REVIEW



Predictive and prognostic value of the neutrophil-to-lymphocyte ratio for acute kidney injury: a systematic review and meta-analysis

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Abstract

The neutrophil-to-lymphocyte ratio (NLR) has been suggested as a potential biomarker for the prediction and risk stratification of acute kidney injury (AKI), but conflicting results were reported by literature. We therefore conducted a pooled analysis to consolidate available evidence regarding the predictive and prognostic value of NLR in AKI patients. A systematic search was performed in the PubMed/Medline, Embase, and Cochrane Central Register of Controlled Trials (Central) databases from inception to March 2025 for cohort studies investigating the association between NLR and AKI. Quality assessment was performed via the Quality Assessment for Studies of Diagnostic Accuracy (QUADAS-2) tool. The predictive and prognostic value of the NLR for AKI was evaluated via pooled estimates of odds ratio (OR), sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NeLR), diagnostic score (DS), diagnostic odds ratio (DOR), summary receiver operating characteristic (SROC) curves, and the Fagan nomogram. Twenty-nine studies with 102.870 patients were pooled in this meta-analysis. Higher NLR was associated an increased risk of AKI (OR 1.52, 95% CI 1.29–1.79; p < 0.001). The pooled sensitivity and specificity were 0.70 (95% CI 0.65–0.74) and 0.67 (95% CI 0.60–0.74). The combined values of the PLR, NeLR, DS, and DOR were 2.13 (1.74–2.60), 0.45 (0.38–0.52), 1.56 (1.24–1.89), and 4.78 (3.46–6.60), respectively, with a pooled area under the curve (AUC) for the SROC being 0.74 (95% CI 0.70–0.78). Subgroup analysis suggested that the associations remained statistically significant in contrast-associated AKI (p < 0.001) and surgery-associated AKI (p < 0.001), but of boarder line significance in sepsis-associated AKI (p=0.082). In addition, higher NLR was also found to be related to 1.47-fold increase in mortality among AKI patients (OR 1.47, 95% CI 1.13–1.91, p=0.004). NLR is not only an effective marker for predicting AKI event, but also a prognostic tool to identify AKI patients with higher risk of death. Future studies are needed to justify its value in different AKI subtypes.

Keywords Acute kidney injury · Neutrophil-to-lymphocyte ratio · Diagnosis · Prognosis · Biomarker

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Introduction

Acute kidney injury (AKI) is a prevalent complication among hospitalized patients and is characterized by an elevation in serum creatinine (SCr) levels, a rapid decline in the glomerular filtration rate (GFR), or oliguria or anuria [1], all of which increase the risk of mortality. Currently, the primary diagnosis of AKI in hospital settings is dependent on SCr levels or urine volume. However, many patients are overlooked initially because their SCr levels are already elevated upon admission [2]. Consequently, interest in new biomarkers that can provide earlier and more accurate diagnoses of AKI, as well as predict clinical outcomes such as mortality is increasing.

One promising area of research involves inflammation response biomarkers, which may offer a valuable addition to the diagnostic toolkit for AKI. Research has underscored the pivotal role of the inflammatory response in the progression of AKI [3]. Systemic inflammation markers, such as IL-6, IL-8, CRP and TNF- α , have been utilized to evaluate the risk and severity of diseases [4]. Similarly, the neutrophilto-lymphocyte ratio (NLR), a readily accessible and costeffective marker of inflammation, has garnered attention as a potential predictive and prognostic biomarker across various diseases, including sepsis [5], cancer [6], acute appendicitis [7], and AKI [8]. While the NLR has shown promise in these contexts, its applicability as a reliable predictive and prognostic tool for AKI remains controversial due to a paucity of robust statistical data. To address this gap and consolidate the existing evidence, we conducted a systematic review and meta-analysis aimed at verifying the predictive value of the NLR for AKI and other clinical outcomes. This comprehensive analysis will help clarify the role of the NLR in AKI management and inform future research directions.

Methods

Study search strategy

The protocol of systematic review and meta-analysis was registered in PROSPERO (CRD42024558959). And the study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement standards [9]. A systematic search was performed in the PubMed/Medline, Embase, and Cochrane Central Register of Controlled Trials (Central) databases from their inception until March 2025. The search terms included ("neutrophilto-lymphocyte" or "neutrophil/lymphocyte ratio" or "neutrophil–lymphocyte count ratio" or "neutrophil–lymphocyte ratio" or "NLR") and ("AKI" or "acute kidney injury" or "acute renal failure"). Furthermore, reference lists were further reviewed to identify relevant studies. The detailed search strategy and results from each database have been provided in the Supplementary Appendix.

