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The prognostic values of lymph node ratio for gynecological cancer: a systematic review and meta-analysis

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Background: The aim of this study was to determine the relationship between the lymph node ratio (LNR) and the prognostic values of gynecological cancer.

Materials and methods: PubMed, Web of Science, Embase, and the Central Cochrane Library were used to search for studies on LNR and gynecological cancer published before 18 April 2024. The effect measure for meta-analysis of primary outcomes was the hazard ratio (HR) for overall survival (OS), progression-free survival (PFS), and disease-free survival (DFS). Pooled HRs and 95% confidence intervals (CIs) were calculated using random- or fixed-effects models. Sensitivity analysis was applied to evaluate the robustness of the results. The I^2 statistic was used to measure heterogeneity. Subgroup analysis and meta-regression were chosen to illustrate the potential heterogeneity of the risk factors for outcomes. Publication bias was assessed using Egger's test and Begg's funnel plots.

Results: A total of 34 studies with 23,202 cases were included in this meta-analysis. A meta-analysis found that higher LNR was associated with worse OS (HR = 2.42, 95% CI: 2.07–2.83; I^2 = 77.4%, $p < 0.05$), PFS (HR = 1.97, 95% CI: 1.66-2.32; I^2 = 0.00%, $p > 0.05$), and DFS (HR = 3.18, 95% CI: 2.12–4.76; I^2 = 64.3%, $p < 0.05$). Moreover, meta-analysis revealed significant differences in the association between LNR and OS of cervical cancer (CC) (HR = 2.53, 95% CI: 1.94–3.31; I^2 = 72.6%, $p < 0.05$), ovarian cancer (OC) (HR = 2.05, 95% CI: 1.66–2.54; I^2 = 76.7%, $p < 0.05$), endometrial cancer (EC) (HR = 2.16, 95% CI: 1.48–3.16; I^2 = 53.6%, $p < 0.05$), and vulvar cancer (VC) (HR = 8.13, 95% CI: 3.41–19.43; I^2 = 57.2%, $p < 0.05$).

Conclusion: We observed a clear association between higher LNR and poorer prognosis in our study of patients with gynecological cancer. Further prospective studies are warranted to determine the optimal LNR and whether LNR can guide adjuvant therapy use in gynecological cancer. It is essential to conduct further prospective studies to establish the optimal LNR threshold, determine the minimum threshold of lymph node removal, and investigate whether LNR can

serve as a reliable marker for guiding adjuvant therapy choices in gynecological cancer.

Systematic review registration: https://www.crd.york.ac.uk/PROSPERO/#recordDetails, CRD42024541187.

KEYWORDS

lymph node ratio, gynecological cancer, prognosis, systematic review, meta-analysis

1 Introduction

Lymph node metastasis is a common occurrence in gynecological cancers and has a significant impact on patient prognosis. However, the number of positive nodes during pelvic lymphadenectomy can be influenced by surgical technique and the accuracy of pathological examination. To overcome potential confounding effects, the use of lymph node ratio (LNR) has been proposed. LNR calculates the ratio of positive lymph nodes to the total number of resected lymph nodes and provides a more accurate representation of pelvic lymph node metastasis status. It has been identified as an independent predictor of survival in various cancers, including colon cancer (1), oral cancer (2), pancreatic cancer (3), breast cancer (4), esophageal cancer (5), and lung cancer (6).

Recently, there has been interest in using LNR as a prognostic tool in gynecologic malignancies such as cervical cancer (CC), ovarian cancer (OC), endometrial cancer (EC), and vulvar cancer (VC). However, the conclusions of studies in this area are not consistent. To address this, we conducted a systematic search of scientific databases to identify relevant publications and to explore the relationship between lymph node ratio and overall survival (OS), progression-free survival (PFS), and disease-free survival (DFS) in gynecological cancers.

2 Materials and methods

2.1 Protocol registration

This meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (7). Before data extraction, the review was registered with the International Prospective Register of Systematic Reviews (PROSPERO, Registration Number CRD42024541187).

