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REVIEW

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Systematic review and metanalysis of neutrophil to lymphocyte ratio and prognosis in patients with nasopharyngeal carcinoma

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Abstract

Background: Hematological parameters have been associated with prognosis in patients with nasopharyngeal carcinoma (NPC). The present meta-analysis investigated the utility of neutrophil-lymphocyte ratio (NLR) in the prognosis of patients with NPC.

Methods: Multiple electronic databases, including PubMed, Embase, the Cochrane Library, and the Web of Science, were systematically searched for studies assessing the association between NLR and NPC from 2011 to 2021. The primary outcomes were overall survival (OS) and progression-free survival (PFS). Pooled hazard ratios (HRs) and 95% confidence intervals (CIs) were utilized to estimate effect size. Use of a fixed effect or random effect model was based on heterogeneity stability was tested by sensitivity analysis, and the risk of bias was assessed by funnel plots. Random effects models were used based on the actual results. Because the NLR grouping criteria for the included studies differed, subgroup analyses were performed.

Results: A search of the electronic databases identified 14 studies, encompassing 6693 patients, that met the selection criteria. NLR higher than the cutoff value was significantly associated with poorer OS [HR 1.760, 95% CI 1.470–2.120, p <0.00001] and PFS [HR 1.850, 95% CI 1.430–2.390, $p = .006$]. Sensitivity analysis showed that the results of the meta-analysis were relatively stable, and funnel plots were used to exclude the risk of bias.

Conclusions: Elevated pretreatment NLR in peripheral blood is predictive of poorer OS and PFS in patients with NPC. NLR is an easily measured and important prognostic factor in patients with NPC.

KEYWORDS

meta-analysis, nasopharyngeal carcinoma, neutrophil-to-lymphocyte ratio, overall survival, prognosis

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1 | INTRODUCTION

Nasopharyngeal carcinoma (NPC) is an epithelial carcinoma arising from the nasopharyngeal mucosal lining. Tumors in the nasopharynx are often observed at the pharyngeal recess (fossa of Rosenmüller).[1,2] Epidemiologically, individuals in certain regions, races, ethnic groups, and other parts of the population are particularly susceptible to NPC, as are certain familial aggregates, suggesting a genetic component. Due to its hidden location in the nasopharynx, early NPC is frequently asymptomatic. Pathologically, the tumors involve lymphatic pathways and are prone to local lymph nodes and distant metastases. In 2005, the World Health Organization (WHO) pathologically classified NPCs into type I, consisting of keratinizing squamous cell carcinomas, and type II, consisting of non-keratinizing carcinomas, with the latter subdivided into differentiated and undifferentiated carcinomas.

At present, the main treatment of NPC consists of a combination of radiotherapy and chemotherapy.[3] The 5-year survival rate of patients with early NPC is >90%, whereas the 5-year survival rate of patients with middle and late NPC is only 34%–60%, indicating a need for improvements in the early diagnosis and treatment of NPC. TNM staging is determined by the anatomical structure of the tumor, which does not fully reflect its biological heterogeneity. Thus, the prognosis of patients with the same TNM stage can differ markedly. More accurate, effective, and convenient indicators are needed to predict the prognosis of patients with NPC.

Tumor prognosis is not only associated with the biological characteristics of a tumor but it is also associated with the immune-inflammatory response of the host.[4] Chronic persistent inflammation in the tumor microenvironment can promote tumor growth through a variety of mechanisms, including (1) the promotion cell proliferation, survival, and epithelial-mesenchymal transition; (2) the promotion of angiogenesis and lymphangiogenesis; (3) the promotion of the migration, infiltration, and metastasis of tumor cells; (4) the destruction of anti-tumor adaptive immune responses; and (5) the alteration in the reactivity of malignant cells to hormones and chemotherapeutic drugs.[5,6] Several hematological parameters, including white blood cell, platelet count, and monocyte counts, along with the neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), and platelet-to-lymphocyte ratio (PLR), were shown to be independent factors prognostic of survival in patients with non-small cell lung cancer, gastric cancer, and breast cancer.[7–15] Several studies have evaluated the relationship between NLR and the prognosis of patients with NPC, but the results have been inconsistent.[16–22] The present study was designed to resolve any inconsistency and quantify the effect of NLR on the prognosis of patients with NPC.

2 | MATERIALS AND METHODS

2.1 | Search strategy

This study was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[23] Four electronic databases, PubMed, Embase, the Cochrane Library, and the Web of Science, were searched electronically for studies evaluating the relationship between NLR and NPC. Key search terms included "nasopharyngeal neoplasms," "NPC," "nasopharyngeal diseases," "nasopharynx," "nasophar*," "rhinophar*," "naso phar*," "chonae, "NLR," "neutrophil-to-lymphocyte ratio," and "neutrophil/lymphocyte ratio." The references of retrieved articles were manually searched to identify other relevant studies in retrieved articles. Because all analyses were based on data from previous studies, the present study does not require ethical permission or informed consent.