Eligibility criteria and study selection

A total of 3442 relevant articles were identified by the initial search. The literature inclusion criteria were as follows: (i) human cohort studies with participants \geq 18 years of age, (ii) investigated the association between NLR and AKI, and (iii) reported incidence of AKI, patient mortality or other clinical outcomes. Ineligible literature, such as conference abstracts, protocols, case reports, reviews, meta-analyses, basic studies or those with insufficient data for analysis, were excluded. Two reviewers (WW and YBY) independently

selected studies by reviewing titles, abstracts, and full texts. Furthermore, disagreements on study selection between the two reviewers were resolved by a third reviewer (ZYL).

Data extraction

Two reviewers (WW and YBY) independently extracted data from each study by using a standardized data extraction form, including the first author, publication year, sample size, type of AKI, definitions of AKI, mortality, and time of NLR measurement. Additionally, odds ratio (OR), the area under the curve (AUC), optimal cutoff, sensitivity and specificity of the NLR were obtained from the included articles. Absolute true-positive (TP), false-positive (FP), true-negative (TN), and false-negative (FN) data were also calculated.

Quality assessment and risk of bias

The quality assessment and risk of bias for the 29 included studies were independently elevated by two authors (WW and YBY) following the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) [10]. The risk of bias included the following: (i) patient selection, (ii) index test, (iii) reference standard, and (iv) flow and test timing. Additionally, patient selection, index tests, and reference standards were assessed for applicability concerns.

Statistical analysis

The outcome measures were analyzed via a random effects model, and the pooled effect of NLR-AKI association was calculated as the standardized OR and 95% CI with heterogeneity. Heterogeneity was evaluated via the χ^2 test and I^2 statistic. The diagnostic value of the NLR for predicting AKI was further evaluated via pooled estimates of sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NeLR), diagnostic score (DS), diagnostic odds ratio (DOR), summary receiver operating characteristic (SROC) curves, and the Fagan nomogram, while clinical outcomes AKI patients such as mortality were also evaluated. Additionally, publication bias was assessed via Deek's funnel plot. All the statistical analyses were performed via R studio software (version 4.2.1; R Foundation for Statistical Computing, Vienna, Austria), Review Manager, version 5.4 (RevMan, the Cochrane Collaboration, Oxford, UK), and Stata, version 17.0 (Stata Corporation, College Station, TX, USA). Statistical analyses were performed using R software (version 4.2.1) with the meta-package (version 5.2–0). Specifically, we employed the following functions: (1) the 'metagen' function for effect size calculation and heterogeneity assessment, (2) the 'summary' function for meta-analysis results synthesis, and (3) the 'forest' function for visualization of the forest plots. p < 0.05 was considered statistically significant.

Results

Study identification

The study selection process is shown in Fig. 1. The initial search identified 3442 relevant articles, 374 of which were excluded because of duplication. According to the title and abstract, 2774 irrelevant articles were further excluded. After screening the full texts, 267 records were excluded. Additionally, two articles were identified through the reference lists of relevant articles. Finally, 29 studies were included in the systematic review and meta-analysis [3, 11–38].

Study characteristics

A total of 29 studies involving 102,870 participants were included. Among these studies, 25 reported on the predictive value of the NLR for AKI [11–35], including surgery-associated AKI, contrast-associated AKI and sepsis-associated AKI (SAKI). AKI was defined as an increase in SCr of \geq 0.5 mg/dl or > 25% from baseline and KDIGO definition. Six studies, including 69,883 participants, evaluated the prognostic value of NLR for predicting morality in AKI patients [3, 19, 32, 36–38]. The detailed characteristics of all the included studies are shown in Table 1.

Study quality assessment

The quality of the 29 included studies was assessed using the QUADAS-2 tool (Figure S1). The results of the QUADAS-2 assessment were classified as "low risk," "high risk," or "unclear risk." Base on the reference standard, four studies [11, 13, 14, 25] were labeled as "high risk" and 18 studies [3, 15, 16, 21–24, 26, 27, 29–34, 36–38] were labeled as "low risk." Overall, the studies included exhibited a low level of bias.