2.2 Data collection

PubMed, Web of Science, Embase, and the Central Cochrane Library were used to search for studies on LNR and gynecological cancer published before 18 April 2024. The following keywords were used for literature retrieval: ("lymph node ratio" or "Ratio, Lymph Node") and ("Uterine Cervical Neoplasms" or "Neoplasm, Uterine Cervical " or "Ovarian Neoplasms" or "Neoplasm, Ovary" or "Neoplasm, Endometrial" or "Endometrial Neoplasms" or "Vulvar Neoplasms" or "Neoplasm, Vulva"). Additionally, the references in the obtained papers were examined to find any other relevant research outside of these two key phrases in the query.

2.3 Eligibility criteria and exclusion criteria

Inclusion criteria were as follows: (1) studies that investigated the relationship between LNR and OS, PFS, or DFS; (2) studies with CC, OC, EC, and VC confirmed by pathology; (3) studies that reported a hazard ratio (HR) with 95% CI for OS, PFS, or DFS; and (4) full articles published in English.

Exclusion criteria were as follows: (1) useful data could not be extracted; (2) the survival data or 95% confidence interval (CI) were not reported; and (3) editorials, reviews, and comments. In addition, when the data of a patient were used in multiple studies, we selected the most recent study.

2.4 Data extraction of data and quality assessment

The data extracted mainly included the following: the first author, publication date, sample size, cancer type, country, average age, duration of follow-up, cutoff value for LNR, and patient outcomes, including OS, PFS, and DFS.

In this meta-analysis, the quality assessment for the non-randomized studies was evaluated by two reviewers independently based on the Newcastle–Ottawa quality assessment scale (NOS) (8). The NOS was based on three categories: selected cases, comparability between groups, and outcome assessment. A score ≥ 6 was considered high-quality literature, to be included in our study.

2.5 Main outcomes

OS refers to the period from the date of the initial therapy to the date of all-cause mortality. PFS refers to the time from the date of the initial therapy to the date of disease progression, which was the time following successful treatment without disease progression or symptoms. DFS refers to the time from surgery to the last follow-up with no evidence of recurrence or distant metastasis.

2.6 Statistical analysis

We used STATA 15.0 software (StataCorp LP, College Station, TX, United States) to pool the extracted data for this meta-analysis. Hazard ratios with 95% CI were collected from individual studies, then combined using a random- or fixed-effects model, and finally presented in forest plots. Statistical heterogeneity was quantified by I^2 statistics. A random-effects model was used if there was prominent heterogeneity ($p < 0.1$ or $I^2 > 50\%$); otherwise, a fixed-effects model was adopted ($p > 0.1$ or $I^2 < 50\%$) (9). Sensitivity analysis was used to determine the robustness and stability of the results by calculating the heterogeneity in each situation in which a single study was removed in turn to evaluate the effect of a single study on the overall outcome. The risk of publication was assessed by visual inspection of Begg's funnel plot and Egger's linear regression test. In these two-tailed statistical tests, $p < 0.05$ (95% CI) was regarded as statistically significant. Meta-regression analysis, subgroup analysis, and publication bias were evaluated in analyses that included more than 10 studies.

3 Results

3.1 Study selection

As shown in Figure 1, through electronic searching on PubMed, Web of Science, Embase, and the Central Cochrane Library, 1,428 potential articles were screened. After excluding duplicate studies there were 1,237 records. Then, the titles and abstracts were screened, and 1,109 publications were removed as irrelevant. Finally, 119 full-text articles were identified for qualification, and 85 ineligible papers were eliminated because they did not provide

