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Relationship between neutrophil percentage to albumin ratio and cardiovascular disease mortality in chronic kidney disease patients; a systematic review and meta-analysis

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ABSTRACT

Introduction: Chronic inflammation plays a significant role in cardiovascular disease (CVD)-related mortality among patients with chronic kidney disease (CKD). The neutrophil-to-albumin percentage ratio (NPAR) has emerged as an indicator of an individual's inflammatory status. This study aimed to investigate the association between elevated NPAR and the risk of CVD mortality in patients with CKD.

Materials and Methods: The study was conducted in accordance with the PRISMA reporting guidelines. Comprehensive searches were performed across the Cochrane Library, Scopus, Web of Science, Embase, and PubMed databases, as well as the Google Scholar search engine, up to 30 January 2026. All statistical analyses were carried out using STATA version 14.

Results: Compared with lower NPAR values, elevated NPAR was associated with a higher risk of cardiovascular mortality (OR = 1.54; 95% CI: 1.33–1.78) and all-cause mortality (OR = 1.62; 95% CI: 1.40–1.89) in patients with CKD. In addition, higher NPAR increased the risk of CVD-related death among patients undergoing hemodialysis (OR = 1.66; 95% CI: 1.29–2.15) and peritoneal dialysis (OR = 1.56; 95% CI: 1.25–1.94). Furthermore, the third quartile of NPAR (OR = 1.44; 95% CI: 1.16–1.78), the fourth quartile (OR = 1.92; 95% CI: 1.61–2.30), the second tertile (OR = 1.38; 95% CI: 1.07–1.80), and the third tertile (OR = 1.97; 95% CI: 1.61–2.41) were all associated with increased CVD mortality compared with the lowest category. Elevated NPAR also increased the risk of CVD-related mortality in both men (OR = 1.23; 95% CI: 1.04–1.45) and women (OR = 1.16; 95% CI: 1.08–1.24) with CKD.

Conclusion: Higher NPAR levels were associated with an increased likelihood of cardiovascular and all-cause mortality among individuals with CKD. As NPAR values rose, the risk of CVD-related death increased correspondingly when compared with lower levels. In addition, cardiovascular mortality risk was greater in men than in women, and higher among patients receiving hemodialysis than those undergoing peritoneal dialysis.

Registration: This study has been compiled based on the PRISMA checklist, and its protocol was registered on the PROSPERO (ID: [CRD420261304086](https://doi.org/10.34172/jnp.2026.28709)) and Research Registry (UIN: [reviewregistry2082](https://doi.org/10.34172/jnp.2026.28709)) websites.

Implication for health policy/practice/research/medical education:

In this meta-analysis study, we found that higher neutrophil-to-albumin percentage ratio (NPAR) values signaled a greater probability of both cardiovascular and overall mortality in patients with chronic kidney disease (CKD). As the NPAR increased, the likelihood of cardiovascular disease (CVD)-related death compared with patients who had lower NPAR. The data also point to important subgroup differences; men faced a higher cardiovascular mortality risk than women, and individuals on hemodialysis showed a greater vulnerability than those treated with peritoneal dialysis. In clinical settings, elevated NPAR may serve as a useful signal for identifying CKD patients at heightened risk of both cardiovascular and overall mortality.

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Introduction

Chronic kidney disease (CKD) has become a significant global public health challenge, with mortality attributable to this condition rising steadily over recent decades(1). Its impact on global health is increasingly evident, as CKD has advanced from the nineteenth leading cause of death in 1990 to the eleventh in 2019 (2). Among affected individuals, cardiovascular diseases (CVD) constitute the predominant cause of mortality, accounting for nearly half of all deaths in this population (3).

Chronic inflammation and malnutrition are recognized as key contributors to both all-cause and cardiovascular mortality in individuals with CKD (4). The neutrophil-to-albumin percentage ratio (NPAR) has recently been introduced as a composite biomarker reflecting inflammatory and nutritional status, and has been applied in the prognostic assessment of various clinical conditions (5-7). Evidence suggests that NPAR offers superior predictive value compared with albumin or neutrophil percentage alone (8,9). Moreover, elevated NPAR has been positively associated with mortality across several cardiovascular disorders, including chronic heart failure, cardiogenic shock, and acute myocardial infarction (8,10-12).