Predictive value of the NLR for AKI

There are 25 studies and 77,304 participants in which the predictive value of the NLR as a biomarker for AKI was investigated [11–35]. As shown in Fig. 2, a higher NLR at admission or preoperatively was significantly associated with increased risk of AKI (OR 1.52, 95% CI 1.29-1.79, p < 0.001), whereas the overall I^2 value was 95% (95% CI: 93.4–96.0%, $\chi^2 = 0.09$, p < 0.01), indicating significant heterogeneity. Furthermore, the pooled sensitivity and specificity were 0.70 (95% CI 0.65–0.74) and 0.67 (95% CI 0.60–0.74), respectively, with an AUC of 0.74 (95% CI 0.70-0.78) (Figs. 3, 4). The combined values of the PLR, NeLR, DS, and DOR were 2.13 (1.74-2.60), 0.45 (0.38-0.52), 1.56 (1.24–1.89), and 4.78 (3.46–6.60), respectively (Figure S2, S3). As shown in Fig. S4, Fagan's nomogram for the likelihood ratios indicated that the use of the NLR to diagnose AKI increased the post-test probability to 68% when the results were positive and reduced the post-test probability to 31% when the test was negative.

Fig. 1 Flow diagram of the 3,442 records identified through database searching study selection process 374 dupicate records excluded 3,068 records screened 2,774 irrelevant records excluded 294 full text articles 267 records excluded after detail review: assessed for eligibility studies on pediatric population (n=33) insufficient data (n=67) conference abstracts, protocol, case reports, reviews, meta-analysis (n=115) 27 full text articles basic studies (n=52) assessed for eligibility 2 record identidied through reference list 29 studies included in the meta-analysis

Table 1 Characteristics of the included studies

Study	Country	Design	Age (Years)	Sex (Male)	Sample size	NLR meas- urement	AKI definition	Type of AKI	Outcomes
Kim (2015)	Korea	Single-center retrospec- tive	65 (55–73)	69.7%	590	Preoperative	KDIGO	Surgery- associated AKI	AKI
Yilmaz (2015)	Turkey	Single-center retrospec- tive	N/A	50.8%	118	At admission	KDIGO	SAKI	AKI
Kurtul (2016)	Turkey	Single-center retrospec- tive	62.8±12.6	64.2%	478	At admission	increase in SCr of > 0.5 mg/ dl or > 25% from base- line	CI-AKI	AKI
Ying (2017)	China	Single-center retrospec- tive	N/A	80.7%	1061	At admission	increase in SCr of > 0.5 mg/ dl from baseline	CI-AKI	AKI
Koo (2018)	Korea	Single-center retrospec- tive	N/A	52.4%	1099	Preoperative	KDIGO	Surgery- associated AKI	AKI
Parlar (2018)	Turkey	Single-center retrospec- tive	N/A	59.3%	396	Preoperative	KDIGO	Surgery- associated AKI	AKI
Silberman (2018)	Israel	Single-center retrospec- tive	N/A	68.9%	3027	Preoperative	increase in SCr of > 2 mg/ dl from baseline	Surgery- associated AKI	AKI, mor- tality
Sun (2018)	China	Multicenter retrospec- tive	59.7 (11.2)	77.2%	5719	At admission	increase in SCr of ≥ 0.5 mg/ dl or $\geq 25\%$ from base- line	CI-AKI	AKI
Tanık (2019)	Turkey	Single-center retrospec- tive	57.16±11.55	82.1%	2000	At admission	increase in SCr of > 0.5 mg/ dl, or > 25% from base- line	CI-AKI	AKI
Kim (2019)	Korea	Single-center retrospec- tive	N/A	82.9%	473	Preoperative	KDIGO	Surgery- associated AKI	AKI, mor- tality
Bu (2019)	China	Single-center retrospec- tive	64.83 ± 17.13	55.4%	222	At admission	KDIGO	SAKI	AKI, mor- tality
Fan (2019)	China	Single-center retrospec- tive	65.8±17.3	44.4%	13,678	At admission	KDIGO	/	Mortality
Weedle (2019)	Ireland	Single-center retrospec- tive	66.8 (9.97)	77.7%	906	Preoperative	KDIGO	Surgery- associated AKI	AKI
Bi (2020)	China	Single-center retrospec- tive	60.48 ± 17.74	63.8%	282	At admission	KDIGO	Surgery- associated AKI	AKI

Table 1 (continued)

