BMC Pulmonary Medicine

RESEARCH

Open Access

The prognostic impact of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio on patients with small cell lung cancer receiving first-line platinum-based chemotherapy: a systematic review and meta-analysis

Yuansheng Zhao[1], Yongsheng Wang[1], Yongquan Jiang[1], Jiandong Yang[1] and Yuefen Zhang[2*]

Abstract

Background The prognostic significance of Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) in Small Cell Lung Cancer (SCLC) patients receiving platinum-based chemotherapy is debated.

Methods This study aims to elucidate their roles in survival outcomes. A systematic search across PubMed, Embase, Web of Science, and Cochrane Library identified relevant studies. The Newcastle-Ottawa Scale (NOS) evaluated study quality. Meta-analysis was conducted using random-effects and fixed-effects models, supplemented by sensitivity analysis.

Results A total of 11 studies with 3,634 SCLC patients were included. Patients with high NLR had significantly decreased overall survival (OS) (HR = 1.39, 95% CI: 1.18–1.59, $P < 0.001$) and progression-free survival (PFS) (HR = 1.52, 95%CI: 1.27–1.78, $P < 0.001$). The OS was not statistically different between high and low PLR groups (HR = 1.13, 95%CI: 0.84–1.43, $P = 0.265$). Subgroup analysis revealed that OS in high NLR group was significantly lower across different strata, and OS in the high PLR group was significantly lower among patients with limited-stage SCLC (LS-SCLC) and populations with a PLR cutoff value < 160.

Conclusions High NLR is associated with poor OS and PFS in patients with SCLC receiving first-line platinum-based chemotherapy. PLR does not significantly impact OS, except in LS-SCLC patients and populations with a PLR cutoff value < 160. These findings require further validation from prospective studies.

Keywords Neutrophil-to-lymphocyte ratio, Platelet-to-lymphocyte ratio, Small cell lung cancer, First-line platinum-based chemotherapy, Prognosis, Meta-analysis

*Correspondence:
Yuefen Zhang
zhangyuefen5999@gmail.com
[1]Department of Cardiothoracic Surgery, Sinopharm TongMei General Hosptial, Datong 037000, Shanxi Province, China
[2]Department of Medical Oncology, Sinopharm TongMei General Hosptial, 5999 HeRui Street, Hengan New District, Yungang District, Datong 037000, Shanxi Province, China

© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

Introduction

Small Cell Lung Cancer (SCLC), one of the most aggressive types of lung cancer, is a malignancy that originates from argyrophilic cells of the bronchial mucosa basal layer. It accounts for approximately 13-17% of all lung cancer cases, demonstrating rapid progression, high invasiveness, a high risk of local recurrence, and a tendency for distant metastasis [1, 2]. Despite the generally poor prognosis of SCLC, with a five-year survival rate as low as 6.5% [3], platinum-based chemotherapy remains the cornerstone of treatment. While the initial response rate to platinum-based chemotherapy is approximately 60-65% [4], long-term survival is exceedingly rare. SCLC prognosis is typically consistent across patients receiving platinum-based chemotherapy, with limited variability in long-term survival outcomes. However, differences in treatment response still occur, driven by factors such as genetic mutations, phenotypic variations, and individual patient characteristics. Given these challenges, the need for more reliable prognostic markers is evident, particularly in light of tumor resistance and disease recurrence. Such markers could help personalize treatment and better identify high-risk patients, ultimately optimizing clinical decision-making [5, 6].

In the broader context of tumor pathophysiology, systemic inflammation has been recognized as a significant player. It constitutes a critical part of the tumor microenvironment and impacts multiple facets of cancer biology, from initiation to progression. Current research has shed light on the nexus between several inflammatory markers and the prognosis of solid tumors, including SCLC [7, 8]. Among these, two prominent systemic inflammation-based indices, the Neutrophil-to-Lymphocyte Ratio (NLR) and the Platelet-to-Lymphocyte Ratio (PLR), have drawn considerable attention for their potential prognostic relevance. These markers encapsulate the balance between inflammatory response (neutrophils and platelets) and the adaptive immune response (lymphocytes), which is increasingly appreciated in the context of cancer prognosis [5, 7].

Despite the surge in research on the prognostic value of NLR and PLR in SCLC patients, the findings have yet to converge into a consistent conclusion. Studies from various research groups paint a complex picture. Some research, such as that conducted by Kang et al. [9] and Sakin et al. [10], implies that SCLC patients with elevated NLR and/or PLR could face a more dismal prognosis. In stark contrast, other studies, such as those from Pan et al. [11] and Xie et al. [12], dispute this relationship, finding no significant correlation between these inflammation-based markers and the prognosis of SCLC patients. Recent studies [13], suggest that while NLR may be a useful prognostic marker for OS, it does not necessarily serve as a predictive marker for treatment efficacy, given the standardization of first-line platinum-based chemotherapy in most SCLC patients. This reinforces the idea that NLR, while potentially valuable for prognostication, does not offer individualized predictive insights into treatment response. This divergence in findings reflects the need for further robust analyses to conclusively determine the prognostic value of NLR and PLR in SCLC. In light of these discrepancies, we conduct a meta-analysis to systematically review and synthesize the available studies, with the aim of providing a more accurate assessment of the prognostic value of NLR and PLR in SCLC patients undergoing first-line platinum-based chemotherapy. This approach seeks to offer a useful tool for clinicians to improve prognosis determination and support more informed, efficient clinical decision-making, ultimately enhancing the management and treatment outcomes for SCLC patients.

Materials and methods

Search strategy

Throughout the systematic review process and the subsequent reporting of our findings, we adhered strictly to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [14]. On May 6, 2023, a comprehensive search was conducted across four electronic databases: PubMed, Embase, Web of Science, and the Cochrane Library. The search was not restricted by time limitations. The vocabulary and syntax were modified according to the specific requirements of each database. The search terms used in PubMed included: ("small-cell lung cancer" OR "small-cell lung carcinoma" OR "SCLC") AND ("neutrophil-lymphocyte ratio" OR "NLR" OR "platelet-lymphocyte ratio" OR "PLR"). No language restrictions were imposed. Additionally, a manual screening of reference lists was performed to identify any additional relevant articles.