Findings from previous research in patients with CKD have been inconsistent. Some studies reported no significant association between the second and third quartiles of NPAR and CVD-related mortality when compared with the lowest quartile (13,14). In contrast, other investigations demonstrated that higher NPAR levels were linked to an increased risk of cardiovascular death in this population (15-17). Given these conflicting results, the present study aimed to clarify the relationship between elevated NPAR and the risk of CVD mortality in individuals with CKD through a systematic review and meta-analysis.

Materials and Methods*Study design*

The study protocol was developed in accordance with PRISMA guidelines (18) and was formally registered in

both the PROSPERO database and the Research Registry.

Search strategy

The Cochrane, Scopus, Web of Science, Embase, and PubMed databases, along with the Google Scholar search engine, were comprehensively searched up to 30 January 2026, without applying temporal or geographical restrictions. The search process employed standardized keywords in combination with Medical Subject Headings (MeSH). Boolean operators (AND, OR) were used to construct advanced search strings and optimize retrieval sensitivity. A supplementary manual search was also conducted by examining the reference lists of the studies selected for inclusion.

PECO components

The PECO framework was defined as follows; eligible studies included those investigating the relationship between the NPAR and cardiovascular mortality in individuals with CKD as the population. The exposure of interest was elevated NPAR levels, with lower NPAR values serving as the comparator. The primary outcome was the risk of cardiovascular mortality, while all-cause mortality was considered a secondary endpoint.

Inclusion and exclusion criteria

Inclusion criteria comprised studies that examined the association between the NPAR and cardiovascular mortality among patients with CKD. Exclusion criteria included studies lacking essential data for quantitative analysis; studies that assessed the relationship between NPAR and cardiovascular mortality in mixed populations of CKD and other renal disorders without reporting stratified results; duplicate publications; studies evaluating NPAR in relation to overall mortality among patients with CVD and CKD; studies deemed to have inadequate methodological quality during the qualitative appraisal; case reports; studies for which full texts were unavailable despite contacting the authors; review articles; and conference abstracts.

Quality assessment

The methodological rigor of the included studies was independently assessed by two reviewers using the Newcastle–Ottawa Scale (NOS), which comprises nine criteria scored through a star-based system. Studies earning at least six stars were deemed to have sufficient methodological quality and were therefore eligible for inclusion in the meta-analysis (19).

Data extraction

Data extraction was carried out independently by two reviewers using a predesigned standardized form. The collected information included the first author's name, study timeframe, country of origin, study design, participants' age, underlying disease characteristics, NPAR measurements, and the reported risk estimates for cardiovascular mortality as well as all-cause mortality.

Statistical analysis

Log-transformed hazard ratios (HRs) were conducted to combine effect estimates across studies. Heterogeneity was quantified using the I^2 statistic; a fixed-effects model was applied when heterogeneity was low, whereas moderate to high heterogeneity warranted the use of a random-effects model. All analyses were performed using STATA version 14, and a two-sided P value of <0.05 was considered statistically significant.

Results

A total of 196 records were identified through database searches, of which 94 duplicates were removed before screening. The remaining 102 records were screened, leading to the exclusion of 44 studies. Full texts were sought for 58 reports, but 13 could not be retrieved. Of the 45 reports assessed for eligibility, 33 were excluded for reasons such as combining patients with CKD and other renal diseases without separate reporting, evaluating NPAR in relation to overall rather than cardiovascular mortality, inadequate methodological quality, being case reports, review articles, or conference abstracts. Ultimately, 12 studies met the inclusion criteria and were incorporated into the review (Figure 1).

A total of 12 observational investigations, comprising 1 cross-sectional study and 11 cohort studies, were ultimately included, encompassing an aggregate sample of 39,480 participants (Table 1).

Elevated NPAR, compared with lower levels, was associated with an increased risk of CVD-related mortality in patients with CKD (OR = 1.54; 95% CI: 1.33–1.78) (Figure 2). When stratified by type of kidney disease, higher NPAR similarly increased the risk of CVD mortality among hemodialysis patients (OR = 1.66; 95% CI: 1.29–2.15) and peritoneal dialysis patients (OR = 1.56; 95% CI: 1.25–1.94). However, in patients with diabetic kidney disease (DKD), no significant

