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ORIGINAL RESEARCH

Association of Neutrophil Percentage-to-Albumin Ratio with All-Cause and Cardiovascular Mortality in Maintenance Hemodialysis Patients: A Retrospective Study

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Aim: Patients undergoing maintenance hemodialysis (MHD) are prone to chronic inflammation, which often leads to the elevation of various inflammatory biomarkers. This study aims to investigate whether the neutrophil percentage-to-albumin ratio (NPAR), a novel biomarker linked to inflammation, increases the likelihood of both overall and cardiovascular mortality in these patients.

Methods: This retrospective cohort study, conducted across multiple centers, utilized data from the China Renal Data System (CRDS) Database collected between 2010 and 2022. A total of 10,067 eligible participants were included, with follow-up data available until December 31, 2022. Univariate and multivariate Cox regression analyses, Kaplan-Meier survival curves, competing risk plots, and restricted cubic splines were applied to investigate the association between NPAR and both overall and cardiovascular mortality in patients undergoing MHD. Additionally, time-dependent ROC analysis and C-index were employed to assess the predictive ability of NPAR for short-term and long-term outcomes in MHD patients.

Results: Among 10,067 eligible individuals, 1759 deaths from any cause were recorded over a median follow-up period of 50.9 months, with 453 of these deaths attributed to cardiovascular causes. Multivariate Cox regression models revealed that high NPAR levels were significantly associated with both all-cause mortality (HR 3.73, 95% CI 2.94–4.73) and cardiovascular mortality (HR 2.38, 95% CI 1.50–3.79). In subgroup analysis, the effect of elevated NPAR levels on the prediction of all-cause mortality was consistent across the seven pre-specified subgroup strata (all P for interaction > 0.05). Sensitivity analysis confirmed that NPAR remained significantly associated with all-cause mortality. Time-dependent ROC analysis showed that the AUC for NPAR in predicting all-cause mortality at overall, 1, 3, 5, and 10 years was 0.69, 0.70, 0.68, 0.65, and 0.62, respectively. For cardiovascular mortality, the corresponding values were 0.65, 0.68, 0.65, 0.64, and 0.61, respectively. For all-cause mortality, the adjusted C-index was 0.76 (95% CI: 0.74–0.78), while for cardiovascular mortality, the adjusted C-index was 0.82 (95% CI: 0.79–0.85).

Conclusion: In MHD patients, elevated NPAR levels were significantly associated with an increased risk of both overall and cardiovascular mortality, and demonstrated greater accuracy in predicting short-term outcomes.

Keywords: hemodialysis, neutrophil percentage-to-albumin ratio, cardiovascular mortality, all-cause mortality, China renal data system database

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Introduction

Chronic kidney disease (CKD) has become a significant contributor to the global disease burden, affecting more than 10% of the world's population.[1] Hemodialysis is the most commonly used form of renal replacement therapy for CKD patients once they progress to uremia. Globally, over 3.5 million people receive dialysis treatment, with more than 90% undergoing hemodialysis.[2] Hemodialysis patients generally experience more complications than those with other chronic diseases, with the average 5-year survival rate falling below 50%.[3] Premature cardiovascular and cerebrovascular events, inflammation, malnutrition, and other factors are key contributors to poor patient outcomes.

Hemodialysis patients are prone to developing protein-energy wasting (PEW), a condition with a complex pathogenesis. The core mechanism involves an imbalance between protein synthesis and breakdown. Additionally, proinflammatory factors can exacerbate PEW by increasing the basal metabolic rate and reducing protein synthesis.[4] Albumin not only reflects nutritional status but also indicates the level of inflammation in the body.[5] As the release of proinflammatory factors increases, a vicious cycle is established, ultimately leading to a significant increase in the likelihood of cardiovascular events and adverse outcomes among dialysis patients. Therefore, early assessment of a patient's inflammatory status and nutritional condition becomes crucial.

NPAR is a novel composite marker of systemic inflammation and malnutrition. It has been used to predict the prognosis of various diseases.[6–8] Elevated NPAR has been identified as an independent predictor of higher prevalence of CKD and increased all-cause mortality in peritoneal dialysis patients.[9,10] However, studies investigating the relationship between NPAR and outcomes in MHD patients remain limited. Cardiovascular disease significantly impacts the prognosis of MHD patients, and elevated NPAR levels are strongly associated with an increased risk of cardiovascular death. Therefore, elevated NPAR levels may be linked to a higher likelihood of death in MHD patients. A similar multicenter study published in BMC Nephrology in May 2025 explored the relationship between NPAR and mortality outcomes in maintenance hemodialysis (MHD) patients. The study found that elevated NPAR levels are significantly associated with both all-cause and cardiovascular mortality in MHD patients.[11] This study provides important context for our work. Our study included a larger sample size, offering a more reliable analysis of both all-cause and cardiovascular mortality, while further investigating the potential role of NPAR in predicting long-term outcomes in MHD patients.

Data Collection and Methods

Study Design and Data Source

This multicenter retrospective cohort study investigated the association between the NPAR and both all-cause and cardiovascular mortality in MHD patients. Data were obtained from the CRDS Database, a national clinical registry coordinated by Nanfang Hospital, Southern Medical University (Guangzhou, China). The CRDS collects structured clinical data from over 33 large central hospitals across China, ensuring robust nationwide representation. The study included patients who initiated maintenance hemodialysis between January 1, 2010, and December 31, 2022. These patients underwent physical examinations, laboratory tests, and surveys conducted by trained healthcare personnel. The collected data were then uploaded to the CRDS database. All CRDS data were cleaned, standardized, de-identified, and merged prior to analysis. The dataset includes demographic characteristics, vital signs, chronic diseases, medication records, laboratory test results, and prognostic outcomes.

Study Population

The database was cleaned, standardized, anonymized, and merged. The time horizon for the survival data ranged from the interview date to either the date of death or the cut-off date (December 31, 2022). Inclusion criteria: (1) Aged 18 years or older; (2) On hemodialysis for at least 6 months; (3) Visited the hemodialysis center at least twice a week and provided laboratory data; (4) Outcomes recorded during the monitoring period. Exclusion criteria: (1) History of malignancy or significant organ dysfunction affecting inflammatory biomarkers, specifically involving the heart (eg, NYHA class III–IV heart failure), liver (eg, decompensated cirrhosis), lungs (eg, advanced COPD with frequent exacerbations), or a history of renal transplantation); (2) Active infections within one month prior to enrollment, including catheter-related infections, arteriovenous fistula infections, respiratory infections (eg, influenza, viral, or bacterial pneumonia), and systemic infections (eg, sepsis originating

from the urinary or gastrointestinal tract, bacteremia secondary to skin or soft tissue infections, tuberculosis with systemic signs, or infective endocarditis); (3) Incomplete follow-up data or missing key laboratory results. Ultimately, 10,067 eligible participants were included in the study, as shown in Figure 1.

Data Collection

This study collected a variety of data, including demographic information, vital signs, and laboratory results. These included sex, age, body mass index (BMI), and medical history of cardiovascular disease (CVD), hypertension, diabetes, use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers (RAASi), systolic blood pressure (SBP), hemoglobin (Hb), white blood cell count (WBC), neutrophil count and percentage, albumin levels (ALB), liver enzymes (ALT, AST), creatinine(Scr), uric acid(UA), blood urea nitrogen(BUN), potassium(K), phosphorus(P), cholesterol profiles (HDL-C, LDL-C, TC), and albumin/globulin ratio (A/G). The neutrophil percentage-to-albumin ratio (NPAR), the primary variable, was calculated by dividing the neutrophil percentage by the albumin concentration (g/dL). Missing data were assessed for all variables. Variables with less than 5% missing data were handled using complete case analysis. For variables with 5% to 20% missing data, multiple imputation using chained equations (MICE) was applied under the missing at random (MAR) assumption. Variables with more than 20% missing data were excluded from the analysis.