2.2 | Research selection

Studies were included if they: (1) evaluated patients with nonmetastatic NPC; (2) assessed the effects of pretreatment NLR on the prognosis of patients with NPC; (3) reported treatment outcomes that included overall survival (OS) or progression-free survival (PFS); (4) reported hazard ratios (HRs) and their associated 95% confidence intervals (CIs); and (5) were clinical trials, cohort studies, and case–control studies.

Studies were excluded if they: (1) were non-human or studies published in a language other than English; (2) were duplicate studies; (3) were case reports, meeting proceedings, letters, reviews/meta-analyses, or laboratory studies; or (4) lacked of extractable data.[24–27] Two authors independently evaluated the results of the electronic search, with any differences of opinion resolved by consensus.

2.3 | Information extraction

Data recorded on a standard form for each study included: year of publication; name of the first author; country in which the study was performed; disease stage; research design; number, gender, and ages of patients; treatment; survival outcomes; duration of follow-up; methods of statistical analysis; NLR cutoff value, HR and CI. Two reviewers independently assessed the quality of non-randomized studies based on the Newcastle-Ottawa Quality Assessment Scale (NOS).[28] NOS scores were rated from 0 through 9 points, with studies having a NOS score >6 considered high-quality studies. (Table 1).

2.4 | Statistical analysis

The effects of NLR on OS and PFS were assessed using the pooled HRs and corresponding 95% CIs, which were obtained directly from each included study. Heterogeneity was evaluated using the Cochrane Q test and I^2 statistics. If heterogeneity was significant ($p < .05$ and $I^2 > 50\%$), the results were analyzed using a random effects model; otherwise, the results were analyzed using a fixed effects model. Sensitivity analyses were performed by excluding one study and recalculating the pooled HR. Publication bias was assessed using funnel plots. p-values <.05 were considered

TABLE 1 Newcastle-Ottawa quality assessment scale of the included studies.

Studies included	Selection	Comparability	Outcome	Score
AKÇAY (2019)	★★★★	★★	★	7
Chua (2016)	★★★★	★★	★	7
He (2012)	★★★★	★★	★★★	9
Jiang (2018)	★★★★	★★	★★	8
Li (2021)	★★★★	★★	★★	8
Liao (2018)	★★★★	★★	★	7
Liu (2020)	★★★★	★★	★	7
Lu (2017)	★★★★	★★	★★★	9
Setakornnuku (2021)	★★★★	★★	★★★	9
Song (2021)	★★★★	★★	★★	8
Sun (2016)	★★★★	★★	★★	8
Wang (2021)	★★★★	★★	★★	8
Yao (2019)	★★★★	★★	★★	8
Ye (2018)	★★★★	★★	★	7

Note: Newcastle-Ottawa Scale (NOS) is a commonly used quality assessment tool for case–control studies and cohort studies. It evaluates the quality of included studies through three modules with a total of eight items. Specifically, it includes population selection, comparability, exposure/outcome evaluation. NOS uses the semi-quantification principle of star system to evaluate literature quality. The full score is 9 stars. The higher the score, the higher the research quality.

statistically significant. Forest plots and funnel plots were drawn using RevMan5.4 software.

3 | RESULTS

3.1 | Review of electronic databases

Searches of the PubMed, Embase, Cochrane Library, and Web of Science databases identified 303 studies records. A review of their titles and abstracts to exclude duplicate studies, review articles, meta-analyses, and articles written in languages other than English identified 33 studies. A further examination of their full texts based on the inclusion and exclusion criteria identified 14 studies, which included a total of 6693 patients (Figure 1).

3.2 | Characteristics of the included studies

Table 2 shows the characteristics of the 14 included studies.[21,29–41] All were performed between 2012 and 2021, with study populations ranging in size from 62 to 1550 patients. Geographically, most of the studies were from China,[29–34,36–39,41] whereas the other three were from Thailand,[21] Singapore,[35] and Turkey.[40] Therefore, most of the included patients belonged to the Chinese ethnic group. The disease stages ranged from stage I to stage IV, and almost all patients were treated with intensity-modulated radiotherapy (IMRT). All 14 studies reported OS,[21,29–41] and nine reported PFS.[30,32–34,36–39,41] In most studies, NLR cut-offs were determined using receive operating characteristic (ROC) curves.