Inclusion criteria

The inclusion and exclusion criteria for this meta-analysis were established based on the Population, Intervention, Comparison, Outcomes, and Study Setting (PICOS) guidelines. Studies included in the systematic review had to meet the following criteria: (1) Studies involving patients diagnosed with SCLC who were receiving first-line platinum-based chemotherapy; (2) Patients in the included studies had undergone at least one cycle of platinum-based chemotherapy; (3) NLR and PLR were determined prior to the initiation of first-line platinum-based chemotherapy; (4) The studies evaluated the association between NLR and PLR and the prognosis of SCLC patients; (5) The studies provided hazard ratios (HR) and 95% confidence intervals (CI) for the association between NLR and PLR and SCLC prognosis.

The exclusion criteria were as follows: (1) Studies that did not provide complete follow-up data were excluded; (2) Studies involving patients with other concurrent cancer diagnoses were excluded; (3) Case reports, commentaries, expert opinions, and narrative reviews were excluded.

Data extraction

Data extraction for this meta-analysis was performed by two independent researchers, with any discrepancies in their findings resolved through discussion or by the intervention of a third arbitrator. The extracted data encompassed a range of variables, including the first author's name, year of publication, ethnicity and country of the participants, follow-up period, age range of the participants, sample size, analysis model, cut-off values for PLR and NLR, and study endpoints. For studies missing OS or PFS data, these values were extracted and recalculated using Engauge Digitizer 9.1 software, from the provided Kaplan-Meier survival curves. In cases where data of interest were not available in the published report, the investigators of the original studies were contacted by email to request the unpublished data.

Quality assessment

The quality of the included studies in our meta-analysis was rigorously evaluated by two independent reviewers using the Newcastle-Ottawa Scale (NOS) [15]. NOS is a widely recognized tool for assessing the quality of research studies. It employs a comprehensive framework consisting of nine distinct components, categorized into three main domains: selection, comparability, and outcome. These categories facilitated the evaluation of potential sources of bias inherent in the studies. After a thorough evaluation, each study was assigned a quality score ranging from 0 to 9. The scores were interpreted as follows: studies with scores from 0 to 3 were classified as low quality, those with scores between 4 and 6 were categorized as moderate quality, and studies with scores from 7 to 9 were considered high quality.

Statistical analyses

To assess the heterogeneity among the included studies, chi-square statistics and the I^2 metric were used. An I^2 value of 0% indicated the absence of observed heterogeneity, whereas an I^2 value exceeding 50% suggested significant heterogeneity among the studies. In the presence of substantial heterogeneity ($I^2 > 50\%$), a random-effects model was adopted to compute the overall effect size, accounting for both within-study and between-study variations. Conversely, in the absence of significant heterogeneity ($I^2 \leq 50\%$), a fixed-effects model was applied, which considered only the within-study variation to estimate the overall effect size. A sensitivity analysis was performed to evaluate the robustness of the results and to assess the potential influence of individual studies on the overall effect size. This involved systematically omitting each study from the meta-analysis and recalculating the overall effect size. Publication bias was evaluated by inspecting the symmetry of the funnel plot and performing Egger's test. All statistical tests were two-sided, with a *P*-value of less than 0.05 denoting statistical significance. All statistical analyses were conducted using Stata version 17 (StataCorp, College Station, TX, USA).

Results

Search results and study selection

An initial search of electronic databases identified a total of 1,201 relevant studies. After eliminating duplicates, reviewing titles and abstracts, and applying strict inclusion and exclusion criteria, 25 studies were deemed relevant, while 14 were considered ineligible for further analysis. Ultimately, 11 studies were included in the meta-analysis [9–12, 16–22]. The study selection process and its outcomes are depicted in Fig. 1.

Study characteristics

The characteristics of the studies included in this systematic review are summarized in Table 1. The meta-analysis comprised studies published between 2014 and 2019. These studies were conducted in various regions, including Asia, North America, and Europe, with countries such as Turkey, China, the United States, Germany, and Korea represented. Follow-up periods varied across studies, with data reported in months; however, not all studies provided follow-up information. The participants were generally middle-aged to elderly, although age ranges varied, with some studies reporting mean age and others reporting median age. All studies employed multivariate analysis, and several also included univariate analyses. The NLR cutoffs ranged from 2.9 to 5.0, while PLR cutoffs (where provided) typically ranged from 140.1 to 210.0. Sample sizes ranged from 65 to 938 participants. Most studies used OS as the primary outcome endpoint, with some also considering PFS.

Results of quality assessment

The methodological quality of each study included in the meta-analysis was evaluated using the NOS. The NOS scores varied across studies, with two studies achieving a score of 7 points, five studies scoring 8 points, and the remaining four studies obtaining the highest score of 9 points. However, none of the studies employed blinding procedures or provided evidence of allocation concealment, which are common strategies to reduce bias in observational studies. No evidence of funding bias was found, suggesting that the financial sources of the studies did not influence the outcomes. Additionally, all studies