Study	Country	Design	Age (Years)	Sex (Male)	Sample size	NLR meas- urement	AKI definition	Type of AKI	Outcomes
Butt (2020)	America	Single-center retrospec- tive	N/A	70.25%	1577	At admission	increase in SCr of \geq 0.5 mg/ dl or \geq 25% from base- line	CI-AKI	AKI
Zhu (2020)	China	Single-center retrospec- tive	58 (47, 67)	65.6%	1168	At admission	KDIGO	CI-AKI	mortality
Ösken (2021)	Turkey	Single-center retrospec- tive	68.3±9.3	80.2%	389	At admission	KDIGO	CI-AKI	AKI
Parlar (2021)	Turkey	Single-center retrospec- tive	62.2±9	78.8%	396	Preoperative	KDIGO	Surgery- associated AKI	AKI
Usta (2021)	Turkey	Single-center retrospec- tive	N/A	76.1%	335	Preoperative	KDIGO	Surgery- associated AKI	AKI
He (2021)	China	Single-center retrospec- tive	N/A	67.32%	91	Preoperative	KDIGO	Surgery- associated AKI	AKI
Olasińska (2022)	Poland	Single-center retrospec- tive	80 (75–83)	47.9%	163	At admission	KDIGO	SAKI	AKI, mor- tality
Chen (2022)	China	Single-center retrospec- tive	68.1±16.6	62.2%	10,411	At admission	KDIGO	/	Mortality
Xie (2022)	Chian	Single-center retrospec- tive	58 (46–68)	63.8%	1238	At admission	KDIGO	SAKI	AKI
Zhang (2022)	China	Single-center retrospec- tive	N/A	66.9%	154	Preoperative	KDIGO	Surgery- associated AKI	AKI
Yan (2023)	China	Single-center retrospec- tive	56 (46-64)	60.2%	10,159	Preoperative	KDIGO	Surgery- associated AKI	AKI
Zhou (2023)	China	Single-center retrospec- tive	N/A	69.9%	2230	At admission	KDIGO	CI-AKI	AKI
Wei (2023)	China	Single-center retrospec- tive	57.8±18.1	70.2%	309	At admission	KDIGO	SAKI	Mortality
Wang (2023)	China		53.23 (15.35)	53.1%	44,065	Preoperative	KDIGO	Surgery- associated AKI	AKI, mor- tality
Pan (2024)	China		70.04 ± 16.95	55.3%	217	At admission	KDIGO	SAKI	AKI

NLR neutrophil-to-lymphocyte ratio, AKI acute kidney injury, CI-AKI contrast-associated AKI, SAKI sepsis-associated AKI, SCr serum creatinine; KDIGO Kidney Disease Improving Global Outcomes

The predictive cutoff values of the NLR, initial TP, TN, FP, FN, sensitivity, and specificity for AKI are summarized in Table S1. These results indicate that the NLR has a moderately high diagnostic value for AKI.

Sensitivity analysis

We evaluated the stability of NLR as a risk factor of AKI by sequentially removing one study at a time. As shown in

Fig. 2 Forest plot of the predictive value of the NLR for AKI. NLR neutrophil-to-lymphocyte ratio, AKI acute kidney injury

Study	logOR S	E(logOR)	Odds Ratio	OR	95%-CI	Weight
Kim/2015	1.7750	0.3918	·	5.90	[2.74; 12.72]	2.4%
Yilmaz/2015	1.1787	0.1102			[2.62; 4.03]	4.4%
Kurtul/2016	0.9670	0.4262			[1.14; 6.06]	2.2%
Ying/2017	0.0953	0.0279		1.10	[1.04; 1.16]	4.8%
Parlar/2018	0.5653	0.1224		1.76	[1.38; 2.24]	4.4%
Koo/2018	0.0100	0.0025		1.01	[1.00; 1.02]	4.8%
Silberman/2018	0.3436	0.1486	-	1.41	[1.05; 1.89]	4.2%
Sun/2018	0.3293	0.1020	-	1.39	[1.14; 1.70]	4.5%
Bu/2019	0.0392	0.0220		1.04	[1.00; 1.09]	4.8%
Kim/2019	0.0862	0.0140		1.09	[1.06; 1.12]	4.8%
Tanlk/2019	0.5766	0.1961		1.78	[1.21; 2.61]	3.8%
Weedle/2019	0.0953	0.0390	+	1.10	[1.02; 1.19]	4.8%
Bi/2020	0.2546	0.0317		1.29	[1.21; 1.37]	4.8%
Butt/2020	0.7080	0.2035		2.03	[1.36; 3.03]	3.8%
Ösken/2021	0.6471	0.1627		1.91	[1.39; 2.63]	4.1%
Parlar/2021	0.3148	0.7526		1.37	[0.31; 5.99]	1.0%
Usta/2021	0.0198	0.0920		1.02	[0.85; 1.22]	4.5%
He/2021	0.1310	0.1016		1.14	[0.93; 1.39]	4.5%
Xie/2022	0.0677	0.0072		1.07	[1.06; 1.09]	4.8%
Zhang/2022	1.5913	0.6216		- 4.91	[1.45; 16.60]	1.3%
Olasiń ska/2022	1.2179	0.1672			[2.44; 4.69]	4.0%
Yan/2023	0.3920	0.1027	-	1.48	[1.21; 1.81]	4.5%
Zhou/2023	0.8329	0.2176		2.30	[1.50; 3.52]	3.6%
Wang/2023	0.3507	0.0850		1.42	[1.20; 1.68]	4.6%
Pan/2024	0.0100	0.0051		1.01	[1.00; 1.02]	4.8%

0.1

Heterogeneity: $I^2 = 94.8\%$, $\tau^2 = 0.1481$, p < 0.0001

Fig. S5, the pooled effect for AKI remains consistent after omitting each of the included studies (p all < 0.001), demonstrating the robustness of the finding.