3.3 | Overall survival

3.3.1 | Heterogeneity test

The combined results of the 14 studies, involving 6693 patients, which assessed the ability of NLR to predict OS in patients with NPC, found that elevated NLR was significantly associated with poor prognosis (HR: 1.76, 95% CI: 1.47–2.12). $p < .00001$. $I^2 = 73\%$. Because I^2 was >50% and the p-value of the Q test was 0.00001, the heterogeneity among the 14 included studies was statistically significant and a random-effects model was used for analysis. The heterogeneity among included studies was likely due to their regional differences (Figure 2A).

3.3.2 | Sensitivity analysis

Stability was tested by sensitivity analyses, with these results compared with the original effect size by eliminating each study individually to explore its impact on the pooled effect variable. The present meta-analysis was stable, as the HR of the pooled studies did not change significantly after successive removal of individual studies (Figure 2B).

3.3.3 | Publication bias

The funnel plot in Figure 2B showed no obvious asymmetry, indicating a lack of publication bias.

3.3.4 | Subgroup analysis

Due to the significant heterogeneity among studies, subgroup analyses were performed to evaluate the prognostic value of NLR in patients with NPC. Based on differences in their NLR cut-off values, the studies were divided into two groups, those with the NLR cut-offs <3 and ≥3. The heterogeneity between these two groups was high ($I^2 = 75\%$, $p < .1$), indicating that the NLR cut-off value would greatly affect the results of the meta-analysis. The heterogeneity among studies with NLR cut-off values ≥3 was also high ($I^2 = 71\%$, $p = .009$). The HR reached 1.43 and was significant ($Z = 2.86$, $p = .004$) when the effect size was pooled by the random effect model, indicating that an NLR cut-off ≥3 was associated with poor OS. In contrast, the heterogeneity among studies with NLR cut-off <3 groups were slight ($I^2 = 26\%$, $p = 0.21$), enabling the use of a fixed effects model to combine the effect size (HR: 2.00, 95% CI: 1.76–2.27). Finally, the inter-group heterogeneity was high, reaching 75%, indicating that