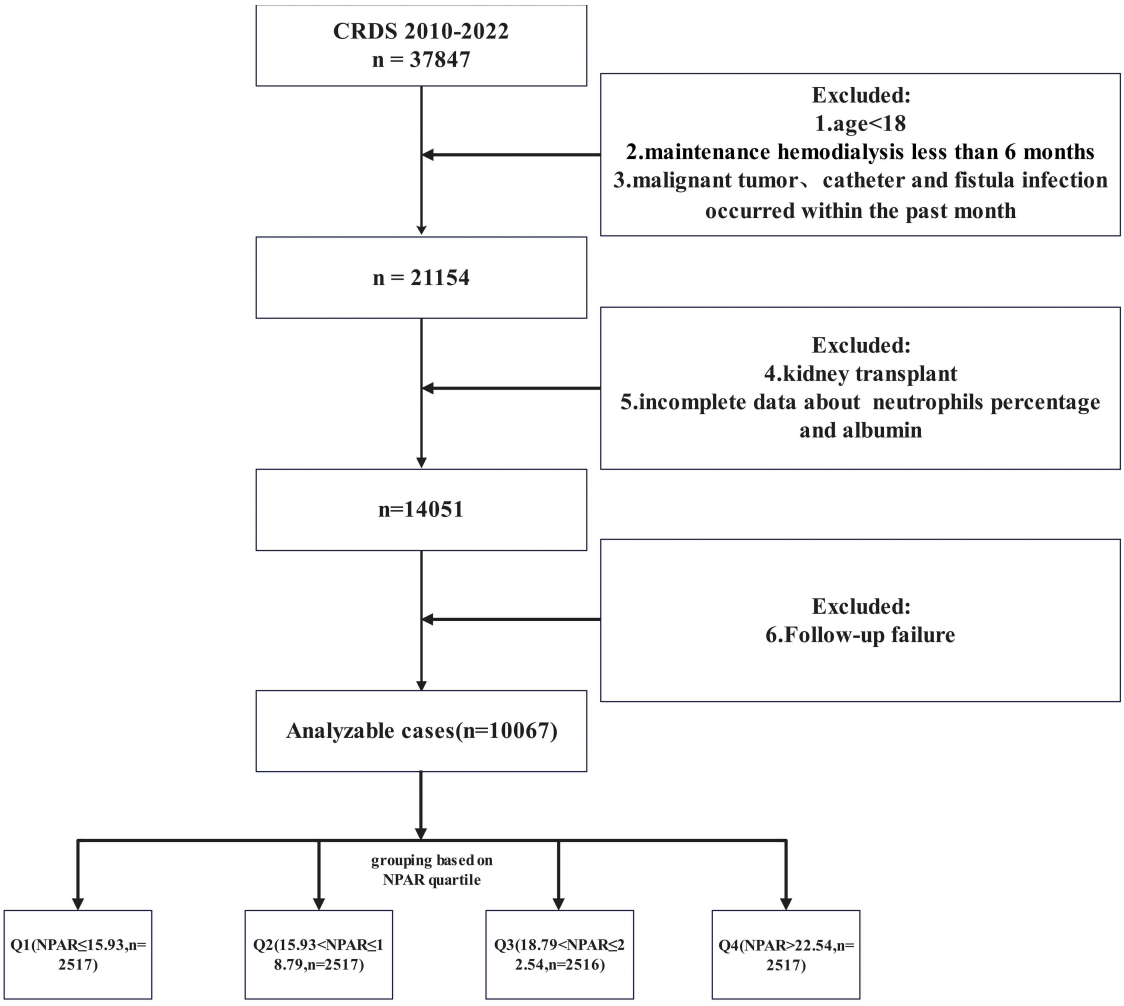

Figure 1 Flowchart of sample selection from the CRDS.

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Follow-Up and Outcomes

Follow-up commenced on the date when the patient initiated maintenance hemodialysis and continued until either the date of death or the prespecified study end date (December 31, 2022), whichever occurred first. The primary outcomes of this study were all-cause mortality and cardiovascular-related mortality. All-cause mortality refers to death from any cause recorded in the CRDS database up to December 31, 2022. Cardiovascular mortality, as defined by the International Classification of Diseases, Tenth Revision (ICD-10), includes deaths resulting from cardiac diseases (codes I00-I09, I11, I13, I20-I51) and cerebrovascular diseases (codes I60-I69).[12]

Statistical Analysis

Descriptive statistical analysis was performed to characterize and summarize the population. For normally distributed variables, continuous data are presented as the mean ± standard error, while skewed data are reported as the median (interquartile range). Categorical variables are summarized as frequencies and percentages. NPAR was classified into quartiles, with the following groups based on NPAR levels: quartile 1 (≤15.93), quartile 2 (>15.93 and ≤18.79), quartile 3 (>18.79 and ≤22.54), and quartile 4 (>22.54). The P trend value was also calculated. Survival estimates and cumulative incidence were compared using Kaplan-Meier analysis and competing risk models. Cox regression models were applied to assess the association between NPAR levels and both overall and cardiovascular-related mortality. Additionally, sensitivity analyses excluded patients from the death group who survived less than 24 months to minimize the risk of reverse causality bias. A subgroup analysis was conducted based on general information, chronic disease history, and medication history to examine the relationship between NPAR and overall mortality, including potential interactions across different stratification factors. Time-dependent ROC and area under the curve (AUC) analyses were conducted to assess the predictive ability of NPAR for overall and cardiovascular-related mortality at different survival times. Statistical analyses were performed using RStudio (version 4.4.1), with a p-value of less than 0.05 considered statistically significant.

Results

Baseline Demographic and Clinical Characteristics

A total of 10,067 participants (2010–2022) were included in the study, with 1759 deaths recorded during the follow-up period, of which 453 were attributed to cardiovascular causes. Men accounted for 63.21% of the deaths, with a mean age of 60.46 ± 14.90 years. The median follow-up duration was 50.9 months, and the mean NPAR was 19.54 ± 4.87. The baseline characteristics according to NPAR quartile grouping are shown in Table 1. Younger individuals and women had lower NPAR levels, as well as a lower prevalence of hypertension, diabetes, and cardiovascular disease.

Table 1 Baseline Characteristics of MHD Patients Based on the 2010–2022 NPAR Quartile Grouping From the CRDS

NPAR Group	Total (n=10067)	Q1 (≤15.93) (n=2517)	Q2 (>15.93 to≤18.79) (n=2517)	Q3 (>18.79 to≤22.54) (n=2516)	Q4 (>22.54) (n=2517)	F/H/χ^2	P
Age(years)	60.46±14.90	59.32±14.97	59.66±14.83	60.97±14.51	61.89±15.14	16.22	<0.001
Sex(%)						26.42	< 0.001
Female	3973(39.5)	1070(42.5)	1024(40.7)	980(39.0)	899(35.7)		
Male	6094(60.5)	1447(57.5)	1493(59.3)	1536(61.0)	1618(64.3)		
Hypertension(%)						4.94	0.176
No	2253(22.4)	544(21.6)	544(21.6)	564(22.4)	601(23.9)		
Yes	7814(77.6)	1973(78.4)	1973(78.4)	1953(77.6)	1916(76.1)		
Diabetes(%)						231.94	0.010
No	6430(63.9)	1802(71.6)	1752(69.6)	1534(61.0)	1342(53.3)		
Yes	3637(36.1)	715(28.4)	764(30.4)	982(39.0)	1176(46.7)		
CVD (%)						62.46	<0.001
No	7539(74.9)	1992(79.1)	1934(76.8)	1848(73.4)	1765(70.1)		
Yes	2528(25,1)	525(20.9)	583(23.2)	668(26.6)	752(29.9)		

(*Continued*)

Table 1 (Continued).

NPAR Group	Total (n=10067)	Q1 (≤15.93) (n=2517)	Q2 (>15.93 to≤18.79) (n=2517)	Q3 (>18.79 to≤22.54) (n=2516)	Q4 (>22.54) (n=2517)	F/H/χ^2	*P*
RAASi(%)						20.48	<0.001
No	5076(50.4)	1281(50.9)	1332(52.9)	1286(51.1)	1177(46.8)		
Yes	4991(49.6)	1236(49.1)	1185(47.1)	1230(48.9)	1340(53,2)		
BMI (kg/m²)	23.14±3.66	22.85±3.60	23.20±3.56	23.25±3.72	23.29±3.76	4.15	0.006
Follow time (months)	50.90[29.60,74.10]	50.20 [30.20, 73.20]	51.80 [31.30, 73.10]	50.85 [29.80, 75.10]	51.00 [26.50, 76.30]	2.02	0.568
SBP(mmHg)	144.40±26.26	140.08±24.71	143.28±24.38	146.69±26.94	146.56±27.77	14.44	<0.001
WBC (10^9/l)	7.35±3.25	6.32±2.35	6.79±2.43	7.45±3.28	8.83±4.06	309.38	< 0.001
Hb (g/dl)	9.33±2.42	10.61±2.36	9.75±2.32	8.89±2.23	8.42±2.17	424.51	< 0.001
N(10^9/l)	5.29±2.93	3.82±1.51	4.71±1.94	5.56±2.88	7.06±3.79	664.66	<0.001
ALT (U/L)	14.00(9.00, 21.85)	14.00(10.00, 21.00)	13.00(9.00,21.00)	13.15(9.00, 21.65)	14.00 (9.16, 23.22)	13.66	0.003
AST (U/L)	18.00(13.20, 24.00)	17.90(13.40, 23.00)	17.00(13.00, 22.82)	17.30(13.20,24.00)	19.00(14.00, 27.20)	94.82	< 0.001
ALB(g/L)	37.16±6.38	43.05±4.47	39.67±4.04	35.90±3.94	30.03±4.22	4498.27	< 0.001
Scr(umol/L)	648.37±396.04	573.29±373.67	659.35±379.43	694.28±398.40	666.56±420.82	44.05	< 0.001
UA(umol/L)	465.88±148.85	446.01±139.93	467.16±145.73	477.55±149.70	474.04±158.49	20.43	< 0.001
BUN(mmol/L)	23.16±12.18	20.06±10.23	22.74±11.24	24.66±12.36	25.17±13.92	91.96	< 0.001
P(mmol/L)	1.78±0.66	1.69±0.57	1.78±0.61	1.84±0.68	1.82±0.74	24.48	< 0.001
K(mmol/L)	4.63±0.83	4.71±0.75	4.68±0.81	4.65±0.85	4.49±0.90	34.70	< 0.001
TC(mmol/L)	4.42±1.44	4.45±1.26	4.33±1.26	4.41±1.43	4.50±1.74	6.74	<0.001
HDL-C(mmol/L)	1.08±0.39	1.12±0.37	1.08±0.37	1.07±0.38	1.05±0.42	13.47	< 0.001
LDL-C(mmol/L)	2.56±1.06	2.50±0.95	2.49±0.94	2.58±1.05	2.66±1.27	13.89	<0.001
A/G	1.32±0.35	1.51±0.34	1.40±0.31	1.28±0.30	1.09±0.29	755.41	<0.001

Abbreviations: CVD, cardiovascular disease; RAASi, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers; BMI, body mass index; SBP, systolic blood pressure; WBC, white blood cell; Hb, hemoglobin; N, neutrophil count; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALB, albumin; Scr, serum creatinine; BUN, blood urea nitrogen; UA, blood uric acid; P, Phosphorus; K, Potassium; TC, Total cholesterol; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; A/G, albumin/globulin.