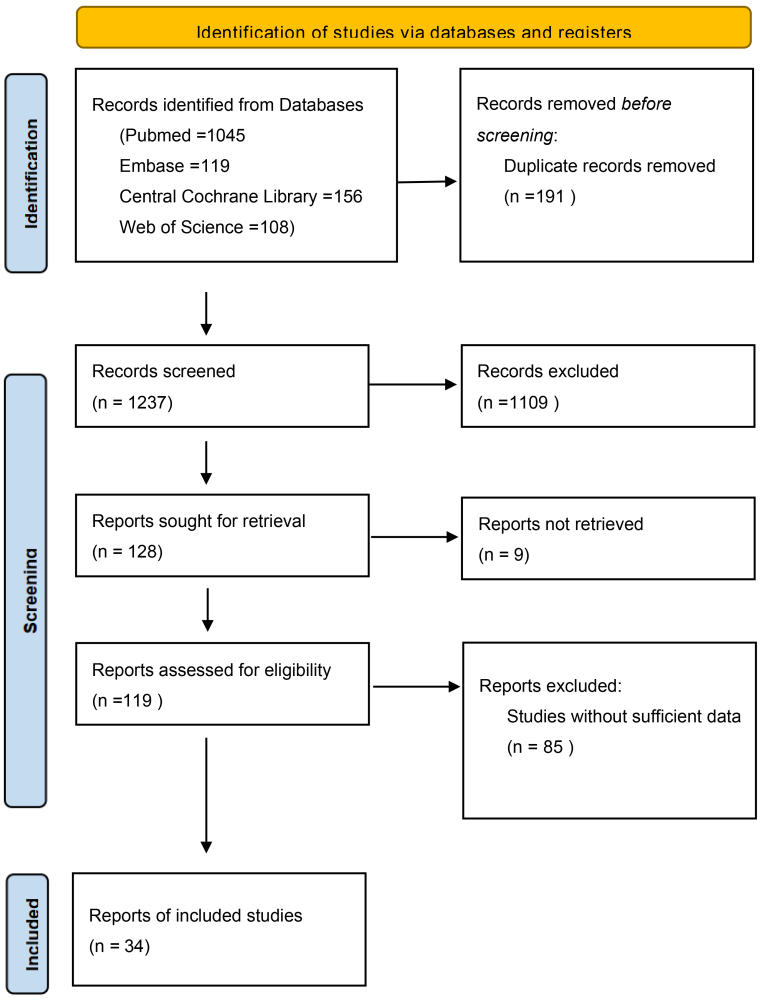

FIGURE 1
Flow diagram of the included studies.

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TABLE 1 Main characteristics of the included literature.

First author	Year	Country	Recruitment period	Size	Cancer type	Age	Mean/median months of follow-up	Survival analysis	Cutoff LNR	NOS score
Ying Chen (10)	2013	China	NM	93	Cervical cancer	46	67	OS	0.05 0.2	8
Qinhao Guo (11)	2020	China	2006–2014	928	Cervical cancer	46.58	35.7	OS PFS	0.16	7
Juan Zhou (12)	2016	China	1988–2010	2,269	Cervical cancer	43	78	OS	0.16	8
Se lk Kim (13)	2021	Republic of Korea	2010–2018	55	Cervical cancer	52.6	NM	DFS	0.08831	7
S Polterauer (14)	2012	Austria	1996–2009	139	Cervical cancer	47.9	45.7	OS	Continuous	7
Xiang Fan (15)	2023	China	2012–2017	102	Cervical cancer	NM	63	OS DFS	0.3	8
Dan Li (16)	2019	China	2008–2013	1,435	Cervical cancer	47	77	OS	0.19	8
Chen Li (17)	2016	China	2007–2009	198	Cervical cancer	44	NM	OS DFS	0.2	7
Juan Zhou (18)	2015	China	1980–2012	60	Cervical cancer	37	30.5	OS	Continuous	7
Yoon Hee Lee (19)	2021	Republic of Korea	2007–2016	49	Cervical cancer	48.5	58	OS DFS	0.0625	7
Nicole D. Fleming (20)	2015	USA	1990–2011	95	Cervical cancer	39.7	64.8	OS PFS	0.076	8
S Polterauer (21)	2010	Austria	1995–2008	88	Cervical cancer	49.9	37.1	OS DFS	0.1	7
Koray Aslan (22)	2020	Türkiye	2006–2018	185	Cervical cancer	50	45.5	OS DFS	0.05	7
E Olthof (23)	2021	Netherlands	1995–2020	593	Cervical cancer	NM	NM	OS	0.177	7
Koray Aslan (24)	2020	Türkiye	1997–2017	62	Ovarian cancer	47	45	OS PFS	0.09	7
Ali Ayhan (25)	2018	Türkiye	2007–2016	229	Ovarian cancer	56	36	OS	0.1 0.5	7
Xiaoxia Tong (26)	2019	China	1973–2013	7,819	Ovarian cancer	NM	NM	OS	0.42	7
Dan Nie (27)	2019	China	2008–2014	265	Ovarian cancer	56	40	OS DFS	0.25	7
Beyhan Ataseven (28)	2014	Germany	2000–2013	398	Ovarian cancer	NM	45	OS	0.25	7
Katarzyna Lepinay (29)	2020	Poland	2010–2015	144	Ovarian cancer	NM	NM	OS	0.1	7
Juan Zhou (30)	2016	China	1990–2012	5,926	Ovarian cancer	59	33	OS	0.42	7
M.A. Ayadi (31)	2018	Tunisia	2000–2010	84	Ovarian cancer	54	65	OS	0.5	8
P. Widschwendter (32)	2017	Germany	2000–2012	131	Ovarian cancer	NM	NM	OS	Continuous	7