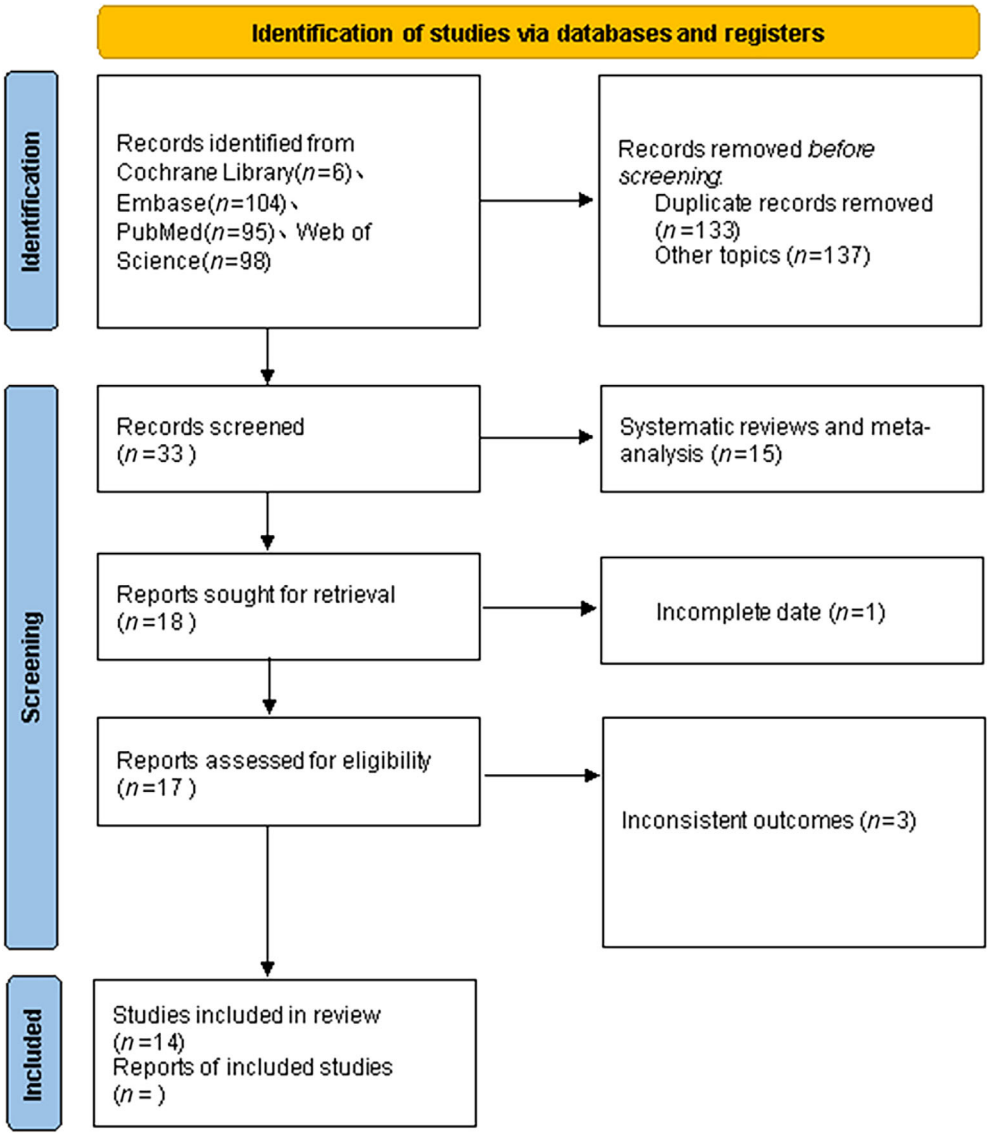

FIGURE 1 Flow diagram of study selection.

NLR cut-off values had a significant effect on OS, with NLR cut-off values being more closely related with poor OS (Figure 3A).

Although NLR cutoff values were associated with OS HRs, the magnitude of this association was very small and unlikely to affect the interpretation of these results, especially because the NLR cutoff values in the included studies fell within a relatively narrow range. Similarly, the 14 included studies were divided into those that evaluated ≥300 and < 300 patients. Heterogeneity between these groups was high ($I^2 = 73\%$, $p < .00001$). Because the intra-group heterogeneity was also high in both groups, a random effects model was used for analyses. These results suggested that the number of patients per study was not one of the sources of heterogeneity. (Figure 3B) According to the research methodology, the subgroups were divided into those in which variables were compared by univariate and multivariate analysis. These intra-group and inter-group differences were large, indicating that the research method was not the main cause of study heterogeneity (Figure 3C).

The 14 studies were also divided into those that assessed Chinese and non-Chinese patients. There was strong heterogeneity between these two groups ($I^2 = 73\%$, $p < .00001$), suggesting that nationality/ethnicity may be the main source of the pooled effect size heterogeneity of the meta-analysis results. There was no heterogeneity within the Chinese group ($I^2 = 0$, $p = .52$), with the 11 studies performed in China having a combined HR of 1.94 and statistical significance ($Z = 12.17$, $p < .00001$). Because there was little heterogeneity within the three studies of non-Chinese patients (HR: 1.21, 95% CI: 1.08–1.35). These findings, indicating that the difference in nationality was the main cause of heterogeneity, suggested that the influence of regional differences on the pooled effect size of the meta-analysis should be considered when determining the inclusion and exclusion criteria (Figure 3D).

3.4 | Progression-free survival

Of the 14 studies, nine, including 4658 patients, reported HRs for PFS. Figure 4A shows these forest plots. All studies showed statistically significant HR, with an overall HR of 1.85 for

TABLE 2 Characteristics of the included studies.