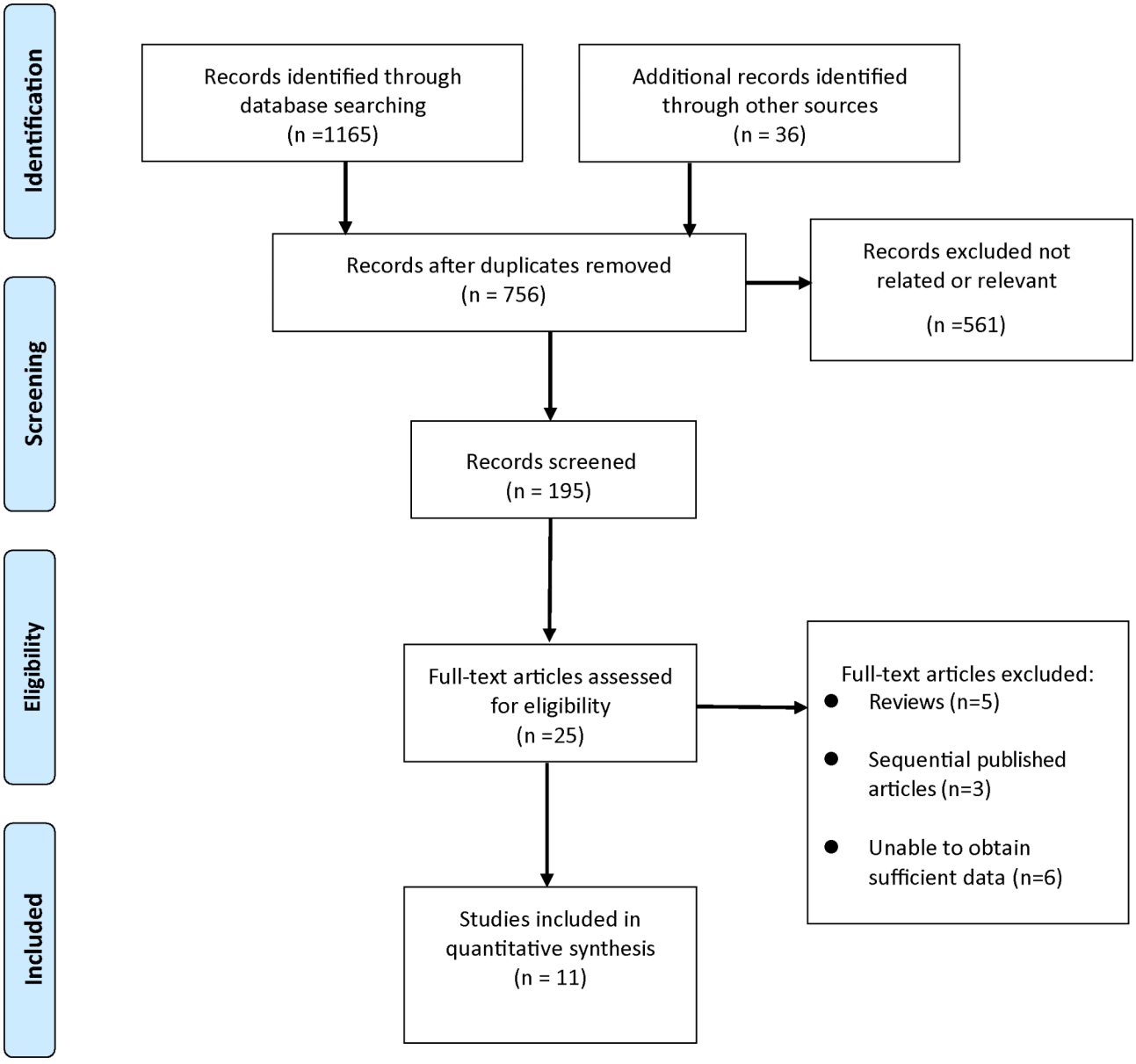

Fig. 1 Selection process of included studies

provided complete outcome data, demonstrating thorough data collection and reporting. No issues related to early stoppage bias or baseline imbalances were identified, further supporting the overall quality and reliability of the studies. For a detailed overview of the risks of bias and their corresponding ratios across the studies, refer to Table 2.

Meta-analysis of primary outcomes

The meta-analysis was based on 11 studies encompassing a total of 3,634 SCLC patients undergoing first-line platinum-based chemotherapy [9–12, 16–22]. This cohort was used to evaluate the correlation between the NLR and OS/PFS. The included studies displayed moderate heterogeneity (I^2=48.1%, P=0.037). Therefore, a random-effects model was employed to combine the effect sizes. The results revealed a significant decrease in OS in the high NLR group compared to the low NLR group (HR=1.39, 95% CI: 1.18–1.59, P<0.001) (Fig. 2). Similarly, PFS was significantly lower in the high NLR group compared to the low NLR group (HR=1.52, 95%CI: 1.27–1.78, P<0.001) (Fig. 3), showing no heterogeneity (I^2=0.0%, P=0.894).

By including five studies with a total of 1,612 SCLC patients undergoing first-line platinum-based chemotherapy, the correlation between the PLR and OS was assessed [9, 10, 12, 19, 20]. These studies demonstrated heterogeneity (I^2=70.0%, P=0.010). However, using a

Table 1 Characteristics of studies included in the meta-analysis

First Author	Publication Year	Region	Country	Follow-up (Months)	Analysis Mode	NLR Cutoff	PLR Cutoff	Sample Size	Age (Years)	Outcome Endpoint
Sakin et al. [10]	2019	Asia	Turkey	Median 6 (1–33)	MV + UV	3.00	150.0	113	Median 61 (35–81)	OS
Pan et al. [11]	2019	Asia	China	NA	UV	3.80	NG	73	Mean 61.64 (39–83)	OS, KM, PFSKM
Suzuki et al. [18]	2018	North America	America	NA	MV + UV	4.00	194.7	252	Median 63 (56–69)	OS
Suzuki et al. [19]	2018	North America	America	NA	MV + UV	2.90	140.1	122	Median 65 (60–72)	OS
Wen et al. [21]	2017	Asia	China	Median 35.1	MV	4.00	NG	452	Median 56 (27–82)	OS, PFS
Käsmann et al. [16]	2017	Europe	Germany	NA	MV	4.00	180.0	65	NG	OS
Cao et al. [15]	2016	Asia	China	NA	MV	3.18	176.5	707	Mean 56.24 (23–75)	OS
Shao et al. [17]	2015	Asia	China	Median 68.5	MV	4.15	150.0	112	Median 62 (45–82)	OS, PFS
Xie et al. [12]	2015	North America	America	Median 10.8	MV	5.00	210.0	938	Median 68 (27–91)	OS
Kang et al. [9]	2014	Asia	Korea	Median 40.28 (2.60–89.20)	MV	4.00	160.0	187	Median 68 (43–84)	OS, PFS
Wang et al. [20]	2014	Asia	China	NA	MV	3.00	150.0	613	Mean 59.31	OS

NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; OS: Overall survival; PFS: Progression-free survival; NA: Not available; UV: Univariate; MV: Multivariate; KM: Extracting data by calculating Kaplan-Meier curves

random-effects model to combine effect sizes, no statistically significant difference in OS was found between the high and low PLR groups (HR = 1.13, 95%CI: 0.84–1.43, $P = 0.265$) (Fig. 4).

Meta-analysis of subgroup analysis

Subgroup analysis was conducted based on the NLR cutoff values, disease stage, pathology type, race, and analysis mode of the included studies. The results indicated that the OS in high NLR group was significantly lower than the low NLR group across different strata, including limited-stage SCLC (LS-SCLC) (HR = 1.56, 95%CI: 1.15–2.16, $P < 0.001$), extensive-stage SCLC (ES-SCLC) (HR = 1.51, 95%CI: 1.21–1.73, $P < 0.001$), pure SCLC (P-SCLC) (HR = 1.41, 95%CI: 1.20–1.69, $P < 0.001$), combined SCLC (C-SCLC) (HR = 1.46, 95%CI: 1.23–1.66, $P < 0.01$), Asian population (HR = 1.39, 95%CI: 1.13–1.81, $P < 0.001$), Non-Asian population (HR = 1.43, 95%CI: 1.32–1.61, $P < 0.001$), and NLR cutoff value ≥ 4 (HR = 1.47, 95%CI: 1.31–1.63, $P < 0.001$) (Table 3).