(Continued)

TABLE 1 Continued

First author	Year	Country	Recruitment period	Size	Cancer type	Age	Mean/median months of follow-up	Survival analysis	Cutoff LNR	NOS score
Katarzyna Gorzelnik (33)	2022	Poland	2000–2015	75	Endometrial cancer	60	NM	OS	0.3	7
Nicole D. Fleming (34)	2015	Brazil	2000–2011	124	Endometrial cancer	60	49.4	OS PFS	0.4 (OS) 0.5 (PFS)	7
Ali Ayhan (25)	2017	Türkiye	1998–2016	207	Endometrial cancer	58	40	OS PFS	0.15	7
Siriwan Tangjitgamol (35)	2019	Thailand	1995–2017	82	Endometrial cancer	59.5	NM	PFS	0.1	7
Stephan Polterauer (36)	2012	Now York	1993–2008	216	Endometrial cancer	65.5	30.5	OS PFS	0.1 0.5	7
Nicole D. Fleming (20)	2015	USA	1990–2011	95	Endometrial cancer	39.7	64.8	OS PFS	0.66 (OS) 0.076 (PFS)	8
Tayfun Toptas (37)	2015	Türkiye	2005–2013	38	Endometrial cancer	32.5	64	OS PFS	0.065	8
B. Akkus Yildirim (38)	2018	Türkiye	2001–2016	180	Endometrial cancer	60	50.5	OS PFS	0.1	7
Stephan Polterauer (39)	2017	Germany	NM	370	Vulvar cancer	64.5	26.4	OS DFS	0.1 0.2	7
E. Serre (40)	2019	France	2005–2015	176	Vulvar cancer	68.7	NM	OS	0.2	7
Stephan Polterauer (41)	2020	Poland	2001–2005	292	Vulvar cancer	69.9	NM	OS	0.2	7

primary outcome measurements. In the end, a total of 34 studies with 23,202 cases were eligible for the current meta-analysis.

3.2 Characteristics of the included studies

The main characteristics of the included studies are presented in Table 1. In this study, all necessary data were extracted from 34 studies from different countries including China (n = 10), Türkiye (n = 6), USA (n = 3), Germany (n = 3), Poland (n = 3), Republic of Korea (n = 2), Austria (n = 2), Thailand (n = 1), Brazil (n = 1), Tunisia (n = 1), Netherlands (n = 1), and France (n = 1). All included studies were retrospective studies. Among these articles, 14 studies involved 6,289 patients diagnosed with CC, 9 studies involved 15,058 patients diagnosed with OC, 8 studies involved 1,017 patients diagnosed with EC, and 3 studies involved 838 patients diagnosed with VC. All studies were retrospective cases, and all were rated seven or more stars according to the NOS criteria (Table 2).