Author (year)	Country	Patients (*n*) (M/F)	Median age (years)	Stage	NLR	HR (OS) (95% CI)	Treatment	HR (PFS) (95% CI)	Median follow-up time (months)
Wang (2021)	China	923 (672/251)	49.3 ± 11.5	I, II, III, IV AJCC 8th	>3 ≤3	2.36 (1.56–3.56)			28.3 ± 16.3
Li (2021)	China	342 (247/95)	49 (16–83)	I, II, III, IV AJCC 8th	≥2.65 <2.65	2.66 (1.40–5.02)	IMRT	1.72 (1.10–2.69)	66 (3–110)
Setakornnuku (2021)	Thailand	463 (326/137)	50	I, II, III, IVa AJCC 8th	>3 ≤3	1.43 (1.09–1.89)	IMRT		70.8
Liu (2020)	China	207 (112/95)	45	I, II, III, IV AJCC	≥2.49 <2.49	1.908 (2.135–2.860)	IMRT		
Yao (2019)	China	1550 (1167/383)	45 (14–78)	II-IVb AJCC 8th	>2.5 ≤2.5	1.72 (131–2.24)	IMRT	1.29 (1.04–1.59)	54.3 (1.3–85.6)
Sun (2016)	China	251 (180/71)	46 (15–76)	I-IV AJCC	≥2.6(OS) ≥2.7(PFS) <2.6 <2.7	2.41 (1.20–4.83)		2.78 (1.81–4.27)	50 (5–84)
He (2012)	China	1410 (1027/383)	46.1 (13–79)	I, II, III, IV AJCC 6th	>2.74 ≤2.74	1.57 (1.04–2.39)	RT ± CT	1.68 (1.19–2.38)	41 (2–60)
Chua (2016)	Singapore	380 (305/75)	47.8 (14.30–75.95)	III/IVA,B AJCC1997	≥3 <3 <4.2 ≥4.2	1.05 (0.76–1.46) 1.30 (0.87–1.93)	2D RT + IMRT		
Lu (2017)	China	140 (101/39)	47 (10–76)	I, II, III, IVa	≥2.28 <2.28	2.38 3 (1.041–5.457)		2.615 (1.206–5.672)	68 (5–77)
Jiang (2018)	China	247 (197/50)	46 (18–86)		2.73	3.259 (1.473–7.208)	IMRT	7.093 (2.685–18.732)	53 (3–64)
Liao (2018)	Taiwan	180 (144/36)	50 (24–71)	AJCC 7th	3.6	1.89 (1.08–3.29)		1.38 (0.76–2.48)	
Ye (2018)	China	427 (307/120)	48 (17–82)		2.32	1.872 (1.118–3.137)	IMRT	1.747 (1.181–2.585)	
AKÇAY (2019)	Eskişehir-Turkey	62 (42/20)	50 (20–76)	I, II, III, IVa AJCC 7th	≥3 <3	1.19 (1.04–1.35)	IMRT non-IMRT		
Song (2021)	China	111 (77/34)	63 (12–74)	I-IV AJCC8th	<2.02 ≥2.02	8.480 (1.693–42.461)	RT/CCRT	1.298 (0.550–3.063)	59

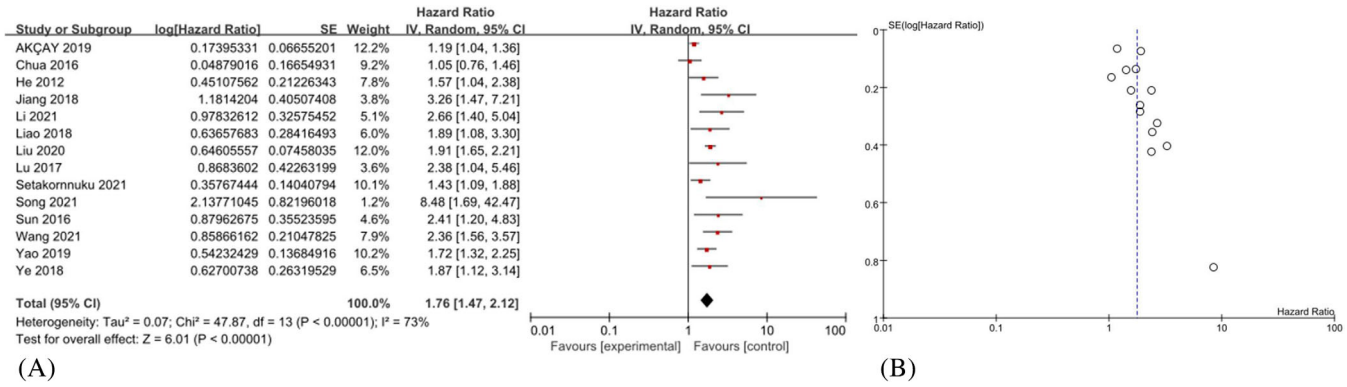

FIGURE 2 (A) Forest plot showing the hazard ratios for overall survival in each of the included studies. The sizes of the squares and the horizontal lines crossing the squares represent the weight of each study in the meta-analysis and the 95% confidence intervals (CIs), respectively. The middle and width of the diamond indicate the pooled hazard ratio (HR) and its 95% CI. (B) Funnel plot of the NLR for OS. NLR, neutrophil-to-lymphocyte ratio; OS, overall survival.