A further subgroup analysis based on the PLR cutoff values and disease stages in the included studies indicated that OS in the high PLR group was significantly lower than the low PLR group among LS-SCLC patients (HR = 1.63, 95%CI: 1.26–2.12, $P < 0.001$) and in populations with a PLR cutoff value < 160 (HR = 1.76, 95%CI: 1.26–2.21, $P < 0.001$) (Table 3).

Sensitivity analysis

Given the significant variability observed among the studies included in the meta-analysis, a sensitivity analysis was performed to assess the robustness and reliability of the aggregated findings. This analysis involved systematically excluding each study individually and recalculating the combined effect estimates based on the remaining studies. The results of the sensitivity analysis showed that the overall findings remained consistent and stable even after excluding any individual study. This suggests that no single study exerted undue influence on the overall outcomes, thereby contributing to the robustness of our findings. The consistency observed across these analyses further supports the reliability of the main conclusions derived from this meta-analysis (Fig. 5).

Publication bias

The funnel plots generated from the observed study data exhibited a symmetrical distribution, indicating the absence of substantial publication bias, as evidenced by the lack of significant asymmetry (Fig. 6). To further evaluate publication bias, Egger's linear regression test was conducted across the meta-analyses for various variables. The results revealed no statistically significant publication bias ($P > 0.05$ for all variables). These findings provide additional evidence supporting the reliability and validity of the meta-analysis results.

Discussion

The tumor microenvironment, consisting of vasculature, extracellular matrix, and inflammatory cells, plays a crucial role in cancer progression [23, 24]. Inflammatory markers such as the NLR and PLR have been linked to cancer prognosis, including in SCLC. Elevated NLR and PLR reflect an inflammatory response that may promote tumor growth and metastasis by modulating immune cells and vascular signaling within the tumor microenvironment [25, 26]. This meta-analysis aims to systematically evaluate the prognostic significance of NLR and PLR in SCLC patients undergoing first-line platinum-based

Table 2 The quality assessment according to Newcastle-Ottawa scale

Study	Selection				Comparability	Outcome			Total score
	Representativ-eness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough	Adequacy of follow up of cohorts	
Sakin et al. [10]	★	★	★	★	★★	★	★	★	9
Pan et al. [11]		★	★	★	★★	★	★	★	8
Suzuki et al. [18]	★	★	★	★	★★	★	★	★	9
Suzuki et al. [19]	★	★	★	★	★★	★		★	8
Wen et al. [21]	★		★	★	★★		★	★	7
Käsmann et al. [16]	★	★	★	★	★	★	★	★	8
Cao et al. [15]	★	★	★	★	★★	★	★	★	9
Shao et al. [17]	★		★	★	★	★	★	★	7
Xie et al. [12]	★	★	★	★	★★	★	★	★	9
Kang et al. [9]	★	★	★	★	★	★	★	★	8
Wang et al. [20]		★	★	★	★★	★	★	★	8

★: each individual asterisk ('★') signifies one point

chemotherapy. By consolidating existing data, we seek to provide a more reliable assessment of these biomarkers' role in predicting survival outcomes, offering clinicians valuable insights for prognosis and treatment decision-making in SCLC management [27, 28]. This meta-analysis provides a comprehensive evaluation of the prognostic value of NLR and PLR in SCLC patients undergoing first-line platinum-based chemotherapy. The novel contribution of this study lies in its systematic assessment of both NLR and PLR across a large cohort of 3,634 patients, revealing that high NLR is significantly associated with poorer OS and PFS, while PLR showed no significant association with OS. The findings highlight the potential utility of NLR as a simple, cost-effective prognostic biomarker in clinical practice, offering valuable insights into patient outcomes.

In this study, we analyzed data from 11 studies involving a total of 3,634 SCLC patients receiving first-line platinum-based chemotherapy, focusing on the prognostic value of NLR and PLR. Previous research, such as that by Yang et al. [29], has highlighted the potential prognostic significance of NLR and PLR in lung cancer, though their study did not specifically link these markers with treatment outcomes. Our findings suggest that elevated NLR is associated with poorer OS and PFS, which is consistent with prior research. However, high PLR did not show a statistically significant association with OS, in line with some earlier studies. Subgroup analyses indicated that high NLR values were particularly associated with worse OS in certain patient groups, including those with LS-SCLC, C-SCLC, non-Asian populations, and in studies using a univariate analysis model. In the LS-SCLC group, high PLR was also associated with worse OS, though this