Random effects model

Publication bias

Publication bias was further evaluated using Deek's funnel chart. As illustrated in Fig. S6, among the 25 studies examining the relationship between NLR and AKI, funnel plot revealed no significant publication bias (p=0.77).

Subgroup analysis

Although the pool analysis suggested that NLR was statistically significant for predicting AKI, the heterogeneity was substantial. Therefore, we further conducted subgroup analysis of different types of AKI, including surgery-associated AKI, contrast-associated AKI, and SAKI. Surgeryassociated AKI was reported in 13 studies [11, 15–17, 20, 22, 23, 25, 27–29, 32, 33] with 61,888 patients, contrastinduced AKI in 7 studies [13, 14, 18, 21, 24, 26, 34] with 13,454 patients, and SAKI in 5 studies [12, 19, 30, 31, 35] with 2,012 patients. As shown in Fig. 5, the results of the subgroup analyses suggest that the NLR is a potential biomarker for diagnosing contrast-associated AKI (OR 1.67, 95% CI 1.32–2.12, p < 0.001) and surgery-associated AKI (OR 1.31, 95% CI 1.14–1.52, *p* < 0.001). However,

the significance of the NLR for predicting SAKI was less robust (OR 1.63, 95% CI 0.94–2.83; *p* = 0.082).

10

2

0.5 1 1.52 [1.29; 1.79] 100.0%

Recognizing the variability in AKI diagnostic criteria among included studies (Table 1), we conducted additional subgroup analyses. Under both the traditional definition (serum creatinine increase ≥ 0.5 mg/dl or > 25% from baseline; OR 1.542, 95% CI 1.26–1.89, *p* < 0.001) and KDIGO definition (OR 1.51, 95% CI 1.21–1.89, *p* = 0.0003) of AKI, NLR demonstrated robust predictive power. Given the wide range of NLR cutoff values (2.17-17.11) adopted across the studies, we conducted meta-regression analysis to assess their impact on AKI prediction. The metaregression analysis revealed different NLR cutoff values might be a potential source of heterogenicity (p = 0.0854)(Table S2). To address the considerable heterogeneity, we further performed stratification into low-cutoff (< 3.46, n = 7 studies) [16, 18, 26, 27, 29, 32, 33] and high-cutoff $(\geq 3.46, n = 8 \text{ studies})$ [12–14, 19, 20, 23, 28, 31] subgroups. As illustrated in Fig. S7, the low NLR cutoff subgroup exhibited predictive value for AKI (OR 1.526, 95% CI 1.38–1.68, p < 0.001) without significant interstudy heterogenicity ($I^2 = 29.1\%$), whereas the high-cutoff group showed limited predictive utility with marginal significance (OR 1.334, 95% CI 1.00–1.79, p=0.0535) and the heterogenicity in this subgroup remained significant $(I^2 = 93\%).$

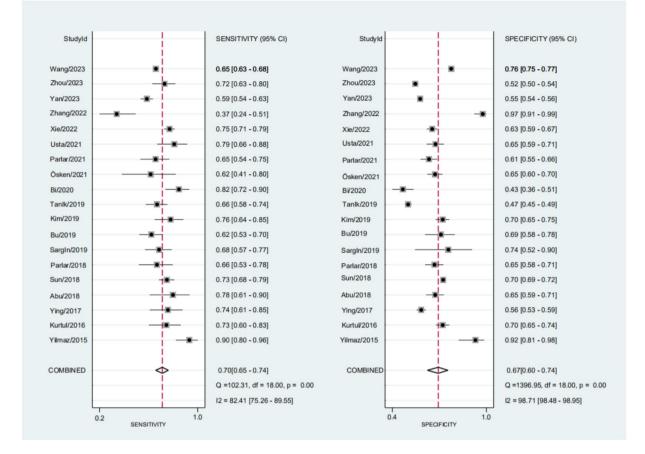


Fig. 3 Forest plot of the sensitivity and specificity of the NLR for the prediction of AKI. NLR neutrophil-to-lymphocyte ratio, AKI acute kidney injury

Prognostic value of the NLR for mortality in AKI patients

Six studies, including 69,883 participants, were included in the evaluation of the prognostic value of the NLR for risk of death in AKI patients [3, 19, 32, 36–38]. As shown in Fig. 6, a higher NLR at admission or preoperatively was associated with mortality in AKI patients (OR 1.47, 95% CI 1.13–1.91; p=0.004). However, only one study [3] has reported other major adverse events, such as the need for renal replacement therapy (RRT) and transfer to the ICU in AKI patients. More studies are required to verify the potential prognostic value of NLR for other major adverse events.