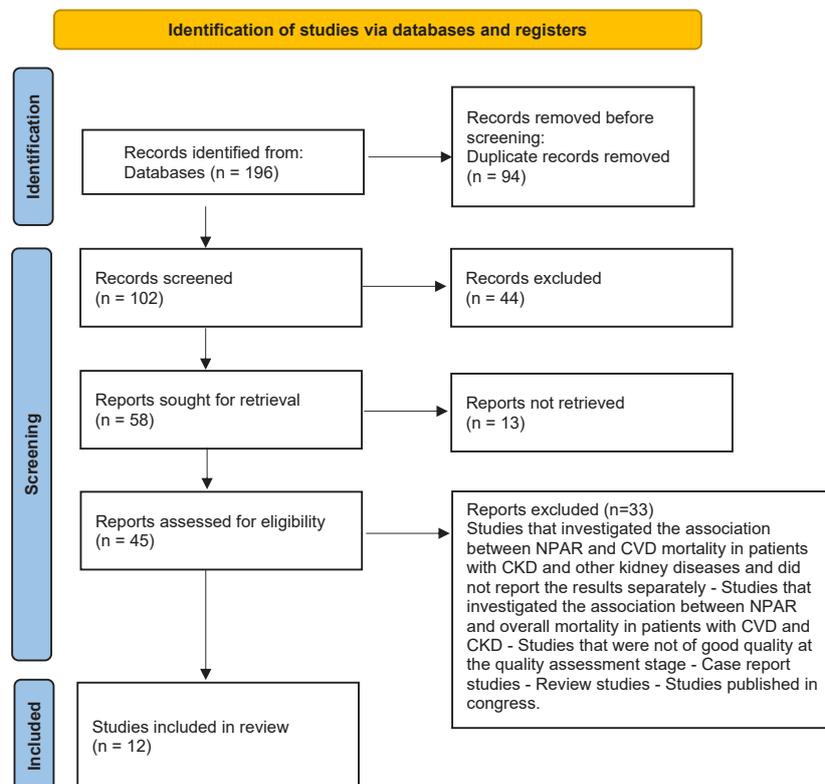


Figure 1. The PRISMA flowchart of study selection.

Table 1. Basic information about the articles reviewed

Author, year	Country	Type of study	Duration of study	Number of patients	Mean age (year)	Level	CVD mortality			All causes mortality		
							HR	Low limit	Up limit	HR	Low limit	Up limit
Chen X, 2026 (13)	USA	Cohort	1999 to 2018	2496	62.47	Quartile2	0.99	0.57	1.73	1.08	0.83	1.40
						Quartile3	1.54	0.96	2.46	1.62	1.25	2.10
						Quartile4	2.24	1.47	3.39	2.05	1.62	2.59
Han Y, 2025 (15)	USA	Cohort	1999 to 2018	3029	≥18	Tertile 2	1.67	1.1	2.56	1.43	1.16	1.77
						Tertile 3	2.49	1.8	3.44	1.71	1.36	2.16
Liu M, 2025 (20)	USA	Cohort	from 2001 to 2018	7854	≥20	Quartile2	1.20	0.87	1.65	1.4	1.17	1.68
						Quartile3	1.44	1.03	2	1.54	1.29	1.85
						Quartile4	1.91	1.42	2.58	2.24	1.88	2.66
Tan J, 2025 (21)	USA	Cross-sectional	1999 to 2018	2699	≥20	Quartile2	1.01	0.68	1.48	0.99	0.72	1.36
						Quartile3	0.90	0.55	1.49	1.45	1.02	2.06
						Quartile4	1.44	0.95	2.18	2.07	1.55	2.76
Chen J, 2025 (14)	USA	Cohort	up to Dec 31, 2019	1121	54	Quartile2	1.07	0.52	2.20	1.24	0.82	1.89
						Quartile3	1.72	0.96	3.07	1.46	1	2.14
						Quartile4	1.87	1.1	3.20	1.66	1.18	2.33
Rao J, 2025 (16)	USA	Cohort	2003–2018	3331	72.45	Total	2.33	1.93	2.82	2.14	1.95	2.35
Jiang H, 2025 (22)	China	Cohort	between 2010 and 2022	10067	60.46	Quartile2	1.45	0.95	2.22	1.77	1.41	2.22
						Quartile3	1.75	1.14	2.7	2.75	2.21	3.44
						Quartile4	2.38	1.50	3.79	3.73	2.94	4.73
Zhu J, 2025 (23)	China	Cohort	from Jan to Dec 2020	1803	54	Tertile 2	1.01	0.55	1.84	0.89	0.62	1.28
						Tertile 3	1.84	1.05	3.21	1.55	1.11	2.166
Xu M, 2024 (24)	China	Cohort	between Jan 2009 and Dec 2019	807	60	Tertile 2	1.94	1.15	2.37	2.16	1.44	3.22
						Tertile 3	2.30	1.34	3.91	3.13	2.12	4.62
Gao Y, 2024 (25)	China	Cohort	From Jan 1, 2010, to May 31, 2016	1229	49	Tertile 2	1.06	0.64	1.75	1.12	0.78	1.61
						Tertile 3	1.62	1.01	2.60	1.47	1.04	2.08
Li X, 2024 (17)	USA	Cohort	from 2001 to 2018	3078	63	Total	1.12	1.08	1.16	1.13	1.11	1.16
Yu Y, 2023 (10)	China	Cohort	from Jan 2006 to Dec 2016	1966	46.83	Tertile 2	1.17	0.77	1.78	1.14	0.85	1.53
						Tertile 3	1.57	1.07	2.31	1.51	1.14	1.98