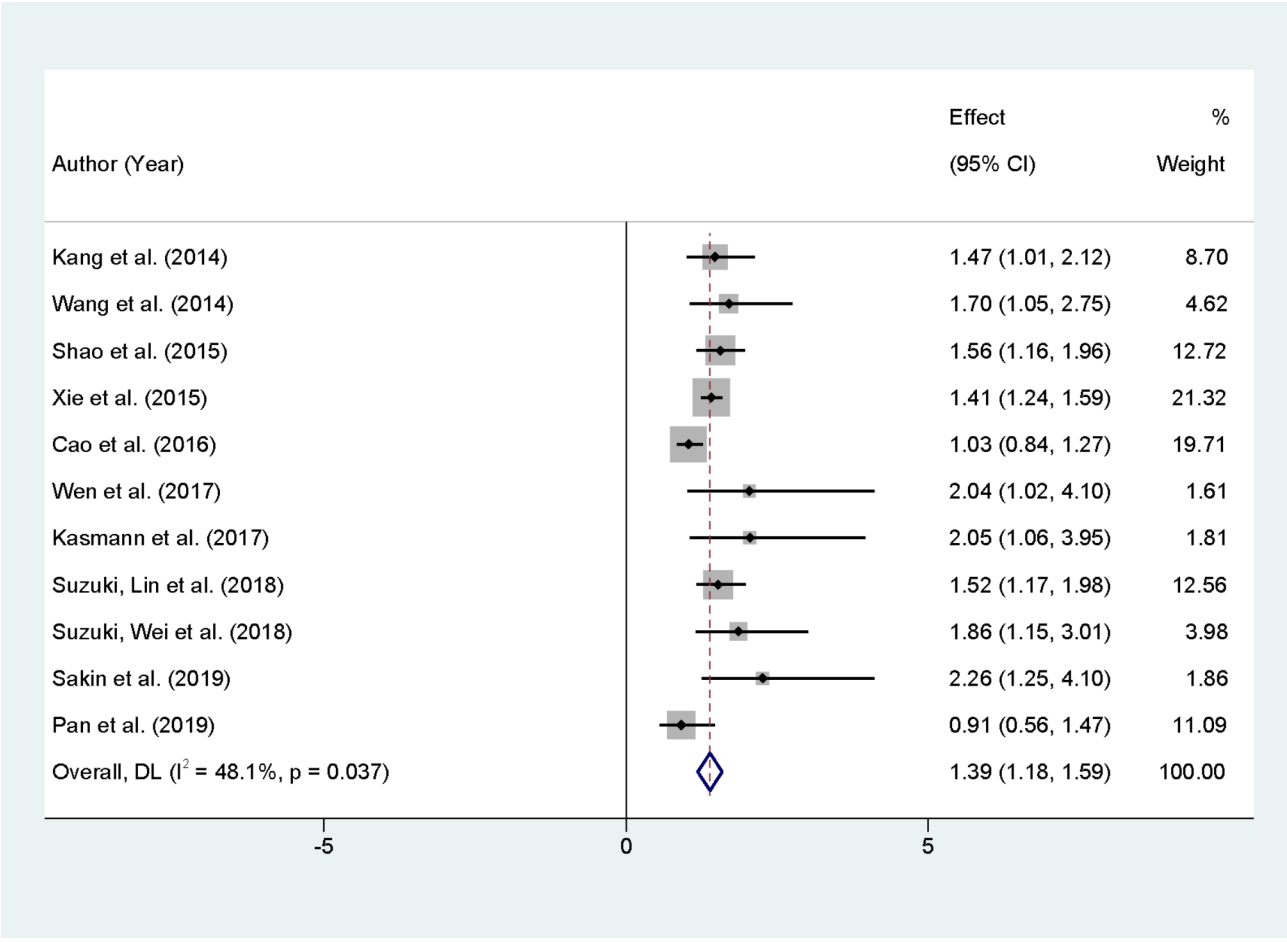

Fig. 2 Forest plots of the effect of NLR on OS in SCLC patients received platinum-based first-line chemotherapy

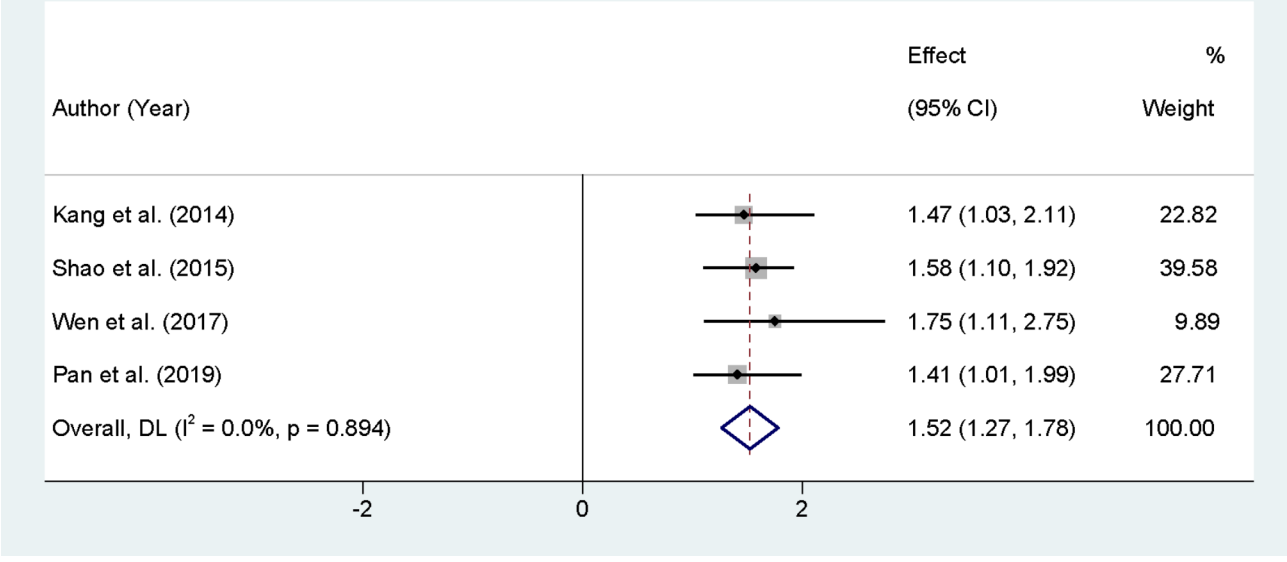

Fig. 3 Forest plots of the effect of NLR on PFS in SCLC patients received platinum-based first-line chemotherapy

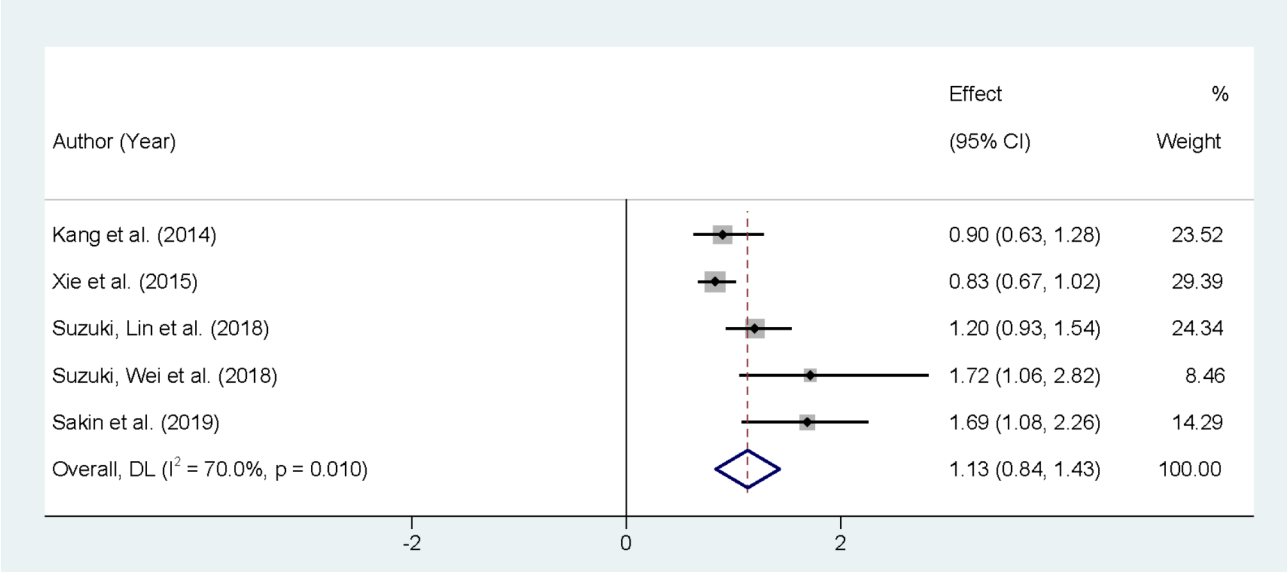

Fig. 4 Forest plot of the effect of PLR on OS in SCLC patients received platinum-based first-line chemotherapy