3.3 Meta-analysis

3.3.1 Primary outcomes

3.3.1.1 LNR and OS

Out of the 34 (10–41) eligible studies, 32 (10–12, 14–34, 36–41) studies, namely, 13 (10–12, 14–23) studies with CC, 9 (24–32) studies with OC, 7 (20, 25, 33, 34, 36–38) studies with EC, and 3 (39–41) studies with VC, analyzed the association between LNR and OS. Using a random-effects model, the pooled results of HR and OS statistics from these 32 studies showed that higher levels of LNR were associated with worse OS (HR = 2.42, 95% CI: 2.07–2.83; I^2 = 77.4%, $p < 0.05$), as shown in (Figure 2A). However, the results also indicated a high heterogeneity between studies (I^2 = 77.4%, $p < 0.05$).

3.3.1.2 LNR and PFS

Seven studies (20, 25, 34–38) with EC, two studies (11, 15) with CC, and one study (24) with OC explored the association between LNR and PFS. Using a fixed-effects model, pooled results of HR and PFS statistics from 10 studies indicated that higher LNR levels were associated with worse PFS (HR = 1.97, 95% CI: 1.66–2.32; $I^2 < 50\%$, $p > 0.05$) (Figure 2B). The results showed that there was low heterogeneity between studies ($I^2 < 50\%$, $p > 0.05$).

3.3.1.3 LNR and DFS

Eight studies, consisting of six studies (13, 15, 17, 19, 21, 22) with CC, one study (24) with OC, and one study (39) with VC, were included in the analysis of the association between LNR and PFS. Using a random-effects model, the pooled results indicated that higher levels of LNR were associated with worse DFS (HR = 3.18, 95% CI: 2.12–4.76; I^2 = 64.3%, $p < 0.05$) (Figure 2C). However, there was high heterogeneity between studies ($I^2 > 50\%$, $p < 0.05$).

TABLE 2 Quality of the included studies.

Study	Selection			Comparability			Outcome		Total
	Representativeness	Selection of non-exposed	Ascertainment of exposure	Outcome not present at the start	Comparability of most important factors	Comparability on other risk factors	Assessment of outcome	Long enough follow-up (median ≥ 5 years)	Adequacy (completeness of follow-up)	
Ying Chen (10)	√	√	√	√	√	×	√	√	√	8
Qinhao Guo (11)	√	√	√	√	√	×	√	×	√	7
Juan Zhou (12)	√	√	√	√	√	×	√	√	√	8
Se lk Kim (13)	√	√	√	√	√	×	√	×	√	7
S Polterauer (14)	√	√	√	√	√	×	√	×	√	7
Xiang Fan (15)	√	√	√	√	√	×	√	√	√	8
Dan Li (16)	√	√	√	√	√	×	√	√	√	8
Chen Li (17)	√	√	√	√	√	×	√	×	√	7
Juan Zhou (18)	√	√	√	√	√	×	√	×	√	7
Yoon Hee Lee (19)	√	√	√	√	√	×	√	×	√	7
Nicole D. Fleming (20)	√	√	√	√	√	×	√	√	√	8
S Polterauer (21)	√	√	√	√	√	×	√	×	√	7
Koray Aslan (22)	√	√	√	√	√	×	√	×	√	7
E. Olthof (23)	√	√	√	√	√	×	√	×	√	7
Koray Aslan (24)	√	√	√	√	√	×	√	×	√	7
Ali Ayhan (25)	√	√	√	√	√	×	√	×	√	7
Xiaoxia Tong (26)	√	√	√	√	√	×	√	×	√	7
Dan Nie (27)	√	√	√	√	√	×	√	×	√	7
Beyhan Ataseven (28)	√	√	√	√	√	×	√	×	√	7
Katarzyna Lepinay (29)	√	√	√	√	√	×	√	×	√	7

(Continued)