HR: Hazard ratio, NR: Not reported, CVD: Cardiovascular disease.

association was observed between elevated NPAR and CVD-related mortality (OR = 1.11; 95% CI: 0.85–1.46) (Figure 3).

Higher NPAR levels were associated with an increased risk of CVD-related mortality among patients with CKD. Specifically, the third quartile (OR = 1.44; 95% CI: 1.16–1.78), the fourth quartile (OR = 1.92; 95% CI: 1.61–2.30), the second tertile (OR = 1.38; 95% CI: 1.07–1.80), and the third tertile (OR = 1.97; 95% CI: 1.61–2.41) all showed significantly higher risks compared with the lowest category. In contrast, no significant

association was observed between the second quartile of NPAR and CVD mortality in CKD patients (OR = 1.16; 95% CI: 0.96–1.40) (Figure 4).

Elevated NPAR, compared with lower levels, increased the risk of CVD-related mortality among patients with CKD in both China (OR = 1.60; 95% CI: 1.37–1.88) and the United States (OR = 1.51; 95% CI: 1.24–1.84) (Figure 5). Similarly, in cohort studies, higher NPAR was associated with a greater risk of CVD-related mortality in CKD patients (OR = 1.61; 95% CI: 1.37–1.88). In contrast, the cross-sectional study showed no significant association between elevated NPAR and CVD-related mortality (OR = 1.11; 95% CI: 0.85–1.46) (Figure 6).

Elevated NPAR, compared with lower levels, increased the risk of CVD-related mortality in both men (OR = 1.23; 95% CI: 1.04–1.45) and women (OR = 1.16; 95% CI: 1.08–1.24) with CKD (Figures 7 and 8).

The results also indicated that elevated NPAR, compared with lower levels, increased the risk of all-cause mortality in patients with CKD (OR = 1.62; 95% CI: 1.40–1.89) (Figure 9).

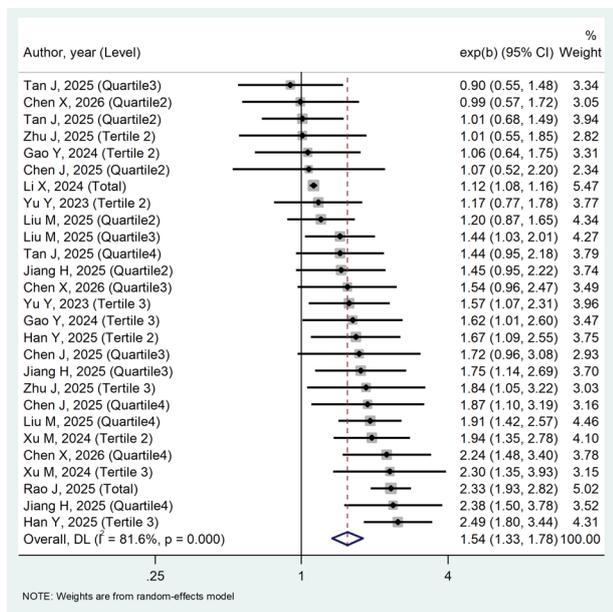


Figure 2. Forest plot showing the association between NPAR and CVD mortality in CKD patients.