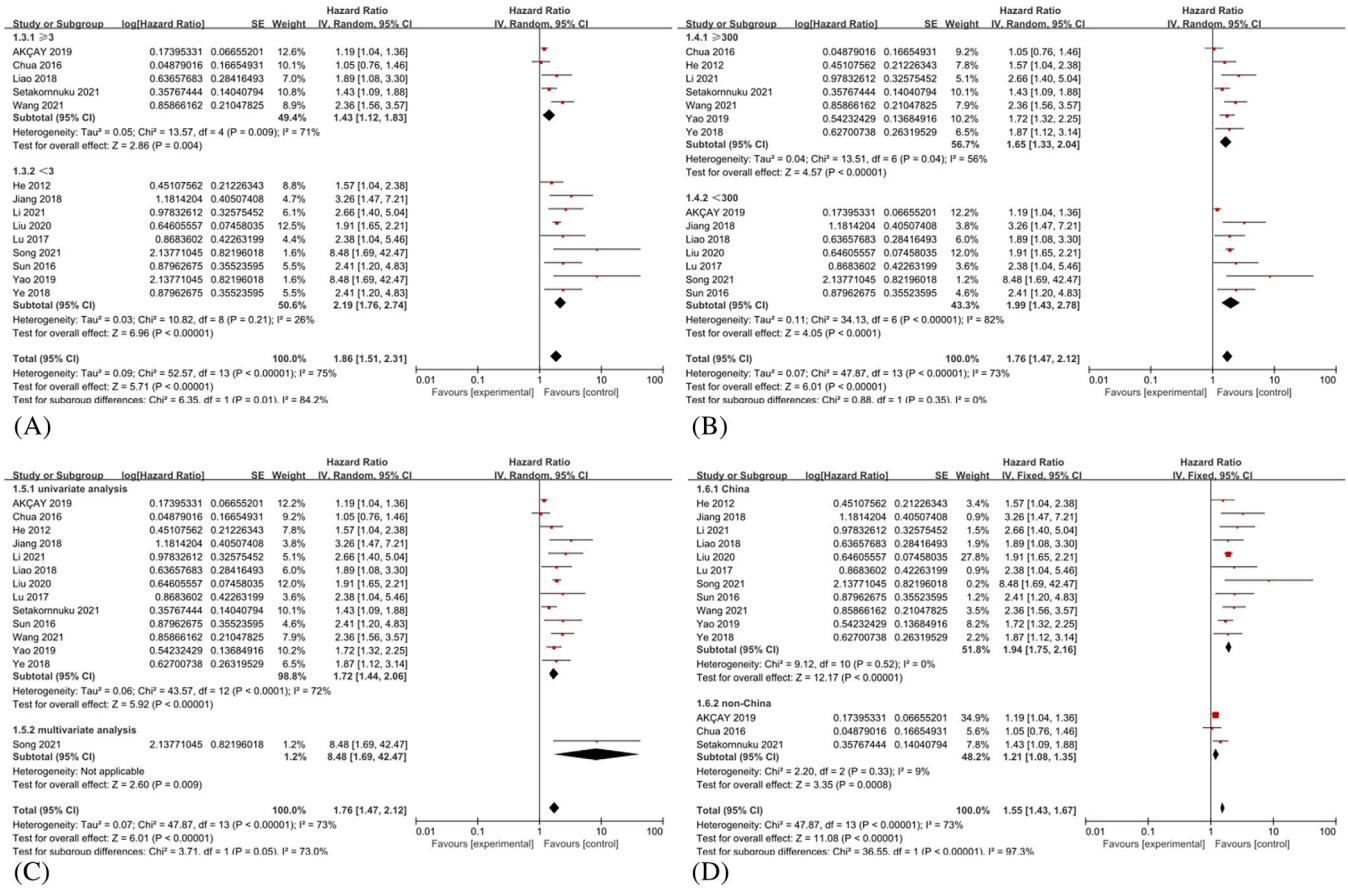

FIGURE 3 Forest plots of the studies categorized by (A) NLR cut-off, (B) number of patients, (C) analytic methods, and (D) nationality/ethnicity.

PFS (95% CI 1.43–2.39), indicating a significant inverse correlation between NLR and PFS. The heterogeneity among the selected studies was statistically significant, allowing the use of a random effect model was used. In order to test stability, sensitivity analysis of PFS was performed by removing each study individually and comparing these effect sizes to the original effect size. There were no significant changes in the combined HR, indicating that the results of this study were stable. A funnel plot evaluating the risk of bias showed no significant asymmetry (Figure 4B), indicating that there was no significant publication bias. Due to the small number of studies evaluating DSS and DMFS, their pooled effect sizes are not shown.