Relationship Between NPAR and MHD Prognosis

As shown in Figures 2 and 3, Kaplan-Meier survival curves and competing risk models revealed that individuals with elevated NPAR levels faced a significantly higher risk of both overall and cardiovascular-related mortality compared to those with lower NPAR levels. Given that the median survival time was 50.9 months, we chose to display survival data up to 100 months, beyond which few participants remained at risk. Extending the survival curve beyond 100 months would not yield relevant or informative data, this adjustment ensured that the survival curve highlighted the most informative portion of the data, where the majority of participants remained at risk.

Multivariate Cox regression analysis, adjusted for demographic factors (age, gender, body mass index [BMI]), medical history (cardiovascular disease, hypertension, diabetes), medication use (use of ACEI/ARB), and laboratory results (hemoglobin, triglycerides, LDL-C cholesterol, HDL-C cholesterol, absolute neutrophil count, creatinine, blood urea nitrogen, white blood cell count, potassium, inorganic phosphorus, alanine aminotransferase, aspartate aminotransferase), identified a significant association between elevated NPAR levels and adverse prognostic outcomes. As shown in Table 2, the multivariate-adjusted all-cause mortality rate increased progressively across NPAR groups (≤15.93, 15.93–18.79, 18.79–22.54, and >22.54), with corresponding hazard ratios (HRs) of 1.00 (reference), 1.77 (1.41, 2.22), 2.75 (2.21, 3.44), and 3.73 (2.94, 4.73), respectively (trend p-value < 0.05). Table 3 presents the corresponding subhazard ratios (SHRs) and 95% confidence intervals (CIs) for cardiovascular death, which were 1.00 (reference), 1.45 (0.95, 2.22), 1.75 (1.14, 2.70), and 2.38 (1.50, 3.79) (P for trend < 0.05). Moreover, as a continuous variable, each one-unit increase in NPAR was associated with a 10% higher likelihood of all-cause mortality in MHD patients, while the probability of cardiovascular mortality increased by 7%.

Restricted Cubic Splines and Adverse Prognosis Outcomes in MHD

As shown in Figure 4A and 4B, the restricted cubic spline curve demonstrates that, after adjusting for various potential confounders, the nonlinear relationship between NPAR and mortality remains significant (P < 0.05). Additionally, NPAR levels are positively correlated with both overall and cardiovascular-related mortality.

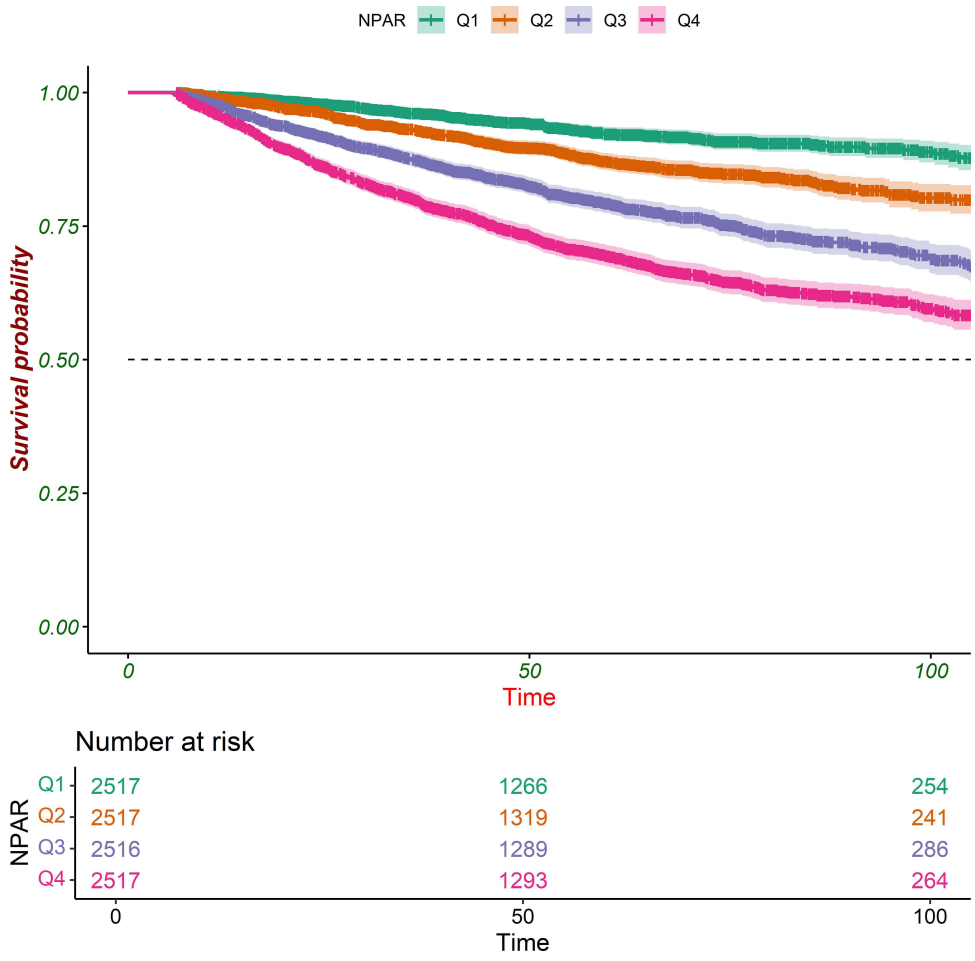

Figure 2 Kaplan-Meier analysis of all-cause mortality in NPAR quartile subgroups (P for Log-rank< 0.0001).

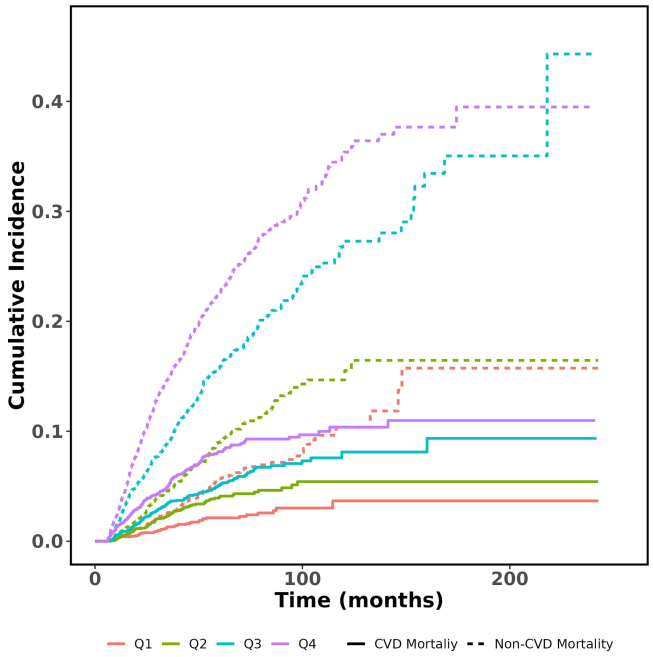

Figure 3 Competing risk analysis of cumulative incidence of cardiovascular disease mortality (Gray = 87.78, p<0.001).

Table 2 Correlation Between NPAR and All-Cause Mortality (Cox Regression Model) (n=10067)

NPAR	Model 1		Model 2		Model 3	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Continuous variables Group	1.11 (1.10,1.12)	<0.001	1.09 (1.08,1.11)	<0.001	1.10 (1.07,1.12)	<0.001
Q1	Reference		Reference		Reference	
Q2	1.73 (1.43,2.09)	<0.001	1.71 (1.29,2.27)	<0.001	1.77 (1.41,2.22)	<0.001
Q3	3.10 (2.60,3.69)	<0.001	2.71 (2.09,3.53)	<0.001	2.75 (2.21,3.44)	<0.001
Q4	4.70 (3.97,5.56)	<0.001	3.67 (2.86,4.72)	<0.001	3.73 (2.94,4.73)	<0.001
P for trend	<0.001		<0.001		<0.001	

Notes: Model 1: unadjusted; Model 2: adjusted for gender, age, BMI, cardiovascular history, hypertension, diabetes, and use of RAASi drugs; Model 3: adjusted for gender, age, BMI, cardiovascular disease, hypertension, diabetes, use of RAASi drugs, hemoglobin, triglycerides, LDL cholesterol, HDL cholesterol, absolute neutrophil count, creatinine, urea nitrogen, white blood cell ratio, potassium, inorganic phosphorus, alanine aminotransferase, aspartate aminotransferase.