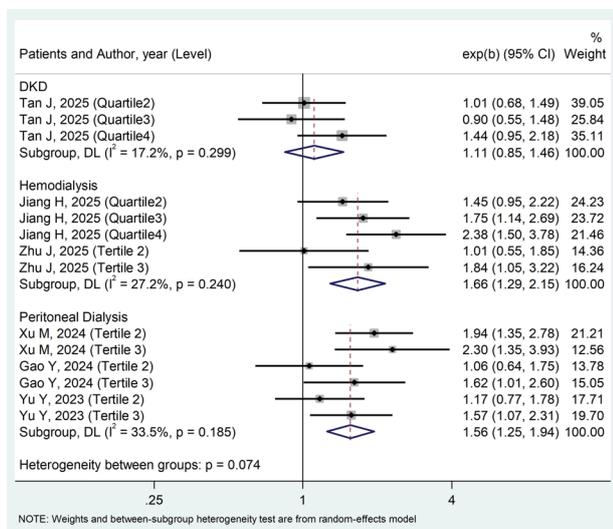


Figure 3. Forest plot showing the association between NPAR and CVD mortality in hemodialysis, peritoneal dialysis, and CKD patients.

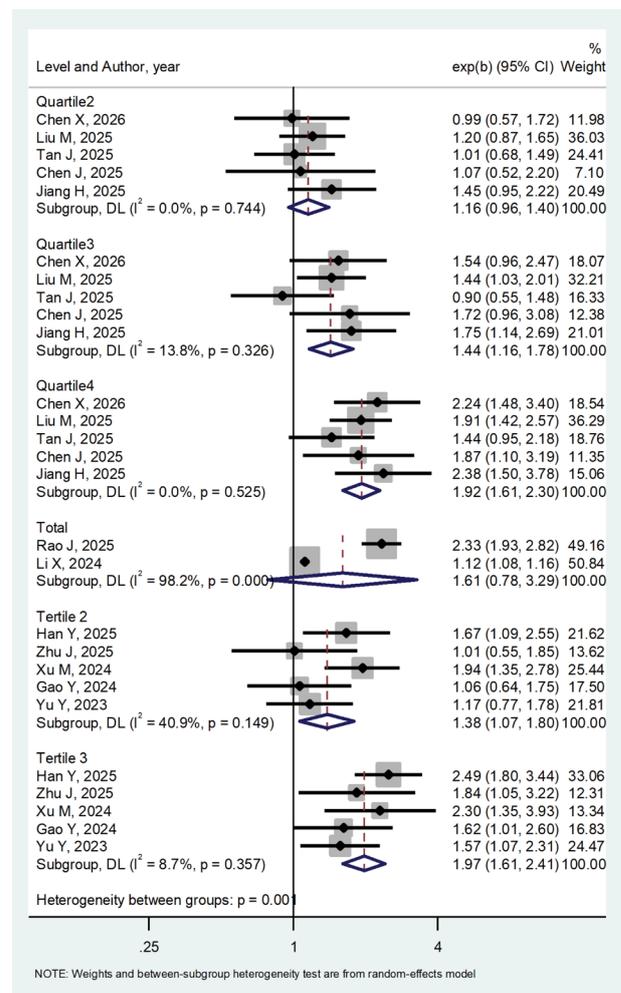


Figure 4. Forest plot showing the association between NPAR and CVD mortality in CKD patients by NPAR level.

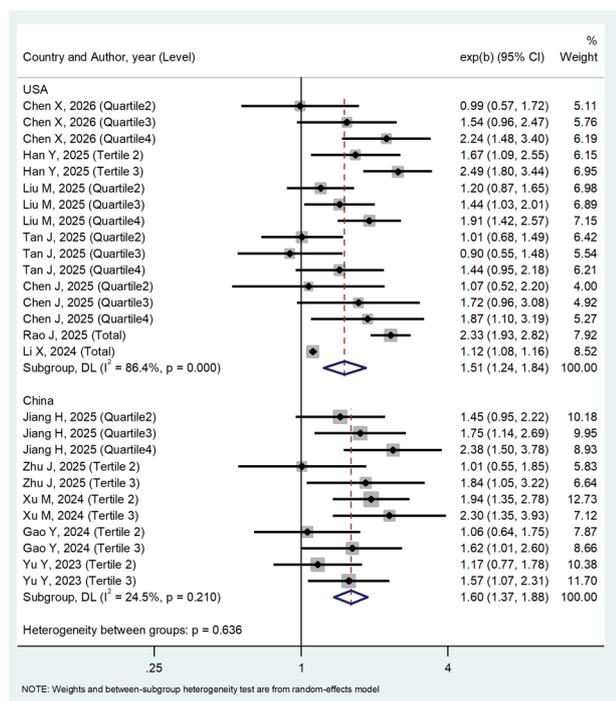


Figure 5. Forest plot showing the association between NPAR and CVD mortality in CKD patients by country.