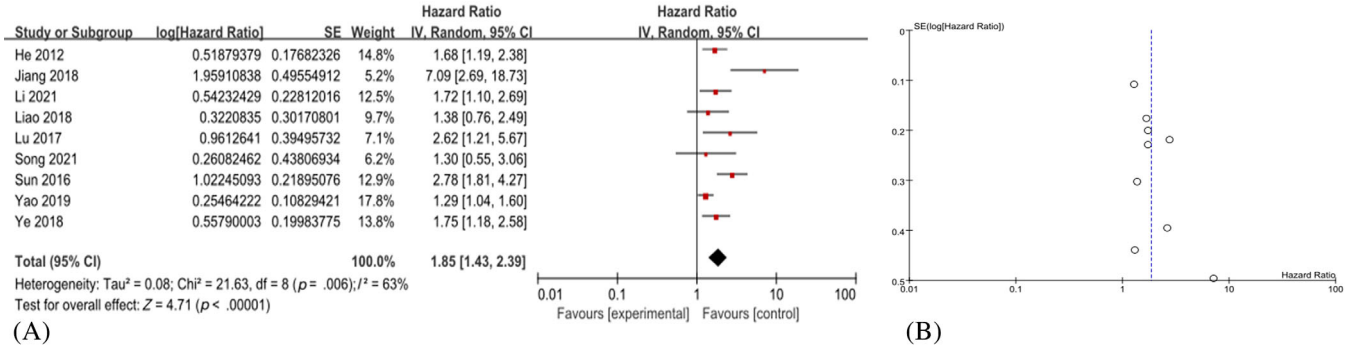

FIGURE 4 (A) Forest plot of NLR for PFS. (B) Funnel plot showing the risk of bias of the NLR for PFS. PFS, progression-free survival.

4 | DISCUSSION

Research on the relationship between inflammation and tumors began in the 19th century. Studies showed that measurable parameters in the blood that reflect systemic inflammatory responses are altered in patients with cancer, including hypoalbuminemia and elevated levels of C-reactive protein, pro-inflammatory cytokines, and leukocyte subtypes. Biochemical markers of inflammatory response have been incorporated into prognostic scores for several cancers.[42,43] Chronic inflammatory lesions often occur secondary to tumors, with inflammatory cells frequently present in tumor biopsy samples.[4,5] Epidemiological studies have confirmed the correlation between inflammation and the occurrence of tumors, with 25% of tumors developing from inflammatory lesions. Inflammatory cells and regulatory factors are present in the microenvironment of most tumors, whether or not they promote tumor progression. Tumor-associated inflammation is not only present during early stages of tumors, but inflammatory regulators and inflammatory cells are also involved in the migration, invasion, and metastasis of malignant cells. Some inflammatory factors can increase the invasive ability of malignant cells, possibly by their up-regulation of chemokine receptor expression. Therefore, sufficient attention should be paid to long-term chronic inflammation to prevent the occurrence and development of tumors.[6] To date, many hematological parameters have been utilized to predict tumor prognosis, such as NLR, PLR, CPR/ALB, and GPS.[13–15] Tests for these markers are accurate, inexpensive, and readily available. Elevated NLR in peripheral blood has been shown to be an indicator of poor prognosis in various cancers. NLR can be easily measured in daily clinical practice and can aid in stratifying patients in clinical trials. Multiple meta-analyses have shown that elevated NLR before treatment is significantly associated with poor prognosis in patients with various solid tumors,[9] such as mesothelioma, pancreatic cancer, renal cell carcinoma, colorectal cancer, gastroesophageal cancer, non-small cell lung cancer,[7] cholangiocarcinoma, and hepatocellular carcinoma. Few studies to date, however, have evaluated the prognostic significance of NLR in patients with NPC.

Currently, NLR is widely used in almost all medical disciplines as a reliable and readily available marker of immune responses to a variety of infectious and noninfectious stimuli. The immunological and biological aspects of the dynamics of neutrophils and lymphocytes in circulating blood have been analyzed during endocrine stress, autonomic nervous system imbalance, and systemic inflammation. NLR reflects the dynamic relationship between innate (neutrophils) and adaptive (lymphocytes) cellular immune responses in diseases and other pathological states. Neutrophils are involved in tumor cell growth, angiogenesis, and metastasis by producing cytokines and releasing angiogenic factors. Lymphocytic infiltration is of great significance in improving tumor prognosis and response to treatment.[44] Low numbers of lymphocytes are associated with the inability to mount a strong immune response. Thus, higher NLR may represent a rough indicator of the relationships among tumors, inflammatory responses, and the overall immune system.

NLR is influenced by many factors, including age; medications; chronic diseases, such as coronary heart disease, stroke, and diabetes; obesity; psychiatric conditions; solid organ cancers; anemia, and stress. Normally, NLR ranges from 1 to 2. In adults, an NLR >3.0 or <0.7 is indicative of pathological conditions, with NLRs ranging from of 2.3 to 3.0 regarded as an early warning of pathological states or processes, such as cancer, atherosclerosis, infection, inflammation, mental disorders, and stress. NLR is a reliable and inexpensive marker of persistent cancer-related inflammation and an effective prognostic indicator of outcomes in patients with solid tumors. Most meta-analyses investigating the prognostic value of NLR in patients with various solid tumors have found that a cutoff >3.0 (IQR 2.5–5.0) was indicative of a poorer prognosis.