Discussion

This systematic review and meta-analysis, which included 29 studies with 102,870 patients, revealed that higher NLR was significantly associated with a 1.5-fold increased risk of AKI. NLR has a moderately high predictive value for AKI with a pooled estimated AUC of 0.74, sensitivity of 0.70 and

specificity of 0.67. Moreover, NLR also has a substantial prognostic value for mortality in AKI patients (OR 1.47). Subgroup analysis suggested that NLR's predictive value of AKI events remained statistically significant in surgery-associated AKI and CI-AKI, while only achieved boarder line significance in SAKI patients.

Current diagnostic criteria rely on classical parameter including SCr level and urine volume [39], which was disadvantaged by the delayed increase in SCr and inaccurate monitoring of urine output. A number of studies have focused on the predictive methods for AKI. Potential early biomarkers, such as kidney injury molecule-1 (KIM-1), neutrophil gelatinase associated-lipoprotein (NGAL), y-glutamyl transpeptidase (GGT), excess reactive oxygen species (ROS), tissue inhibitor of matrix metalloproteinase-2 (TIMP-2) and insulin-like growth factor binding protein 7 (IGFBP7), have been identified to be promising in the prediction of AKI [40]. However, most of the early biomarkers of AKI have not yet become clinical routine tests and the unavailability has hindered their clinical application. Cost-effective biomarker which are readily available has always been an area of interest in AKI research.

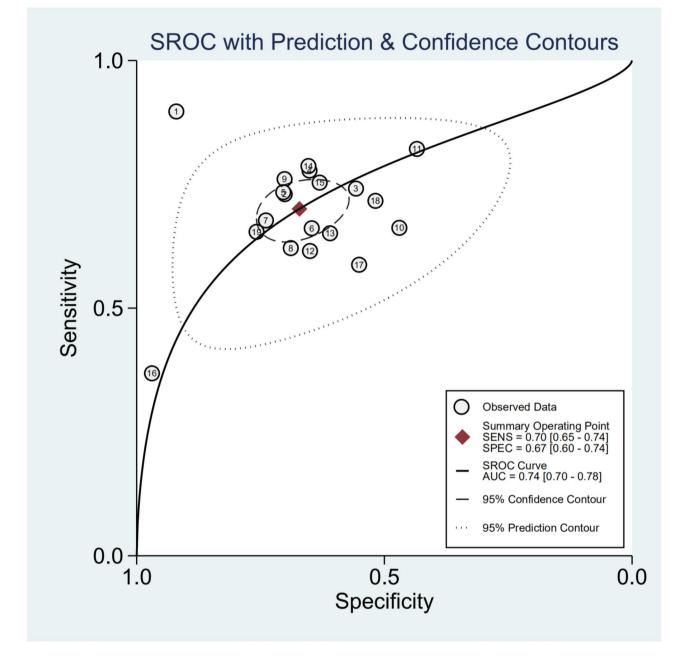


Fig. 4 SROC curve of the NLR for the included studies. SROC summary receiver operating characteristic, NLR neutrophil-to-lymphocyte ratio

The NLR is a combination of blood neutrophil and lymphocyte counts that are economical and easily obtained. Clinical and experimental studies [41] have reported that the systemic inflammatory response plays pivotal roles in the pathophysiological process of AKI. Increasing evidence has shown that the NLR may serve as a predictive marker for various diseases, including bacteraemia [42], atrial fibrillation [43] as well as AKI [20]. NLR measurement offers valuable clinical utility for AKI risk stratification across multiple healthcare settings. In preoperative evaluation, particularly for high-risk surgeries like cardiac procedures, NLR assessment can identify subclinical inflammation, guide perioperative optimization strategies, and inform surgical decision-making. For emergency department patients presenting with sepsis, early NLR measurement enables rapid AKI risk stratification and may help to guide fluid resuscitation protocols. In critical care settings, serial NLR monitoring provides dynamic assessment of AKI risk and other outcomes. NLR's particular strength lies in its cost-effectiveness and immediate availability through routine complete blood count analysis, making it especially valuable for resource-limited settings. Fig. 5 Subgroup analysis of AKI for the predictive value of the NLR. NLR neutrophil-tolymphocyte ratio, AKI acute kidney injury