Table 3 Association of NPAR with Mortality From Cardiovascular Disease (CVD) (Competing Risk Model)

NPAR	Model 1		Model 2		Model 3	
	SHR (95% CI)	P	SHR (95% CI)	P	SHR (95% CI)	P
Continuous variables Group	1.09 (1.07,1.11)	<0.001	1.05 (1.03,1.08)	<0.001	1.07 (1.04, 1.10)	0.023
Q1	Reference		Reference		Reference	
Q2	1.81 (1.26,2.59)	0.001	1.78 (1.05,3.00)	0.032	1.45 (0.95,2.22)	0.088
Q3	2.55 (1.82,3.57)	<0.001	2.07 (1.25,3.41)	0.004	1.75 (1.14,2.70)	0.011
Q4	3.83 (2.77,5.28)	<0.001	2.56 (1.58,4.17)	<0.001	2.38 (1.50,3.79)	<0.001
P for trend	<0.001		<0.001		<0.001	

Notes: Model 1: unadjusted; Model 2: adjusted for gender, age, BMI, cardiovascular history, hypertension, diabetes, and use of RAASi drugs; Model 3: adjusted for gender, age, BMI, cardiovascular disease, hypertension, diabetes, use of RAASi drugs, hemoglobin, triglycerides, LDL cholesterol, HDL cholesterol, absolute neutrophil count, creatinine, urea nitrogen, white blood cell ratio, potassium, inorganic phosphorus, alanine aminotransferase, aspartate aminotransferase.

Subgroup and Sensitivity Analyses

As shown in Figure 5, we performed subgroup analyses to assess whether demographic factors and comorbidities influence the relationship between NPAR and mortality. The analysis revealed no significant interaction with NPAR ($P > 0.05$) across age (<60, ≥60), gender (male, female), BMI (<25, ≥25), hypertension, diabetes, cardiovascular disease, and RAASi drug use histories. Notably, the relationship between NPAR and mortality was not significant ($P > 0.05$) in patients without hypertension or diabetes. As shown in Table 4, sensitivity analysis yielded similar results after excluding participants in the mortality group who survived less than 24 months, further enhancing the robustness of our findings.

Time-Dependent ROC and AUC Curve Analysis and C-Index for Adverse Prognosis Outcomes in MHD

This study evaluated the relationship between NPAR and mortality in MHD patients using time-dependent ROC and AUC analyses. Additionally, we further explored the predictive power of NPAR for mortality risk by analyzing AUC values at overall, 1, 3, 5, and 10 years. The findings revealed that the AUC for NPAR in predicting all-cause mortality at overall, 1, 3, 5, and 10 years were 0.69 (0.68–0.71), 0.70 (0.67–0.73), 0.68 (0.66–0.70), 0.65 (0.63–0.67), and 0.62

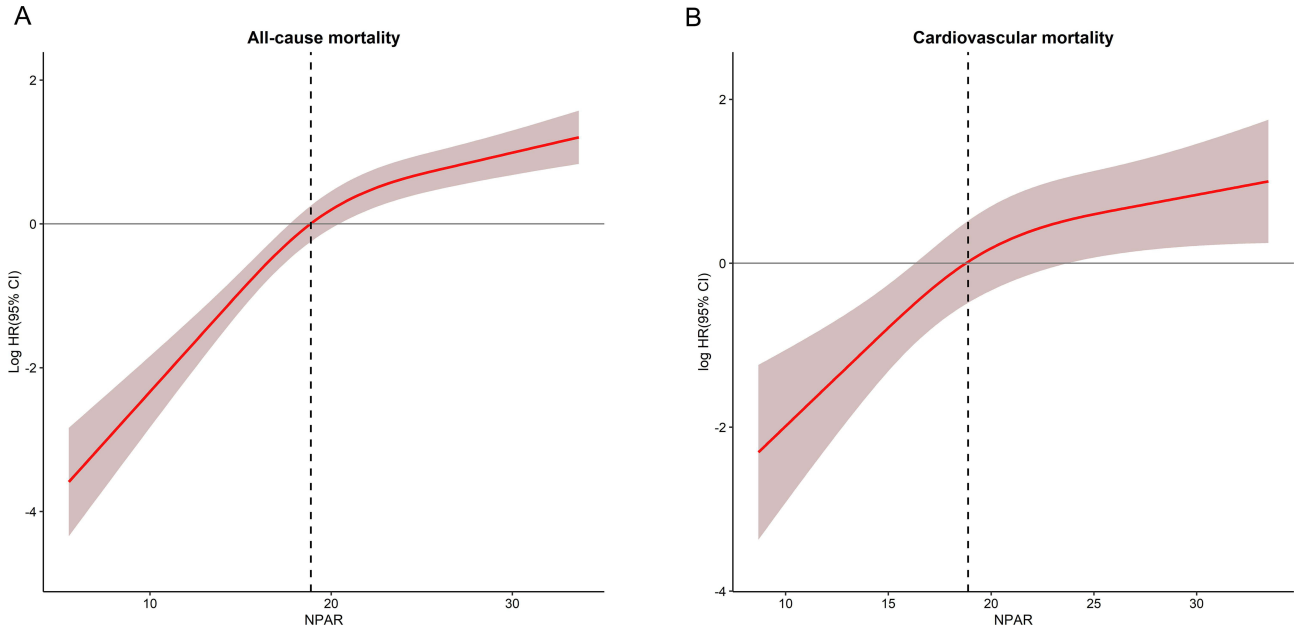

Figure 4 Restricted cubic spline for NPAR and all-cause and cardiovascular mortality. (**A**) all-cause mortality, P for nonlinear<0.001, P for overall < 0.001, knot = 18.88). (**B**) cardiovascular mortality, P for nonlinear<0.014, P for overall <0.001, knot = 18.88.

Notes: Adjustments were made for gender, age, BMI, cardiovascular disease, hypertension, diabetes, use of RAASi drugs, hemoglobin, triglycerides, LDL cholesterol, HDL cholesterol, absolute neutrophil count, creatinine, urea nitrogen, white blood cell ratio, potassium, inorganic phosphorus, alanine aminotransferase, aspartate aminotransferase.

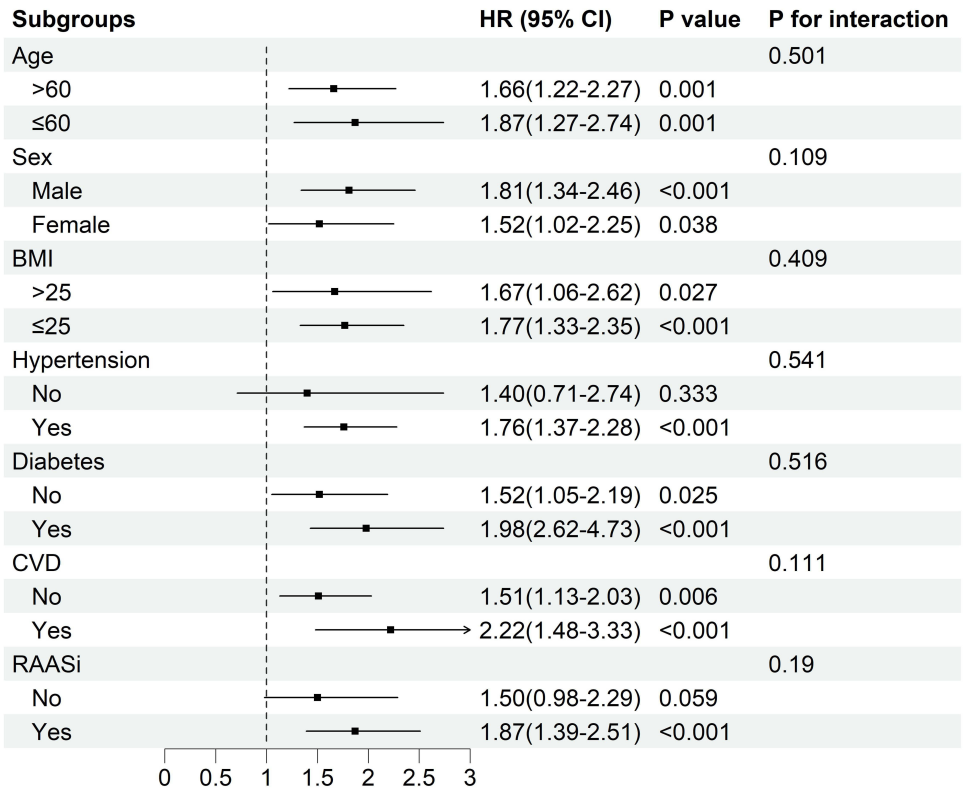

Figure 5 Subgroup analysis of the relationship between NPAR and all-cause mortality.