Table 3 Meta-analysis of subgroup analysis

Indicator	Number of included studies	I^2(%)	The model of meta-analysis	HR (95%CI)	*P*Value
NLR on OS in SCLC patients					
LS-SCLC	4	66.2	R	1.56 (1.15–2.16)	< 0.001
ES-SCLC	3	16.8	F	1.51 (1.21–1.73)	< 0.001
P-SCLC	9	56.6	R	1.41 (1.20–1.69)	< 0.001
C-SCLC	2	0	F	1.46 (1.23–1.66)	< 0.001
Asia	7	61.8	R	1.39 (1.13–1.81)	< 0.001
Non-Asia	4	0	R	1.43 (1.32–1.61)	< 0.001
NLR cutoff value ≥ 4	6	47.8	F	1.47 (1.31–1.63)	< 0.001
NLR cutoff value < 4	5	71.1	R	1.39 (0.99–1.97)	0.065
PLR on OS in SCLC patients					
LS-SCLC	2	0	F	1.63 (1.26–2.12)	0.091
ES-SCLC	3	81.1	R	1.16 (0.79–1.71)	0.361
PLR cutoff value ≥ 160	3	56.1	R	0.95 (0.76–1.22)	0.551
PLR cutoff value < 160	2	5	7	1.76 (1.26–2.21)	< 0.001

NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; LS-SCLC: limited-stage small-cell lung cancer; ES-SCLC: extensive-stage small-cell lung cancer, R: random-effects model; F: fixed-effects model; P-SCLC: pure- small-cell lung cancer; C-SCLC: combined small-cell lung cancer;

finding was not consistent across all subgroups. While these findings contribute to the growing body of study on prognostic markers in SCLC, it is important to note that these markers should be viewed as additional tools for prognostication rather than definitive guides for treatment decisions. They may help identify patients at higher risk of poor outcomes, potentially aiding in the identification of those who could benefit from closer monitoring or more aggressive treatment approaches [10].

Our analysis indicates significant heterogeneity among the included studies, as reflected in the *P*-value and I^2 statistics. To explore the source of this heterogeneity, we conducted a subgroup analysis, which suggested that elevated PLR is associated with poorer OS in the LS-SCLC population and in groups with a PLR cutoff < 160. However, in studies using a PLR cutoff ≥ 160, no significant association was observed between elevated PLR and OS. This variation in cutoff values across studies appears to be a key factor contributing to the observed heterogeneity. To assess the robustness of our findings, we performed sensitivity analyses, which examine the influence of individual studies on the overall results. The consistency of our primary outcomes, even when any single study was excluded, suggests that no individual study disproportionately affected the aggregate results. This reinforces the reliability of our findings across different study conditions, although the possibility of residual bias cannot be completely ruled out. We also addressed potential concerns about publication bias using funnel plots and Egger's regression test. The symmetrical distribution of

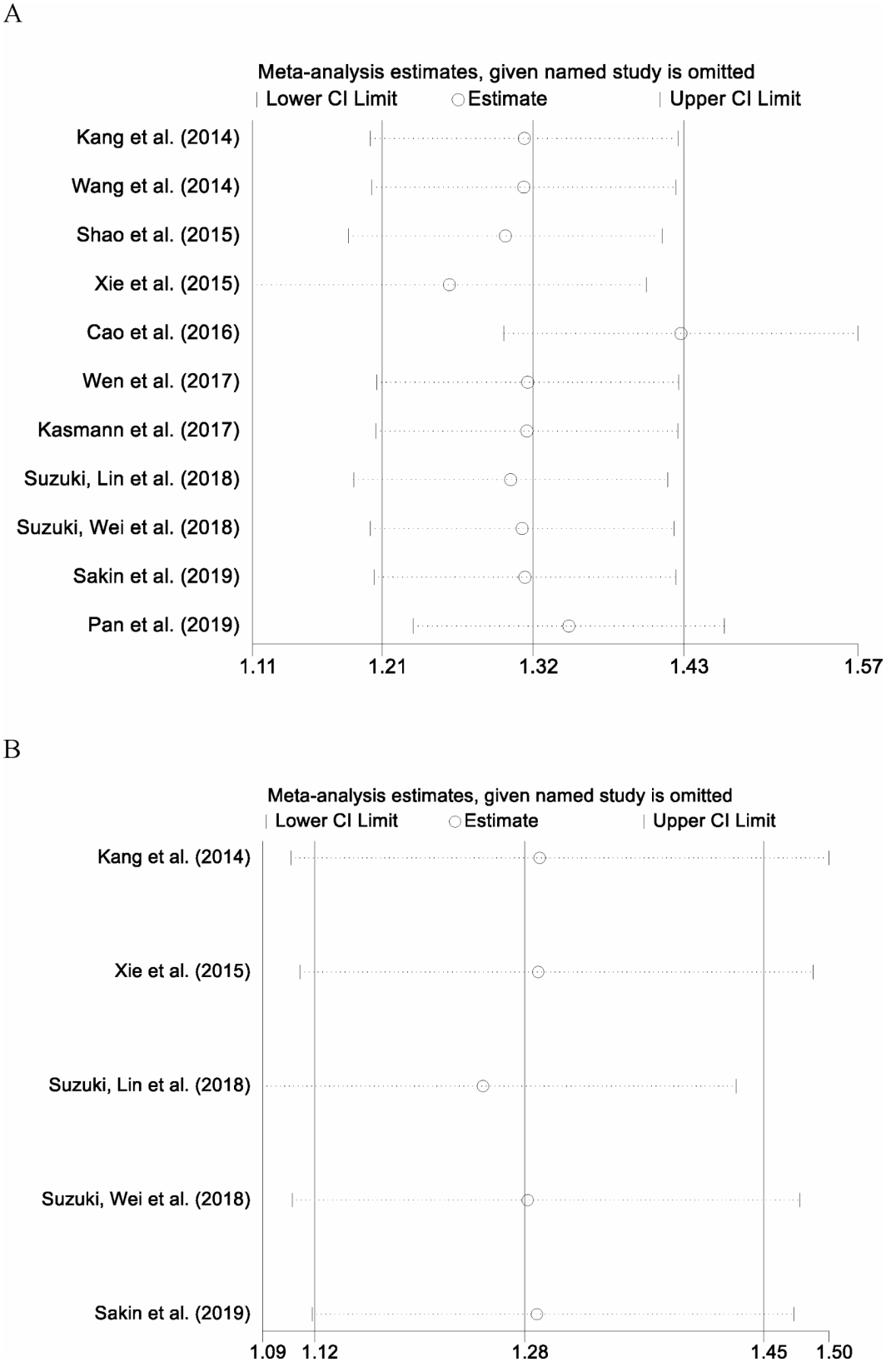

Fig. 5 Sensitivity analysis of the effect of NLR on OS (**A**) and the effect of PLR on OS (**B**)