Fig. 6 Forest plot of the prog-

nostic value of the NLR for

AKI acute kidney injury

ine	(2025) 25:201					Page 9 of 12	201
	Study	logHR S	E(logHR)	Hazard Ratio	HR	95%-CI	Weight
•	Contract consolities			1.1			
	Contrast-associate		0 4000		0.00	14 44. 0 001	0.00/
	2016 Kurtul	0.9670	0.4262			[1.14; 6.06]	
	2017 Ying	0.0953	0.0279	Task.		[1.04; 1.16]	
	2018 Sun	0.3293	0.1020			[1.18; 1.76]	
	2019 Tanlk	0.5766	0.1961	1.00		[1.21; 2.61]	
	2020 Butt 2021 Ösken	0.7080 0.6471	0.2035			[1.36; 3.02]	
			0.1627	-		[1.39; 2.63]	
	2023 Zhou Random effects mo	0.8329	0.2176			[1.50; 3.52]	
					1.67	[1.32; 2.12]	26.7%
	Heterogeneity: $I^2 = 85$	$1.7\%, \tau = 0.0688$	s, p < 0.0001				
	Surgery-associated	AKI					
	2015 Kim	1.7750	0.3918		5.90	[2.74; 12.73]	2.4%
	2018 Parlar	0.5653	0.1224	÷=		[1.38; 2.23]	
	2018 Koo	0.0100	0.0025		1.01	[1.00; 1.01]	4.8%
	2018 Silberman	0.3436	0.1486	1	1.41	[1.05; 1.88]	4.2%
	2019 Kim	0.0862	0.0140		1.09	[1.06; 1.12]	4.8%
	2019 Weedle	0.0953	0.0390		1.10	[1.03; 1.20]	4.8%
	2020 Bi	0.2546	0.0317		1.29	[1.21; 1.37]	4.8%
	2021 Parlar	0.3148	0.7526 -	-		[0.09; 1.72]	
	2021 Usta	0.0198	0.0920	-	1.02	[0.99; 1.42]	4.5%
	2021 He	0.1310	0.1016	-	1.14	[0.94; 1.40]	4.5%
	2022 Zhang	1.5913	0.6216		- 4.91	[1.45; 16.58]	1.3%
	2023 Yan	0.3920	0.1027		1.48	[1.21; 1.81]	4.5%
	2023 Wang	0.3507	0.0850	-	1.42	[1.24; 1.73]	4.6%
	Random effects mo	odel		0	1.31	[1.14: 1.52]	50.4%

Random effects model 1.31 [1.14; 1.52] 50.4% Heterogeneity: $I^2 = 93.1\%$, $\tau^2 = 0.0503$, p < 0.0001Sepsis-associated AKI 2015 Yilmaz 1.1787 0.1102 3.25 [2.72; 4.19] 4.4% 2019 Bu 0.0392 0.0220 1.04 [1.00; 1.09] 4.8% 2022 Xie 0.0677 0.0072 1.07 [1.05; 1.08] 4.8% 2022 Olasiń ska 1.2179 0.1672 3.38 [2.43; 4.68] 4.0% 2024 Pan 0.0100 0.0051 1.01 [1.00: 1.02] 4.8% Random effects model 1.63 [0.94; 2.83] 22.9% Heterogeneity: $I^2 = 98\%$, $\tau^2 = 0.3872$, p < 0.0001Random effects model 1.52 [1.29; 1.79] 100.0% \diamond

0.1 0.5 1 2 Heterogeneity: $I^2 = 94.8\%$, $\tau^2 = 0.1481$, p < 0.0001

Test for subgroup differences: $\chi_2^2 = 3.17$, df = 2 (p = 0.2046)

Study logOR SE(logOR) **Odds Ratio** OR 95%-CI Weight mortality in AKI patients. NLR Fan/2019 0.3920 0.1343 1.48 [1.14; 1.93] 16.7% 0.0078 neutrophil-to-lymphocyte ratio, Bu/2019 -0.01010.99 [0.98; 1.01] 20.0% Zhu/2020 0.9322 0.1938 2.54 [1.74; 3.71] 14.1% Chen/2022 0.1655 0.0759 1.18 [1.02; 1.37] 18.8% Wei/2023 0.6313 0.2669 1.88 [1.11; 3.17] 11.2% Wang/2023 0.4574 0.0631 1.58 [1.40; 1.79] 19.2% Random effects model 1.47 [1.13; 1.91] 100.0% 0.5 1 2

Heterogeneity: $I^2 = 95\%$, $\tau^2 = 0.0897$, p < 0.01

However, current studies on the association between NLR and AKI are heterogenous and baring conflict results. Hence, to consolidate available evidence and verify the predictive and prognostic value of the NLR for different types of AKI, we provided the one of the first systematic review and meta-analysis which justify the future clinical application of NLR in the timely recognition and risk stratification of AKI and subsequent outcomes.