Notes: Adjustments were made for gender, age, BMI, cardiovascular disease, hypertension, diabetes, use of RAASi drugs, hemoglobin, triglycerides, LDL cholesterol, HDL cholesterol, absolute neutrophil count, creatinine, urea nitrogen, white blood cell ratio, potassium, inorganic phosphorus, alanine aminotransferase, aspartate aminotransferase.

Table 4 The Relationship Between NPAR and All-Cause Mortality After Excluding Patients on Maintenance Hemodialysis with a Survival Time of Less Than 24 months (n=9678)

NPAR	Model 1		Model 2		Model 3	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Continuous variables Group	1.09 (1.08,1.11)	<0.001	1.08 (1.06,1.10)	<0.001	1.08 (1.05,1.11)	<0.001
Q1	Reference		Reference		Reference	
Q2	1.73 (1.38,2,17)	<0.001	1.87 (1.33,2.61)	<0.001	1.88 (1.25,2.84)	0.002
Q3	2.75 (2.23,3.40)	<0.001	2.74 (2.00,3.76)	<0.001	2.99 (2.00,4.49)	<0.001
Q4	3.83 (3.13,4.70)	<0.001	3.41 (2.52,4.63)	<0.001	3.50 (2.26,5.43)	<0.001
P for trend	<0.001		<0.001		<0.001	

Notes: Model 1: unadjusted; Model 2: adjusted for gender, age, BMI, cardiovascular history, hypertension, diabetes, and use of RAASi drugs; Model 3: adjusted for gender, age, BMI, cardiovascular disease, hypertension, diabetes, use of RAASi drugs, hemoglobin, triglycerides, LDL cholesterol, HDL cholesterol, absolute neutrophil count, creatinine, urea nitrogen, white blood cell ratio, potassium, inorganic phosphorus, alanine aminotransferase, aspartate aminotransferase.

(0.59–0.66), respectively (see Figures 6A and 7A). For cardiovascular mortality, the AUC at overall, 1, 3, 5, and 10 years was 0.65 (0.63–0.68), 0.68 (0.61–0.74), 0.65 (0.62–0.68), 0.64 (0.61–0.67), and 0.61 (0.56–0.65), respectively (see Figures 6B and 7B). The results indicate that NPAR is a stronger predictor of short-term all-cause and cardiovascular mortality in MHD patients compared to long-term prognosis.

As shown in Table 5, the C-index for NPAR was calculated to assess its predictive accuracy across different models. For all-cause mortality, the C-index values for Model 1, Model 2, and Model 3 were 0.67 (0.66–0.68), 0.71 (0.69–0.73), and 0.76 (0.74–0.78), respectively, indicating a progressive improvement in model performance with the inclusion of additional variables. Similarly, for cardiovascular mortality, Model 1, Model 2, and Model 3 showed C-index values of 0.65 (0.63–0.68), 0.77 (0.74–0.81), and 0.82 (0.79–0.85), respectively. These results suggest that as more covariates are included in the models, predictive accuracy increases for both all-cause and cardiovascular mortality. Overall, the findings highlight that the inclusion of additional variables can enhance the model's ability to predict mortality outcomes, with cardiovascular mortality being more accurately predicted than all-cause mortality.

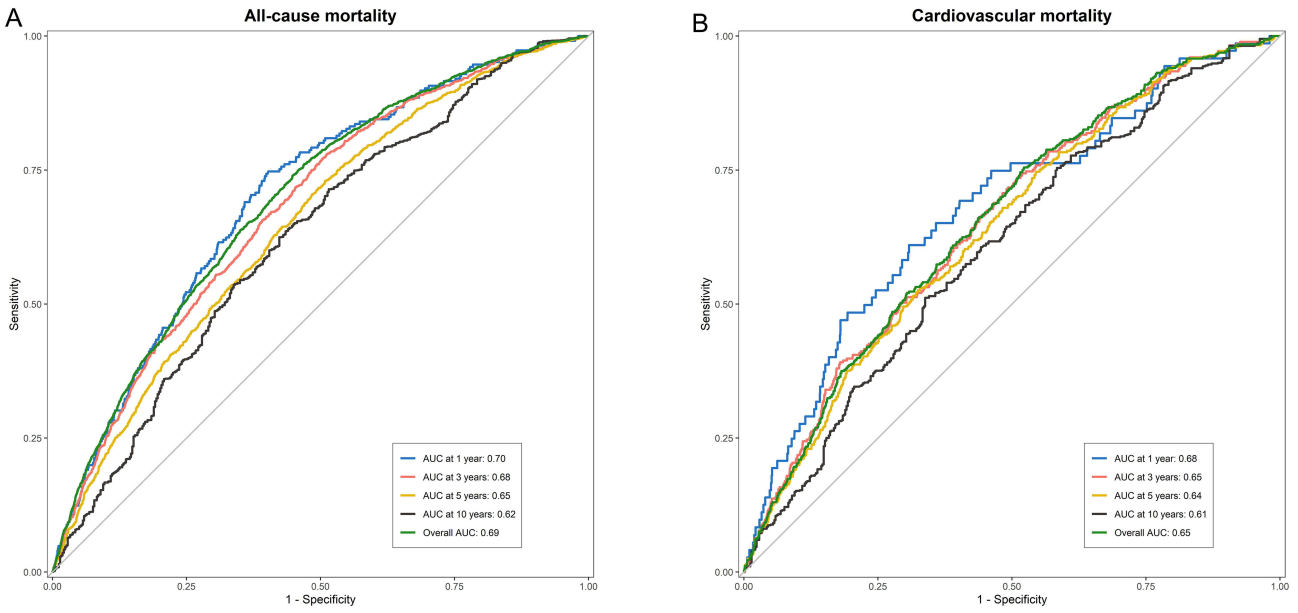

Figure 6 Time-dependent ROC curve for all-cause mortality and cardiovascular mortality in MHD. (**A**) all-cause mortality). (**B**) cardiovascular mortality.

https://doi.org/10.2147/JIR.S532319

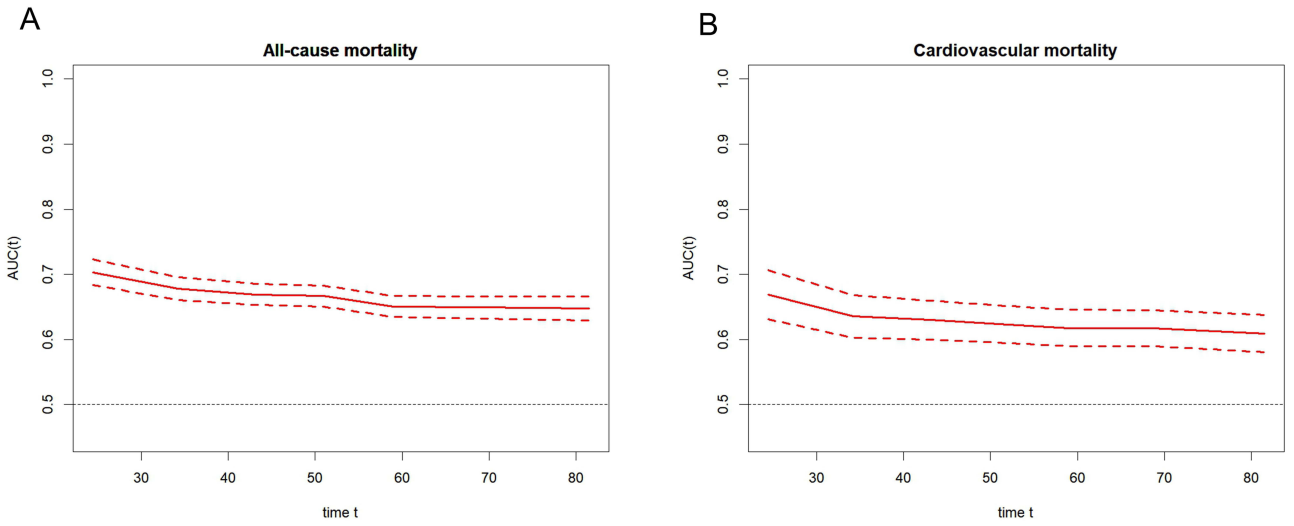

Figure 7 Time-dependent AUC curves for all-cause and cardiovascular mortality in MHD. (**A**) all-cause mortality). (**B**) cardiovascular mortality.

Discussion

To date, this study is the first multicenter, large-sample study to investigate the association between NPAR and adverse outcomes in maintenance hemodialysis (MHD) patients. Multivariable-adjusted analyses demonstrated that elevated NPAR levels are independently associated with a higher risk of both overall and cardiovascular-related mortality. These associations were consistently replicated across predefined subgroup and sensitivity analyses, particularly after excluding the death group with a survival time of less than 24 months. Furthermore, the restricted cubic spline analysis revealed a nonlinear increasing relationship between NPAR and poor prognostic outcomes in MHD patients. These results indicate that NPAR is an independent risk factor for both all-cause and cardiovascular mortality in MHD. As NPAR increases, the likelihood of adverse outcomes rises.