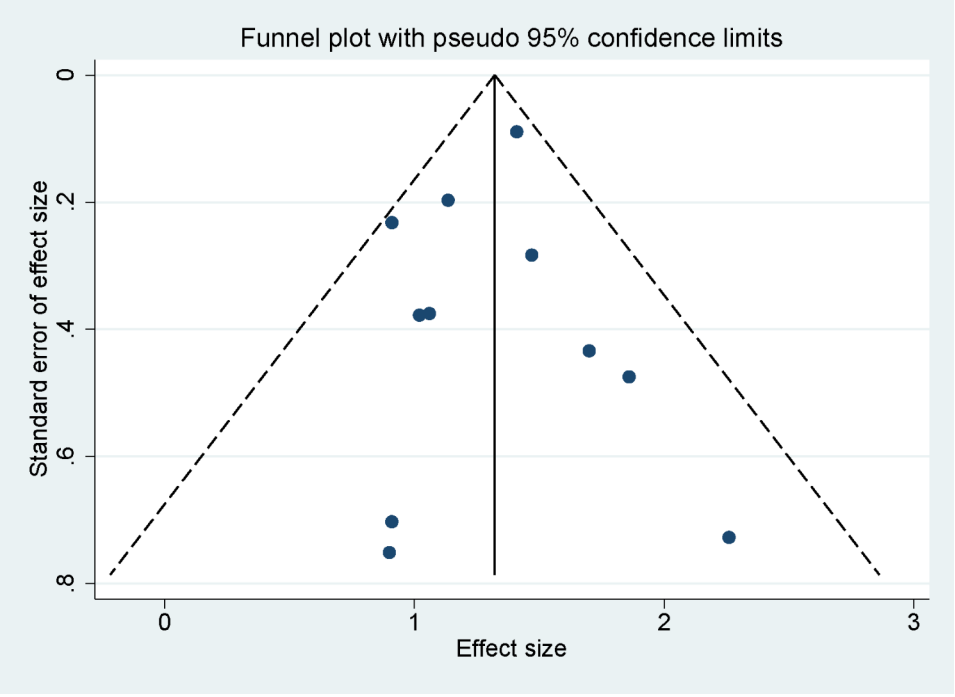

Fig. 6 Funnel plot for publication bias in all included studies

the funnel plots and the absence of significant publication bias in Egger's test further support the validity of our results, suggesting that the observed findings are likely a reliable reflection of the broader body of research on this topic. Sensitivity analysis and evaluation of publication bias provide additional confidence in the reliability of our findings. However, it is important to emphasize that the observed associations between NLR, PLR, and survival outcomes in SCLC patients receiving first-line platinum-based chemotherapy should be interpreted with caution. Further validation through larger-scale, prospective studies is needed to better establish the clinical applicability and real-world utility of these prognostic markers.

This study has several limitations that should be considered when interpreting the findings. First, our analysis focused specifically on patients with SCLC undergoing first-line platinum-based chemotherapy. As such, the results are specific to this patient group and may not be directly applicable to other types of lung cancer or patients receiving alternative treatments. Second, the majority of the included studies were retrospective in design, which inherently introduces potential biases, including selection and reporting biases. Although we attempted to mitigate these risks through a rigorous quality assessment process, the retrospective nature of the studies limits the ability to draw definitive causal conclusions. Lastly, there was notable variability in the cutoff values for NLR and PLR across the included studies, which likely contributed to the observed heterogeneity in the results. To enhance the precision and comparability of future analyses, it would be beneficial to standardize these cutoff values across studies.

Conclusions

In conclusion, our meta-analysis suggests that a high NLR is associated with poorer OS and PFS in patients with SCLC undergoing first-line platinum-based chemotherapy. However, PLR did not show a statistically significant association with OS in this cohort. While our study contributes to the existing body of research on the prognostic value of NLR and PLR in SCLC, it is important to emphasize that NLR is a prognostic marker of survival rather than a predictive marker of treatment efficacy. The retrospective nature of the analysis, along with variability in NLR and PLR cutoff values across studies, limits the ability to draw definitive clinical conclusions. Further prospective studies with standardized cutoff values are needed to validate these findings and explore their potential prognostic implications.

Acknowledgements
None.

Author contributions
ZYS contributed to the conception of the study; WYS contributed significantly to literature search, data extraction, quality assessment, data analyses and manuscript preparation; JYQ contributed improving the article for language and style and protocol preparation; YJD helped perform the analysis with constructive discussions; ZYF revised the manuscript and approved the final version.

Funding
None.

Data availability
The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 18 April 2024 / Accepted: 10 December 2024
Published online: 22 December 2024