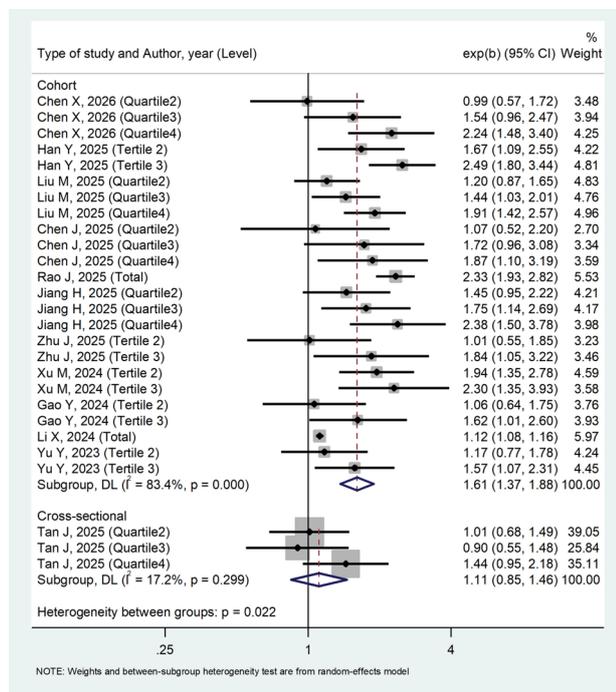


Figure 6. Forest plot showing the association between NPAR and CVD mortality in CKD patients by type of study.

In the additional analyses, the meta-regression indicated that the association between elevated NPAR and the risk of CVD-related mortality in patients with CKD was not significantly influenced by either the year of publication ($P = 0.490$) or the sample size of the included studies

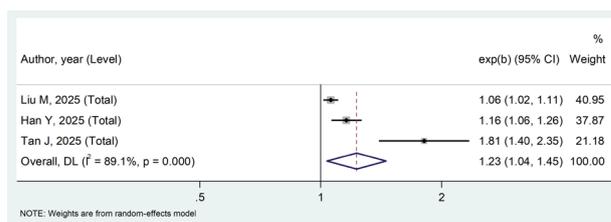


Figure 7. Forest plot showing the association between NPAR and CVD-related mortality in males with CKD.

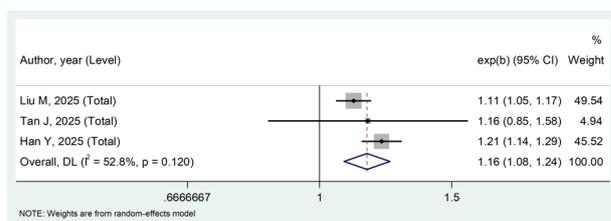


Figure 8. Forest plot showing the association between NPAR and CVD mortality in females with CKD.

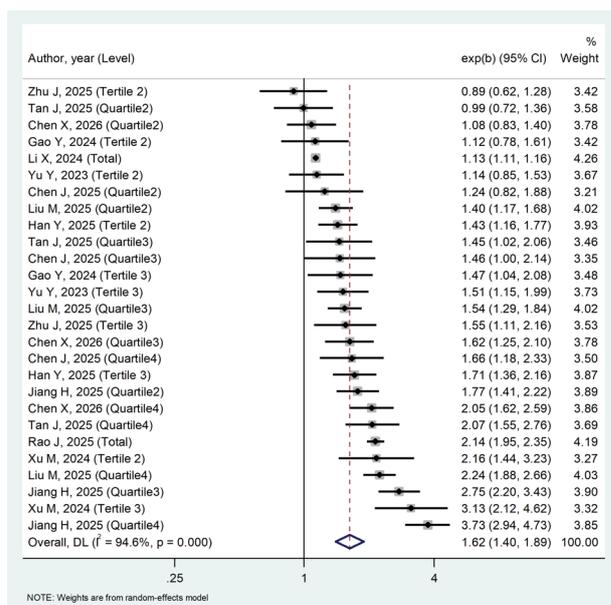


Figure 9. Forest plot showing the association between NPAR and all-cause mortality in CKD patients.

($P = 0.957$) (Figures 10 and 11).