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AKI is a clinical syndrome with complex etiologies. In addition to the overall pool analysis, we further conducted a subgroup analysis to assess the predictive value of the NLR for different types of AKI, such as surgery-associated

AKI [34], contrast-associated AKI [14], and SAKI [31]. Our results indicate that the NLR serves as an effective biomarker for contrast- or surgery-associated AKI. However, for SAKI, the predictive value of the NLR was less pronounced with only boarder line significance. The relation between NLR and sepsis has been reported by various studies. Schupp et al. reported that an elevated NLR was associated with an increased risk of sepsis [44]. A meta-analysis demonstrated that a higher NLR was predictive of a poorer prognosis for sepsis patients [45]. In our subgroup analysis focusing on SAKI enrolling five primary studies with 2012 patients, four studies [12, 19, 30, 31] identified significant association between the NLR and risk of SAKI in multivariate analysis, which remained significant when pooled together, whereas one SAKI research [35] failed to verify the predictive value. Notably, these studies were retrospective studies with limited samples, which might compromise the stability of the results. Furthermore, the performance of NLR may also vary depending on the AKI stage, severity of sepsis, complications, as well as covariates included in the multivariate analyses; therefore, more studies are required to draw a solid conclusion.

The high heterogeneity ($I^2 = 94.8\%$) in NLR's predictive performance for AKI may stem from various factors. Subgroup analyses revealed consistent results across AKI definitions, aligning with prior meta-analyses on CI-AKI [46]. However, NLR showed limited predictive value with borderline significance in the subgroup with high NLR cutoff values. Our analysis showed considerable variation in NLR cutoffs across studies, as demonstrated in the distribution bar chart (Fig. S8). For AKI subgroups, we observed that for contrast-associated AKI, the study by Kurtul et al. [13] reported optimal performance at a cutoff of 3.46 (AUC 0.787), while for surgery-associated AKI, a cutoff of 3.35 showed the best discriminative ability (AUC 0.778) [32]. For septic AKI, existing data suggest a potential optimal cutoff around 10.15 (AUC) [12]. These findings underscore the need for tailored NLR cutoffs and adjusted analyses for comorbidities in future studies to improve clinical applicability in different AKI subgroups.

In addition to forecasting AKI itself, NLR has also been found as a prognosticator for disease severity and clinical outcome [5, 45]. Hwang et al. demonstrated that the NLR was independently associated with mortality in patients with sepsis and septic shock [47]. Zhou et al. reported that a high NLR was independently associated with all-cause mortality in rheumatoid arthritis (RA) patients [48]. In our previously cohort study on SAKI patients, we demonstrated that NLR and NLR dynamics were associated with incidence of mortality, the need for RRT, and transfer to the ICU [3, 49]. The results of current meta-analysis were consistent with past literature findings, confirming that NLR was positively associated with mortality in AKI patients and might be used as a viable predictor of prognosis in AKI patients. However, as only six retrospective, single-center studies were included, larger-scale studies are required to conclude on the prognostic value of NLR on various clinical outcome in different subtypes of AKI.

To our knowledge, this systematic review and meta-analysis is among the first to evaluate the relationships between the NLR and AKI incidence and prognosis. However, several limitations should be considered. First, the etiologies of AKI are diverse and the application of NLR in other types of AKI, for example ischemic-reperfusion injury-associated AKI and cisplatin-induced AKI, was not analyzed because of the limited source studies. Second, in the analysis on AKI prognosis, we only compared on patient mortality and did not include other clinical outcomes such as need for RRT, transfer to ICU, renal non-recovery at discharge and rehospitalization. Third, NLR is a dynamic index along with the disease progression. Although most studies mainly focused on NLR at hospital admission or pre-operation, the fluctuation of NLR afterward was also informative for AKI patient prognosis [49] but it had not been evaluated through metaanalysis. Fourth, due to the study-level nature of our metaanalysis and significant methodological heterogeneity across included studies, we cannot definitively recommend specific NLR cutoff values. Future studies with standardized protocols are needed to establish optimal NLR cutoffs for AKI prediction in different clinical contexts.

Conclusion

Our systematic review and meta-analysis suggested that the NLR not only emerges as an effective predictive marker for AKI but also serves as a potential predictor of mortality in AKI patients. Further studies of larger sample sizes and higher quality are imperative to better understand the potential value of NLR and NLR dynamics in the prediction of different AKI subtypes and risk stratification of various patient outcomes.

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Availability of data and materials The datasets analyzed in the current study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

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