A prospective study of 21,317 participants published in 2024 found that elevated NPAR levels were strongly associated with poor prognostic outcomes in the general population. Under tertile grouping, both all-cause and cardiovascular mortality increased by 46% and 54%, respectively, in the highest tertile compared to the lowest tertile.[13] These findings suggest a significantly elevated mortality risk in the third group. Another cross-sectional study involving 26,225 participants showed that high NPAR levels significantly increased the probability of cardiovascular events, with the prevalence of cardiovascular disease (CVD) being 46% higher in the highest quartile compared to the first quartile, indicating a clear upward trend.[14] A retrospective analysis by Xu et al in peritoneal dialysis patients also demonstrated that higher NPAR levels substantially elevate the risk of adverse prognostic outcomes. Rates of all-cause

Table 5 C-Index for All-Cause Mortality and Cardiovascular Mortality in MHD Patients

NPAR	Model 1	Model 2	Model 3
All-cause mortality	0.67(0.66–0.68)	0.71(0.69–0.73)	0.76(0.74–0.78)
P value	<0.001	<0.001	<0.001
Cardiovascular mortality	0.65(0.63–0.68)	0.77(0.74–0.81)	0.82(0.79–0.85)
P value	<0.001	<0.001	<0.001

Notes: Model 1: unadjusted; Model 2: adjusted for gender, age, BMI, cardiovascular history, hypertension, diabetes, and use of RAASi drugs; Model 3: adjusted for gender, age, BMI, cardiovascular disease, hypertension, diabetes, use of RAASi drugs, hemoglobin, triglycerides, LDL cholesterol, HDL cholesterol, absolute neutrophil count, creatinine, urea nitrogen, white blood cell ratio, potassium, inorganic phosphorus, alanine aminotransferase, aspartate aminotransferase.

and cardiovascular mortality in the highest NPAR tertile were 3.13 and 2.30 times higher, respectively, compared to the lowest tertile.[15] The findings of this study align with previous research, confirming that higher NPAR levels correlate with an elevated risk of adverse prognostic outcomes in maintenance hemodialysis (MHD) patients.

Moreover, our findings indicated that elevated NPAR levels are associated with reduced hemoglobin levels in MHD patients. Chronic anemia is highly prevalent in CKD, and studies have confirmed that inflammation directly affects hemoglobin levels.[16] In addition to insufficient erythropoietin (EPO) production and hypersensitivity associated with CKD, the primary mechanism behind renal anemia involves the inflammatory environment, which drives the production of iron regulatory proteins, leading to functional iron deficiency and inflammatory anemia.[17] The severity of anemia is directly correlated with poor prognosis in these patients.[18] Given that NPAR reflects the degree of inflammation, the conclusion that NPAR levels are inversely related to hemoglobin levels in MHD patients is credible.

Neutrophils play a critical role in all stages of cardiovascular inflammation.[19] Their activation can lead to excessive secretion of reactive oxygen species (ROS), endothelial cell activation, extracellular matrix degradation, and enhanced recruitment of monocytes and macrophages.[20,21] These processes contribute to myocardial injury,[22] atherosclerosis, and rupture of intravascular plaques.[23] Additionally, ROS released by neutrophils can influence drug efficacy.[24] Neutrophils also release myeloperoxidase (MPO), which can indirectly cause endothelial dysfunction by interfering with nitric oxide metabolism.[25] Furthermore, MPO and ROS driven by neutrophils can trigger proinflammatory responses,[26,27] accelerate plaque rupture,[28] cause vascular damage and stenosis,[29,30] and promote the development of cardiovascular disease.[31] In chronic kidney disease, various renal cells, such as mesangial cells, podocytes, and tubular epithelial cells, are known to express receptors for several inflammatory mediators.[32] Following cellular injury, these cells secrete a variety of inflammatory mediators,[33] further amplifying the inflammatory environment. Neutrophils are recruited by this heightened inflammation,[34] which further intensifies inflammation and contributes to additional kidney damage.[35] This may lead to uremia and, in severe cases, necessitate dialysis.[36]

Albumin is an essential component for maintaining life. It helps sustain plasma colloid osmotic pressure and fluid balance, provides nutrition, and exerts an anti-shock effect.[37,38] Albumin also acts as a carrier for drug transport in the body.[39] Hypoalbuminemia can lower the effective concentration of drugs, thereby impairing their efficacy.[40,41] It can also result in insufficient circulating blood volume and organ perfusion.[42] In hemodialysis patients, hypoperfusion can rapidly impair the function of the remaining kidney, cause access route embolism, and lead to cerebral ischemia,[43] thereby increasing the likelihood of complications.[44] The causes of hypoalbuminemia include malabsorption, synthesis disorders, and excessive loss, and it is also closely associated with inflammation.[45] An inflammatory environment can significantly reduce albumin synthesis and increase capillary permeability, leading to greater loss.[46] CKD patients are prone to metabolic acidosis, which can enhance albumin catabolism.[47,48] As an important antioxidant molecule, a decrease in albumin reduces the body's antioxidant capacity, and oxidative stress plays a key role in the development of cardiovascular diseases.[49–51] Elevated oxidative stress levels can contribute to an increased risk of cardiovascular events.[52]

Chronic inflammation is a common characteristic in CKD patients and is closely associated with cardiovascular and cerebrovascular complications, as well as high mortality.[53] This inflammatory state is also significant in MHD patients,[54] where it is linked to complications such as protein-energy wasting and adverse cardiovascular events, which severely impact patient prognosis.[55,56] Neutrophils and albumin are key contributors to chronic inflammatory diseases. The Neutrophil-to-Albumin Ratio (NPAR), which combines neutrophil percentage and albumin levels, is simple to use and repeat. It exerts a synergistic effect, enhancing the ability to assess cardiovascular risk, chronic complications, and poor prognosis more effectively than relying on a single marker. A retrospective study of peritoneal dialysis patients concluded that NPAR outperforms other biomarkers, such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR), in predicting adverse outcomes.[57] Previous studies have shown that high levels of NPAR significantly increase the risk of poor outcomes in heart failure patients.[58] NPAR is also an independent risk factor for poor prognosis in patients with hemorrhagic stroke.[59] A prospective study in hypertensive patients revealed that the highest NPAR tertile had a 63% higher probability of poor outcomes compared to the lowest tertile.[60] A follow-up study of atrial fibrillation patients also found a significant association between NPAR and both cardiovascular and overall mortality.[61] This study reaffirms the established link between NPAR and cardiovascular events, emphasizing its predictive value for adverse outcomes in MHD patients. The AUC values of 0.70 and 0.68 for predicting one-year overall and cardiovascular mortality on the time-dependent AUC curve indicate that NPAR is

a stronger predictor for short-term outcomes than long-term prognosis, although its predictive power gradually weakens over time. This suggests that as the follow-up period extends, it may be necessary to combine other indicators or updated assessment tools to enhance prediction accuracy.

In summary, this study confirms that NPAR is a reliable tool for assessing both overall and cardiovascular mortality risk in MHD patients. Monitoring and intervening based on NPAR levels may provide new avenues for improving the prognosis of these patients. The strengths of this study include its large sample size, multicenter design, and broad representativeness. Additionally, common confounding factors were adjusted for, ensuring the reliability of the correlations, and multivariate and subgroup analyses further strengthened the stability of the findings. This study utilized the CRDS database, which is well-established and integrates data from major central hospitals across more than 30 regions. The database features a high-quality patient population, an excellent follow-up rate, and has contributed to numerous high-impact publications,[62–64] enhancing its authority and representativeness. Compared to our previously published study on the prognosis of patients with diabetic kidney disease (DKD) using the CRDS database,[65] this study introduces several new distinctions and key advantages: 1. It comprehensively includes important clinical subgroups, stratified by factors such as age, gender, complications (hypertension, diabetes, cardiovascular disease), BMI, and medication, verifying the generalizability of NPAR's prognostic value and demonstrating its robust predictive ability across diverse patient characteristics. 2. The RCS curve was specifically drawn for cardiovascular outcomes, clarifying the dose-response relationship between NPAR thresholds and mortality risk. This approach provides an evidence-based foundation for dynamically monitoring inflammatory status and adjusting intervention timing. Time-dependent ROC and AUC analysis were employed to quantify NPAR's dynamic predictive ability for short-term and long-term cardiovascular outcomes, enhancing the interpretability of the results.

Despite its strengths, this study has several limitations. First, being a retrospective study based on a database, it is difficult to establish a causal relationship between NPAR and mortality. Second, since NPAR was measured only once, this may have introduced selection bias. Third, although several confounding factors were adjusted for, the influence of other potential covariates cannot be entirely excluded. Future large-scale, multicenter prospective studies are needed to better elucidate the relationship between NPAR and adverse cardiovascular outcomes or mortality.

Conclusion

A non-linear relationship exists between NPAR and mortality, with higher NPAR levels associated with an increased risk of both overall and cardiovascular mortality. As a readily accessible and easily calculable biomarker, NPAR can serve as an effective clinical tool for predicting patient prognosis. Monitoring NPAR levels allows for the identification of high-risk patient groups, enabling timely intervention and preventive measures to reduce mortality risk in these individuals.

Data Sharing Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author Dr.Su.