The publication bias diagram was significant (p -value=0.001) and showed that studies that identified high NPAR levels as a risk factor for cardiovascular mortality in patients with CKD were more likely to be published (Figure 12).

Discussion

The findings of this meta-analysis showed that elevated NPAR in patients with CKD increased the risk of CVD-related mortality by 54% and all-cause mortality

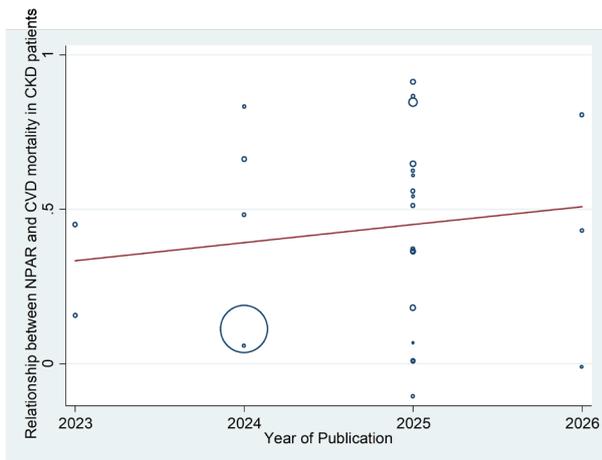


Figure 10. Meta-regression plot of association between NPAR and CVD mortality in CKD patients by year of publication.

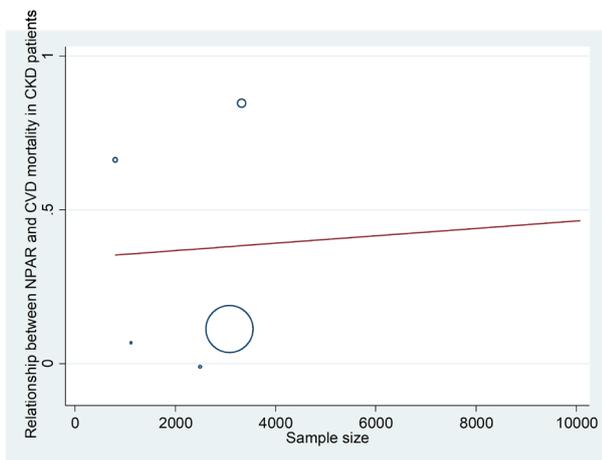


Figure 11. Meta-regression plot of association between NPAR and CVD mortality in CKD patients by sample size

by 62%. Regarding NPAR categories, the third quartile (44%), fourth quartile (92%), second tertile (38%), and third tertile (97%) were all associated with higher CVD mortality compared with the lowest category. In addition, higher NPAR increased the risk of CVD-related death by 23% in men, 16% in women, 60% in studies conducted in China, and 51% in those conducted in the United States. Elevated NPAR also increased the risk of CVD mortality by 66% in hemodialysis patients and by 56% in peritoneal dialysis patients.

Chen et al, in their cohort study, reported that higher NPAR was associated with an elevated likelihood of both all-cause mortality and CVD-related mortality among individuals with CKD (13). Han and colleagues, using a cohort design, reported that higher NPAR in individuals with CKD was linked to a greater likelihood of both all-cause mortality and CVD-related mortality (15). In a cohort study conducted by Jiang et al among hemodialysis patients, elevated NPAR was likewise

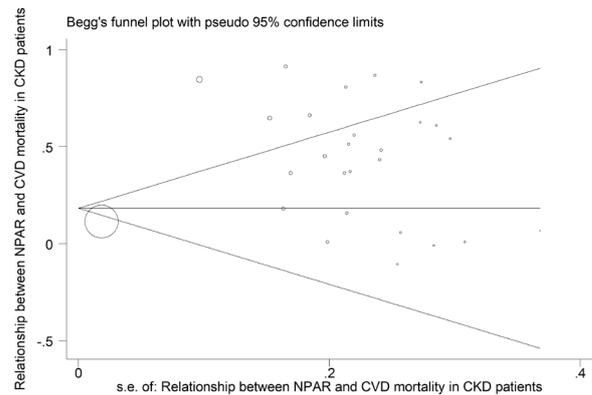


Figure 12. Publication bias of the included studies.

associated with a higher probability of death from any cause as well as death due to CVD events (22). Liu et al found that patients in the highest NPAR category experienced a noticeably greater risk of both all-cause and CVD-related mortality compared with those in the lowest category (20). Similarly, Rao et al observed that increased NPAR levels were accompanied by a heightened risk of mortality from all causes and from CVD-related causes in patients with CKD (16). Evidence from the cohort study by Tan et al, conducted in individuals with DKD, also indicated that higher NPAR was related to an increased likelihood of both all-cause and CVD-related mortality (21). Collectively, these studies align with the findings of the present analysis, reinforcing that elevated NPAR serves as an indicator of greater vulnerability to both overall and cardiovascular-specific mortality in patients with CKD. This pattern suggests that higher NPAR may function as a prognostic marker and a potential risk factor in this population.