References

1. Paz-Ares L, Dvorkin M, Chen Y, Reinmuth N, Hotta K, Trukhin D, Statsenko G, Hochmair MJ, Özgüroğlu M, Ji JH, et al. Durvalumab plus platinum-etoposide versus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): a randomised, controlled, open-label, phase 3 trial. Lancet. 2019;394(10212):1929–39.
2. Käsmann L, Abdo R, Eze C, Dantes M, Taugner J, Gennen K, Roengvoraphoj O, Rades D, Belka C, Manapov F. External validation of a survival score for limited-stage small cell lung cancer patients treated with chemoradiotherapy. Lung. 2020;198(1):201–6.
3. Liu Q, Zhang Y, Liu M, Xu R, Yi F, Wei Y, Zhu S, Zhang W. The benefits and risks of pembrolizumab in combination with chemotherapy as first-line therapy in small-cell lung cancer: a single-arm meta-analysis of noncomparative clinical studies and randomized control trials. World J Surg Oncol. 2021;19(1):298.
4. Zhou K, Zhou J, Huang J, Zhang N, Bai L, Yang Y, Li Q. Cost-effectiveness analysis of atezolizumab plus chemotherapy in the first-line treatment of extensive-stage small-cell lung cancer. Lung Cancer. 2019;130:1–4.
5. Shen XB, Wang Y, Shan BJ, Lin L, Hao L, Liu Y, Wang W, Pan YY. Prognostic significance of platelet-to-lymphocyte ratio (PLR) and mean platelet volume (MPV) during etoposide-based first-line treatment in small cell lung cancer patients. Cancer Manag Res. 2019;11:8965–75.
6. Deng M, Ma X, Liang X, Zhu C, Wang M. Are pretreatment neutrophil-lymphocyte ratio and platelet-lymphocyte ratio useful in predicting the outcomes of patients with small-cell lung cancer? Oncotarget. 2017;8(23):37200–7.
7. Sacdalan DB, Lucero JA, Sacdalan DL. Prognostic utility of baseline neutrophil-to-lymphocyte ratio in patients receiving immune checkpoint inhibitors: a review and meta-analysis. Onco Targets Ther. 2018;11:955–65.
8. Li Y, Zhang Z, Hu Y, Yan X, Song Q, Wang G, Chen R, Jiao S, Wang J. Pretreatment neutrophil-to-lymphocyte ratio (NLR) may predict the outcomes of advanced non-small-cell lung cancer (NSCLC) patients treated with immune checkpoint inhibitors (ICIs). Front Oncol. 2020;10:654.
9. Kang MH, Go SI, Song HN, Lee A, Kim SH, Kang JH, Jeong BK, Kang KM, Ling H, Lee GW. The prognostic impact of the neutrophil-to-lymphocyte ratio in patients with small-cell lung cancer. Br J Cancer. 2014;111(3):452–60.
10. Sakin A, Sahin S, Yasar N, Demir C, Arici S, Geredeli C, Cihan S. The relation between hemogram parameters and survival in extensive-stage small cell lung cancer. Oncol Res Treat. 2019;42(10):506–15.
11. Pan Z, Zhang L, Liu C, Huang X, Shen S, Lin X, Shi C. Cisplatin or carboplatin? Neutrophil to lymphocyte ratio may serve as a useful factor in small cell lung cancer therapy selection. Oncol Lett. 2019;18(2):1513–20.
12. Xie D, Marks R, Zhang M, Jiang G, Jatoi A, Garces YI, Mansfield A, Molina J, Yang P. Nomograms predict overall survival for patients with small-cell lung cancer incorporating pretreatment peripheral blood markers. J Thorac Oncol. 2015;10(8):1213–20.
13. Winther-Larsen A, Aggerholm-Pedersen N, Sandfeld-Paulsen B. Inflammation scores as prognostic biomarkers in small cell lung cancer: a systematic review and meta-analysis. Syst Rev. 2021;10(1):40.
14. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
15. Wells G. The Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomised studies in meta-analyses. In: *Symposium on Systematic Reviews: Beyond the Basics: 2014*; 2014.
16. Cao S, Jin S, Shen J, Cao J, Zhang H, Meng Q, Wang C, Zhang A, Zhang P, Yu Y. Selected patients can benefit more from the management of etoposide and platinum-based chemotherapy and thoracic irradiation-a retrospective analysis of 707 small cell lung cancer patients. Oncotarget. 2017;8(5):8657–69.
17. Käsmann L, Bolm L, Schild SE, Janssen S, Rades D. Neutrophil-to-lymphocyte ratio predicts outcome in limited disease small-cell lung cancer. Lung. 2017;195(2):217–24.
18. Shao N, Cai Q. High pretreatment neutrophil-lymphocyte ratio predicts recurrence and poor prognosis for combined small cell lung cancer. Clin Transl Oncol. 2015;17(10):772–8.
19. Suzuki R, Lin SH, Wei X, Allen PK, Welsh JW, Byers LA, Komaki R. Prognostic significance of pretreatment total lymphocyte count and neutrophil-to-lymphocyte ratio in extensive-stage small-cell lung cancer. Radiother Oncol. 2018;126(3):499–505.
20. Suzuki R, Wei X, Allen PK, Cox JD, Komaki R, Lin SH. Prognostic significance of total lymphocyte count, neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio in limited-stage small-cell lung cancer. Clin Lung Cancer. 2019;20(2):117–23.
21. Wang X, Jiang R, Li K. Prognostic significance of pretreatment laboratory parameters in combined small-cell lung cancer. Cell Biochem Biophys. 2014;69(3):633–40.
22. Wen Q, Meng X, Xie P, Wang S, Sun X, Yu J. Evaluation of factors associated with platinum-sensitivity status and survival in limited-stage small cell lung cancer patients treated with chemoradiotherapy. Oncotarget. 2017;8(46):81405–18.
23. Wu Y, Li C, Zhao J, Yang L, Liu F, Zheng H, Wang Z, Xu Y. Neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios predict chemotherapy outcomes and prognosis in patients with colorectal cancer and synchronous liver metastasis. World J Surg Oncol. 2016;14(1):289.
24. Lucca I, Jichlinski P, Shariat SF, Rouprêt M, Rieken M, Kluth LA, Rink M, Mathieu R, Mbeutcha A, Maj-Hes A, et al. The neutrophil-to-lymphocyte ratio as a prognostic factor for patients with urothelial carcinoma of the bladder following radical cystectomy: validation and meta-analysis. Eur Urol Focus. 2016;2(1):79–85.
25. Rotondo R, Bertolotto M, Barisione G, Astigiano S, Mandruzzato S, Ottonello L, Dallegri F, Bronte V, Ferrini S, Barbieri O. Exocytosis of azurophil and arginase 1-containing granules by activated polymorphonuclear neutrophils is required to inhibit T lymphocyte proliferation. J Leukoc Biol. 2011;89(5):721–7.
26. Jacobsen LC, Theilgaard-Mönch K, Christensen EI, Borregaard N. Arginase 1 is expressed in myelocytes/metamyelocytes and localized in gelatinase granules of human neutrophils. Blood. 2007;109(7):3084–7.
27. Nieswandt B, Hafner M, Echtenacher B, Männel DN. Lysis of tumor cells by natural killer cells in mice is impeded by platelets. Cancer Res. 1999;59(6):1295–300.
28. Placke T, Kopp HG, Salih HR. Modulation of natural killer cell anti-tumor reactivity by platelets. J Innate Immun. 2011;3(4):374–82.
29. Yang HB, Xing M, Ma LN, Feng LX, Yu Z. Prognostic significance of neutrophil-lymphocyteratio/platelet-lymphocyteratioin lung cancers: a meta-analysis. Oncotarget. 2016;7(47):76769–78.

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.