Ethics Approval Statement

The study protocol was approved by the Medical Ethics Committee of Nanfang Hospital, Southern Medical University (NFEC-2019-213) and the China Office of Human Genetic Resources for Data Preservation Application (2021-BC0037).

Informed Consent Statement

The ethics committee formally waived the requirement for informed consent based on the following criteria:

1. Retrospective design: This study analyzed existing anonymized clinical data without direct patient involvement or additional interventions.

2. Full anonymization: All personally identifiable information (including names, hospital IDs, and admission dates) was permanently removed prior to analysis.

3. Impossibility of contact: Due to the multi-center nature and large sample size of the hemodialysis cohort, obtaining consent from all participants was deemed impractical.

The research was carried out in compliance with the Declaration of Helsinki and adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[66]

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

References

1. Kovesdy CP. Epidemiology of chronic kidney disease: an update 2022. *Kidney Int Suppl*. 2022;12(1):7–11. doi:10.1016/j.kisu.2021.11.003
2. Flythe JE, Watnick S. Dialysis for chronic kidney failure: a review. *JAMA*. 2024;332(18):1559–1573. doi:10.1001/jama.2024.16338
3. Zhang P, Xun L, Bao N, Tong D, Duan B, Peng D. Long-term mortality in patients with end-stage renal disease undergoing hemodialysis and peritoneal dialysis: a propensity score matching retrospective study. *Ren Fail*. 2024;46(1):2321320. doi:10.1080/0886022X.2024.2321320
4. Mori K. Maintenance of skeletal muscle to counteract sarcopenia in patients with advanced chronic kidney disease and especially those undergoing hemodialysis. *Nutrients*. 2021;13(5):1538. doi:10.3390/nu13051538
5. Feliciano E, Kroenke CH, Meyerhardt JA, et al. Association of systemic inflammation and sarcopenia with survival in nonmetastatic colorectal cancer: results from the C SCANS study. *JAMA Oncol*. 2017;3(12):e172319. doi:10.1001/jamaoncol.2017.2319
6. Liu CF, Chien LW. Predictive role of neutrophil-percentage-to-albumin ratio (NPAR) in nonalcoholic fatty liver disease and advanced liver fibrosis in nondiabetic US adults: evidence from NHANES 2017-2018. *Nutrients*. 2023;15(8):1892. doi:10.3390/nu15081892
7. Ji W, Li H, Qi Y, et al. Association between neutrophil-percentage-to-albumin ratio (NPAR) and metabolic syndrome risk: insights from a large US population-based study. *Sci Rep*. 2024;14(1):26646. doi:10.1038/s41598-024-77802-y
8. Zhang H, Wu T, Tian X, Lyu P, Wang J, Cao Y. High neutrophil percentage-to-albumin ratio can predict occurrence of stroke-associated infection. *Front Neurol*. 2021;12:705790. doi:10.3389/fneur.2021.705790
9. Li J, Xiang T, Chen X, Fu P. Neutrophil-percentage-to-albumin ratio is associated with chronic kidney disease: evidence from NHANES 2009-2018. *PLOS ONE*. 2024;19(8):e0307466. doi:10.1371/journal.pone.0307466
10. Gao Y, Han Z, Feng X, et al. Association of neutrophil and albumin with mortality risk in patients receiving peritoneal dialysis. *J Ren Nutr*. 2024;34(3):252–259. doi:10.1053/j.jrn.2023.10.009
11. Zhu J, Shi R, Li X, et al. Association between neutrophil percentage-to-albumin ratio and mortality in Hemodialysis patients: insights from a prospective cohort study. *BMC Nephrol*. 2025;26(1):112. doi:10.1186/s12882-025-04027-0
12. Liu Q, Zhang Y, Chen S, et al. Association of the triglyceride-glucose index with all-cause and cardiovascular mortality in patients with cardiometabolic syndrome: a national cohort study. *Cardiovasc Diabetol*. 2024;23(1):80. doi:10.1186/s12933-024-02152-y
13. Liu Y, Qiu Z, Shen G, et al. Associations between neutrophil-percentage-to-albumin ratio level and all-cause mortality and cardiovascular disease-cause mortality in general population: evidence from NHANES 1999-2010. *Front Cardiovasc Med*. 2024;11:1393513. doi:10.3389/fcvm.2024.1393513
14. Wang R, Tao W, Chen H, Ma T, Cheng X. Investigating nonlinear associations between neutrophil percentage to albumin ratio and cardiovascular disease: a nationally representative cross-sectional study. *Sci Rep*. 2024;14(1):23632. doi:10.1038/s41598-024-75111-y
15. Xu M, Huan J, Zhu L, Xu J, Song K. The neutrophil percentage-to-albumin ratio is an independent risk factor for poor prognosis in peritoneal dialysis patients. *Ren Fail*. 2024;46(1):2294149. doi:10.1080/0886022X.2023.2294149

16. Macdougall IC, Bircher AJ, Eckardt KU, et al. Iron management in chronic kidney disease: conclusions from a "kidney disease: improving global outcomes" (KDIGO) controversies conference. *Kidney Int*. 2016;89(1):28–39. doi:10.1016/j.kint.2015.10.002
17. Petzer V, Tymoszuk P, Asshoff M, et al. A fully human anti-BMP6 antibody reduces the need for erythropoietin in rodent models of the anemia of chronic disease. *Blood*. 2020;136(9):1080–1090. doi:10.1182/blood.2019004653
18. Ku E, Del Vecchio L, Eckardt KU, et al. Novel anemia therapies in chronic kidney disease: conclusions from a kidney disease: improving global outcomes (KDIGO) controversies conference. *Kidney Int*. 2023;104(4):655–680. doi:10.1016/j.kint.2023.05.009
19. Luo J, Thomassen JQ, Nordestgaard BG, Tybjærg-Hansen A, Frikke-Schmidt R. Neutrophil counts and cardiovascular disease. *Eur Heart J*. 2023;44(47):4953–4964. doi:10.1093/eurheartj/ehad649
20. Wang Y, Sano S, Oshima K, et al. Wnt5a-mediated neutrophil recruitment has an obligatory role in pressure overload-induced cardiac dysfunction. *Circulation*. 2019;140(6):487–499. doi:10.1161/CIRCULATIONAHA.118.038820
21. Soehnlein O, Lindbom L, Weber C. Mechanisms underlying neutrophil-mediated monocyte recruitment. *Blood*. 2009;114(21):4613–4623. doi:10.1182/blood-2009-06-221630
22. Ruparelia N, Godec J, Lee R, et al. Acute myocardial infarction activates distinct inflammation and proliferation pathways in circulating monocytes, prior to recruitment, and identified through conserved transcriptional responses in mice and humans. *Eur Heart J*. 2015;36 (29):1923–1934. doi:10.1093/eurheartj/ehv195
23. Sugamura K, Keaney JF. Reactive oxygen species in cardiovascular disease. *Free Radic Biol Med*. 2011;51(5):978–992. doi:10.1016/j.freeradbiomed.2011.05.004
24. Sun W, Dai L, Yu H, et al. Monitoring structural modulation of redox-sensitive proteins in cells with MS-CETSA. *Redox Biol*. 2019;24:101168. doi:10.1016/j.redox.2019.101168
25. Abdo AI, Rayner BS, van Reyk DM, Hawkins CL. Low-density lipoprotein modified by myeloperoxidase oxidants induces endothelial dysfunction. *Redox Biol*. 2017;13:623–632. doi:10.1016/j.redox.2017.08.004
26. Yakubenko VP, Cui K, Ardell CL, et al. Oxidative modifications of extracellular matrix promote the second wave of inflammation via β(2) integrins. *Blood*. 2018;132(1):78–88. doi:10.1182/blood-2017-10-810176
27. Dufour A, Bellac CL, Eckhard U, et al. C-terminal truncation of IFN-γ inhibits proinflammatory macrophage responses and is deficient in autoimmune disease. *Nat Commun*. 2018;9(1):2416. doi:10.1038/s41467-018-04717-4
28. Robbins CS, Hilgendorf I, Weber GF, et al. Local proliferation dominates lesional macrophage accumulation in atherosclerosis. *Nat Med*. 2013;19 (9):1166–1172. doi:10.1038/nm.3258
29. Ellison-Hughes GM, Colley L, O'Brien KA, Roberts KA, Agbaedeng TA, Ross MD. The role of MSC therapy in attenuating the damaging effects of the cytokine storm induced by COVID-19 on the heart and cardiovascular system. *Front Cardiovasc Med*. 2020;7:602183. doi:10.3389/fcvm.2020.602183
30. Jeong K, Kim JH, Murphy JM, et al. Nuclear focal adhesion kinase controls vascular smooth muscle cell proliferation and neointimal hyperplasia through GATA4-mediated cyclin D1 transcription. *Circ Res*. 2019;125(2):152–166. doi:10.1161/CIRCRESAHA.118.314344
31. Das S, Senapati P, Chen Z, et al. Regulation of angiotensin II actions by enhancers and super-enhancers in vascular smooth muscle cells. *Nat Commun*. 2017;8(1):1467. doi:10.1038/s41467-017-01629-7
32. Xiao C, Xiao P, Li X, Huang G, Li H, Chen Y. Streptococcus may aggravate inflammatory damage in chronic nephritis via the chemotaxis of Th22 cells. *Am J Transl Res*. 2019;11(12):7432–7440.
33. Zhou D, Liu Y. Renal fibrosis in 2015: understanding the mechanisms of kidney fibrosis. *Nat Rev Nephrol*. 2016;12(2):68–70. doi:10.1038/nrneph.2015.215
34. Bożena P, Daria A, Irena M, Maria N, Adam J, Danuta Z. Elastase, α1-proteinase inhibitor, and interleukin-8 in children and young adults with end-stage kidney disease undergoing continuous ambulatory peritoneal dialysis. *Arch Immunol Ther Exp*. 2014;62(3):239–245. doi:10.1007/s00005-013-0265-7
35. Zhang YM, Zhou XJ, Zhang H. What genetics tells us about the pathogenesis of Iga nephropathy: the role of immune factors and infection. *Kidney Int Rep*. 2017;2(3):318–331. doi:10.1016/j.ekir.2017.02.005
36. Liang Z, Hu X, Lin R, et al. Identification of shared gene signatures and molecular mechanisms between chronic kidney disease and ulcerative colitis. *Front Immunol*. 2023;14:1078310. doi:10.3389/fimmu.2023.1078310
37. Vo E, Massarweh NN, Chai CY, et al. Association of the addition of oral antibiotics to mechanical bowel preparation for left colon and rectal cancer resections with reduction of surgical site infections. *JAMA Surg*. 2018;153(2):114–121. doi:10.1001/jamasurg.2017.3827
38. Boer C, Bossers SM, Koning NJ. Choice of fluid type: physiological concepts and perioperative indications. *Br J Anaesth*. 2018;120(2):384–396. doi:10.1016/j.bja.2017.10.022
39. Callmann CE, LeGuyader C, Burton ST, et al. Antitumor activity of 1,18-octadecanedioic acid-paclitaxel complexed with human serum albumin. *J Am Chem Soc*. 2019;141(30):11765–11769. doi:10.1021/jacs.9b04272
40. Yagi T, Naito T, Doi M, et al. Plasma exposure of free linezolid and its ratio to minimum inhibitory concentration varies in critically ill patients. *Int J Antimicrob Agents*. 2013;42(4):329–334. doi:10.1016/j.ijantimicag.2013.06.015
41. Roberts JA, Stove V, De Waele JJ, et al. Variability in protein binding of teicoplanin and achievement of therapeutic drug monitoring targets in critically ill patients: lessons from the DALI Study. *Int J Antimicrob Agents*. 2014;43(5):423–430. doi:10.1016/j.ijantimicag.2014.01.023
42. Vincent JL, De Backer D, Wiedermann CJ. Fluid management in sepsis: the potential beneficial effects of albumin. *J Crit Care*. 2016;35:161–167. doi:10.1016/j.jcrc.2016.04.019
43. MacEwen C, Sutherland S, Daly J, Pugh C, Tarassenko L. Relationship between Hypotension and Cerebral Ischemia during Hemodialysis. *J Am Soc Nephrol*. 2017;28(8):2511–2520. doi:10.1681/ASN.2016060704
44. Chou JA, Streja E, Nguyen DV, et al. Intradialytic hypotension, blood pressure changes and mortality risk in incident hemodialysis patients. *Nephrol Dial Transplant*. 2018;33(1):149–159. doi:10.1093/ndt/gfx037
45. Arra M, Swarnkar G, Ke K, et al. LDHA-mediated ROS generation in chondrocytes is a potential therapeutic target for osteoarthritis. *Nat Commun*. 2020;11(1):3427. doi:10.1038/s41467-020-17242-0
46. Nie R, Yuan S, Chen S, et al. Prognostic nutritional index is an independent prognostic factor for gastric cancer patients with peritoneal dissemination. *Chin J Cancer Res*. 2016;28(6):570–578. doi:10.21147/j.issn.1000-9604.2016.06.03
47. Kraut JA, Madias NE. Consequences and therapy of the metabolic acidosis of chronic kidney disease. *Pediatr Nephrol*. 2011;26(1):19–28. doi:10.1007/s00467-010-1564-4