Liu et al, in a cohort study of individuals with hypertension, reported that higher NPAR was associated with a greater likelihood of both all-cause and CVD mortality (26). Likewise, Zhu et al, examining adults with non-alcoholic fatty liver disease, likewise found that elevated NPAR corresponded to an increased probability of death from all-cause as well as from CVD events (27). In a study by Yan et al involving patients with coronary artery disease, those in the highest NPAR category experienced a noticeably higher risk of overall and CVD-related mortality compared with those in the lowest category (28). A cohort study by Ji and colleagues in individuals with diabetes and pre-diabetes also demonstrated that increased NPAR was linked to a heightened likelihood of both all-cause and CVD mortality (29). Similarly, Qiu et al, studying a general population sample, observed that participants with the highest NPAR levels faced a greater risk of mortality from all causes and from CVD (30). Collectively, these findings are consistent with

the results of the present study, indicating that elevated NPAR functions as a risk marker for increased all-cause and CVD-related mortality across a range of conditions, including hypertension, non-alcoholic fatty liver disease, coronary artery disease, diabetes, and pre-diabetes.

Shen et al reported findings that did not align with the results of the present study. In their cohort investigation involving individuals with diabetes, the highest NPAR category did not show a meaningful increase in cardiovascular-related mortality when compared with the lowest category. Differences in study design, patient characteristics, sample size, and other methodological factors may reasonably account for this discrepancy (31).

Limitations of the study

The evidence base was relatively narrow, as only a small number of eligible studies were available, and all were conducted exclusively in China and the United States, limiting the geographic and demographic diversity of the included populations. This concentration of data may restrict the generalizability of the findings to broader or more heterogeneous settings. In addition, the available studies did not provide sufficient detail to allow stratified analyses by patient age, preventing assessment of whether the association between NPAR and mortality varies across different age groups.

Conclusion

Elevated NPAR was associated with a greater likelihood of both cardiovascular and all-cause mortality in individuals with CKD. Within this population, progressively higher NPAR levels corresponded to progressively higher cardiovascular mortality risk, indicating that high values function as a stronger risk marker than moderate values, and moderate values carry more risk than low values. When comparing patient subgroups, the association appeared more pronounced in men than in women. A similar pattern emerged across treatment modalities, with hemodialysis patients exhibiting a stronger mortality risk linked to elevated NPAR than those undergoing peritoneal dialysis.

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Authors' contribution

Conceptualization: Mohammad Rostamzadeh and Maede Safari.

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Formal analysis: Abdolmohammad Ranjbar and Ali

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Investigation: Reza Faramarzadeh and Mohammad Rostamzadeh.

Methodology: Ali Emadzadeh and Samaneh Zandifar.

Project administration: Niloofar Khosravi and Roozbeh Roohinezhad.

Supervision: All authors.

Validation: Yaser Abolhasani and Roozbeh Roohinezhad.

Visualization: Amir Heidari and Samaneh Zandifar.

Writing—original draft: All authors.

Writing—review and editing: All authors.

Conflicts of interest

The authors declare that they have no competing interests.

Declaration of generative artificial intelligence (AI) and AI-assisted technologies in the writing process

During the preparation of this work, the authors utilized AI tools (Copilot and Grammarly) to refine grammatical points and language style in their writing. Subsequently, the authors thoroughly reviewed and edited the content as necessary, assuming full responsibility for the accuracy and content of the publication.

Ethical issues

This study has been compiled based on the PRISMA checklist, and its protocol was registered on the PROSPERO (International Prospective Register of Systematic Reviews) website with (ID: [CRD420261304086](https://doi.org/10.1111/PROSPERO.2024040086)) and the Research Registry website with (Unique Identifying Number [UIN]: [reviewregistry2082](https://doi.org/10.21956/RESEARCHREGISTRY.2024040086)). Besides, ethical issues (including plagiarism, data fabrication, and double publication) have been completely observed by the author.

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