NLR has several advantages in oncology. First, NLR can help stratify patients by tumor size, tumor stage, metastatic potential, and lymphatic invasion. NLR is independent prognostic effect of OS, cancer-free survival, and cancer-specific survival, and can assist in monitoring tumor response to treatment, including with biological agents and immune checkpoint inhibitors. NLR is a very sensitive indicator of infection, inflammation, and sepsis. NLR should be monitored daily in patients with acute and critical illnesses, with both absolute NLR and its dynamic course measured. A marked increase in NLR to >11, >17 and even >30 can indicate the severity of critical illness and the levels of stress and serious inflammation. Improvements in the clinical course of sepsis and critical illness, as well as lower risks of mortality, have been associated with a reduction in NLR values <7.[4]

NLR helps distinguish between more and less severe diseases. NLR assays are low in cost, easy to perform, yield a rapid response, have high sensitivity and low specificity, and respond to stress and inflammatory parameters. Dynamic changes in NLR occur several hours before changes in clinical status and may be early indicators of pathological processes. NLR is a novel perspective marker of cellular immune activation and a potent indicator of stress and systemic inflammation, which opens a new dimension to clinical medicine and contributes to a better understanding of the biology of inflammation, the coupling and antagonism between innate and adaptive immunity and its clinical consequences for health and disease.

NLR however, can be affected by pre-existing autoimmune diseases, acute inflammation, and hematological disorders and is therefore a less reliable indicator of pathological processes in patients with these conditions. Moreover, although these biomarkers present a snapshot of inflammation, the immune system and inflammatory markers are dynamic. Thus, biomarkers may not truly reflect the overall situation of a patient. In addition, these markers are systemic and do not necessarily describe the nature of the tumor microenvironment.[8]

The present meta-analysis of 14 studies involving 6693 patients evaluated the effect of NLR on the prognosis of patients with NPC. Pooled HRs showed that elevated NLR was significantly associated with poorer OS (HR: 1.76, 95% CI: 1.47–2.12) and PFS (HR: 1.85, 95% CI: 1.43–2.39) in Asian patients with NPC. OS results were highly heterogeneous, and subgroup analysis was needed to identify the source of heterogeneity. Some subgroups (national populations and NLR cutoff values) showed low heterogeneity. Subgroup analysis that divided nationality into Chinese and non-Chinese groups eliminated the heterogeneity of OS, a heterogeneity that may be due to differences among countries in clinical study methods. These findings suggest that heterogeneity was due to methodological parameters rather than clinical factors. Because this meta-analysis included a limited number of studies, however, patients could not be evaluated by clinical subgroups, such as tumor histology or site. Because some subgroups were highly heterogeneous, both within and between groups, their results could not be combined. Subgroup analyses of studies that included ≥300 and < 300 patients showed that the former group ($I^2 = 56\%$) was less heterogeneous than the latter group ($I^2 = 82\%$). In addition, groups with NLR cutoffs <3.0 were less heterogeneous than those with higher cutoffs.

The present study had several limitations. First, this meta-analysis included only 14 studies, with most studies using univariate analysis to calculate the association between NLR and HR for survival outcomes; other studies did not report the results of univariate analysis but did report the results of multivariate analysis. Several studies included inflammatory markers as covariates in multivariate models along with NLR, which may have led to an underestimation of NLR. Second, most of the patients in this study were from China, and others were from other areas of East Asia. Ethnicity may affect the associations between NLR and survival outcomes in patients with NPC. Although the incidence of NPC is higher in China and Southeast Asia than in other areas of the world, the findings of this study may be applicable only to East Asian populations. Third, the cutoff values of the included studies were determined according to different criteria, resulting in heterogeneity among the cutoff values for hematological parameters. Because the number of studies was limited, meta-regression analyses could not be performed to explore the relationship between boundary values and the effects of NLR. Therefore, the optimal NLR cut-off value for clinical use could not be determined. In general, the present meta-analysis results showed that, in most patients, pretreatment of NLR is a negative prognostic factor in patients with NPC. Application, to clinical biomarkers requires a system of evaluation, with additional clinical data needed to confirm this conclusion.

5 | CONCLUSION

The results of this meta-analysis showed that higher pre-treatment NLR was associated with poorer OS and PFS in patients with NPC. NLR is an accurate, easily determined parameter that can act as a valuable prognostic indicator in patients with NPC.

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CONFLICT OF INTEREST STATEMENT

The authors have declared that no competing interest exists.

DATA AVAILABILITY STATEMENT

Meta-analysis is a secondary analysis in which data are fully available without restrictions, and all materials can be found in the included original studies.

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