48. Siew ED, Ikizler TA. Insulin resistance and protein energy metabolism in patients with advanced chronic kidney disease. *Semin Dial*. 2010;23(4):378–382. doi:10.1111/j.1525-139X.2010.00763.x
49. Karimi Galougahi K, Antoniades C, Nicholls SJ, Channon KM, Figtree GA. Redox biomarkers in cardiovascular medicine. *Eur Heart J*. 2015;36(25):1576–82,1582a–b. doi:10.1093/eurheartj/ehv126
50. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: the task force for the diagnosis and treatment of acute and chronic heart failure of the European society of cardiology (ESC)developed with the special contribution of the heart failure association (HFA) of the ESC. *Eur Heart J*. 2016;37(27):2129–2200. doi:10.1093/eurheartj/ehw128
51. Tsutsui H, Kinugawa S, Matsushima S. Oxidative stress and heart failure. *Am J Physiol Heart Circ Physiol*. 2011;301(6):H2181–90. doi:10.1152/ajpheart.00554.2011
52. Münzel T, Camici GG, Maack C, Bonetti NR, Fuster V, Kovacic JC. Impact of oxidative stress on the heart and vasculature: part 2 of a 3-part series. *J Am Coll Cardiol*. 2017;70(2):212–229. doi:10.1016/j.jacc.2017.05.035
53. Güneş I, Süngü N, Kılıçarslan A, et al. Effects of hydroxyethyl starch 130/0.4 on the kidney tissue of rats with ureteral obstruction. *Drug Des Devel Ther*. 2018;12:3061–3070. doi:10.2147/DDDT.S165695
54. Gupta J, Mitra N, Kanetsky PA, et al. Association between albuminuria, kidney function, and inflammatory biomarker profile in CKD in CRIC. *Clin J Am Soc Nephrol*. 2012;7(12):1938–1946. doi:10.2215/CJN.03500412
55. Cobo G, Lindholm B, Stenvinkel P. Chronic inflammation in end-stage renal disease and dialysis. *Nephrol Dial Transplant*. 2018;33(suppl_3):iii35–iii40. doi:10.1093/ndt/gfy175
56. Gulen MF, Samson N, Keller A, et al. cGAS-STING drives ageing-related inflammation and neurodegeneration. *Nature*. 2023;620(7973):374–380. doi:10.1038/s41586-023-06373-1
57. Yu Y, Zhong Z, Yang W, et al. Neutrophil percentage-to-albumin ratio and risk of mortality in patients on peritoneal dialysis. *J Inflamm Res*. 2023;16:6271–6281. doi:10.2147/JIR.S437256
58. Wu CC, Wu CH, Lee CH, Cheng CI. Association between neutrophil percentage-to-albumin ratio (NPAR), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and long-term mortality in community-dwelling adults with heart failure: evidence from US NHANES 2005-2016. *BMC Cardiovasc Disord*. 2023;23(1):312. doi:10.1186/s12872-023-03316-6
59. Lv XN, Shen YQ, Li ZQ, et al. Neutrophil percentage to albumin ratio is associated with stroke-associated pneumonia and poor outcome in patients with spontaneous intracerebral hemorrhage. *Front Immunol*. 2023;14:1173718. doi:10.3389/fimmu.2023.1173718
60. Liu Z, Dong L, Shen G, et al. Associations of neutrophil-percentage-to-albumin ratio level with all-cause mortality and cardiovascular disease-cause mortality among patients with hypertension: evidence from NHANES 1999-2010. *Front Cardiovasc Med*. 2024;11:1397422. doi:10.3389/fcvm.2024.1397422
61. Cai J, Li M, Wang W, Luo R, Zhang Z, Liu H. The relationship between the neutrophil percentage-to-albumin ratio and rates of 28-day mortality in atrial fibrillation patients 80 years of age or older. *J Inflamm Res*. 2023;16:1629–1638. doi:10.2147/JIR.S400924
62. Zhou S, Chen R, Liu J, et al. Comparative effectiveness and safety of atorvastatin versus rosuvastatin: a multi-database cohort study. *Ann Intern Med*. 2024;177(12):1641–1651. doi:10.7326/M24-0178
63. Xu X, Nie S, Xu H, et al. Detecting Neonatal AKI by Serum Cystatin C. *J Am Soc Nephrol*. 2023;34(7):1253–1263. doi:10.1681/ASN.0000000000000125
64. Zhou S, Su L, Xu R, et al. Statin initiation and risk of incident kidney disease in patients with diabetes. *CMAJ*. 2023;195(21):E729–E738. doi:10.1503/cmaj.230093
65. Bai Y, Huang L, Li Y, et al. Neutrophil/lymphocyte ratio and all-cause mortality in diabetic kidney disease: a retrospective cohort study. *J Inflamm Res*. 2024;17:10739–10753. doi:10.2147/JIR.S483637
66. Vandenbroucke JP, von Elm E, Altman DG, et al. Strengthening the reporting of observational studies in epidemiology (STROBE): explanation and elaboration. *PLoS Med*. 2007;4(10):e297. doi:10.1371/journal.pmed.0040297