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TABLE 2 Continued

Study		Selection			Comparability			Outcome		Total
	Representativeness	Selection of non-exposed	Ascertainment of exposure	Outcome not present at the start	Comparability of most important factors	Comparability on other risk factors	Assessment of outcome	Long enough follow-up (median ≥ 5 years)	Adequacy (completeness of follow-up)	
Juan Zhou (30)	√	√	√	√	√	×	√	×	√	7
M.A. Ayadi (31)	√	√	√	√	√	×	√	√	√	8
P. Widschwendter (32)	√	√	√	√	√	×	√	×	√	7
Katarzyna Gorzelnik (33)	√	√	√	√	×	×	√	×	√	7
Nicole D. Fleming (34)	√	√	√	√	√	×	×	×	×	7
Ali Ayhan (25)	√	√	√	√	√	×	×	×	×	7
Siriwan Tangjitgamol (35)	√	√	√	√	√	×	×	×	×	7
Stephan Polterauer (36)	√	√	√	√	√	×	×	×	×	7
Nicole D Fleming (20)	√	√	√	√	√	×	×	√	√	8
Tayfun Toptas (37)	√	√	√	√	√	×	√	√	√	8
B. Akkus Yildirim (38)	√	√	√	√	√	×	√	×	√	7
Stephan Polterauer (39)	√	√	√	√	√	×	√	×	√	7
E. Serre (40)	√	√	√	√	√	×	√	×	√	7
Stephan Polterauer (41)	√	√	√	√	√	×	√	×	√	7

"√" indicates that the criteria are met, while "×" indicates that the criteria are not met.

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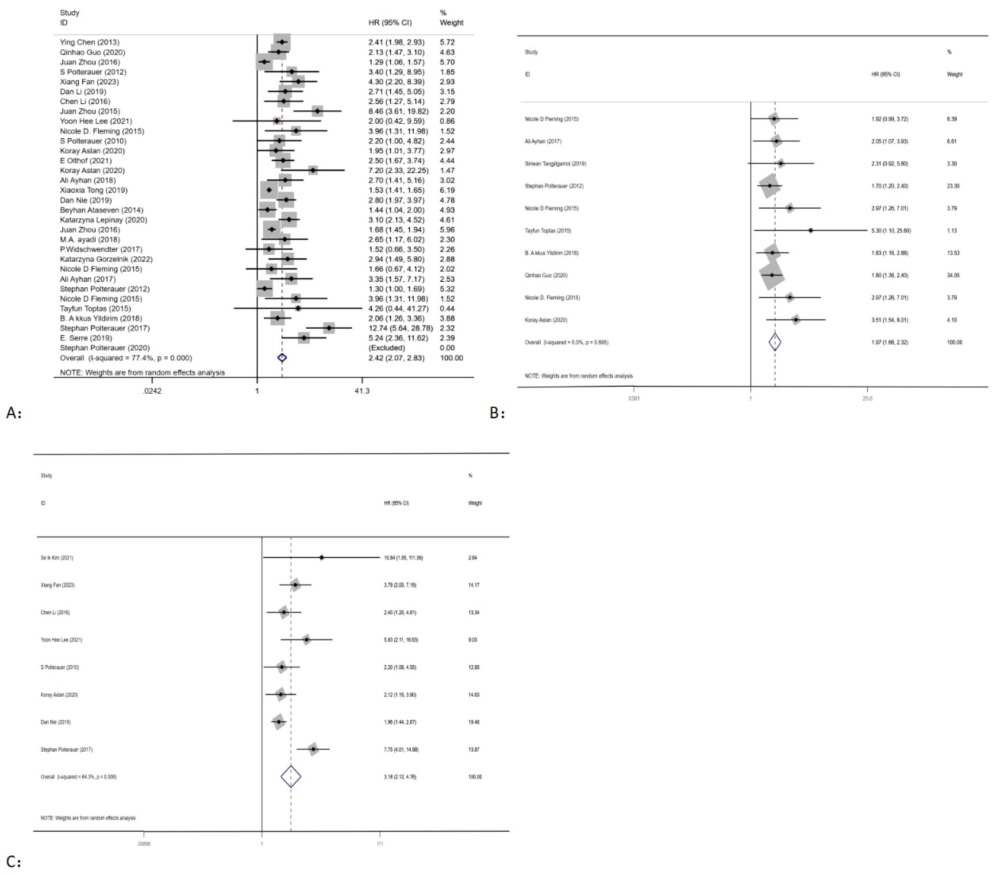

FIGURE 2
Forest plots and pooled estimates of the effect for meta-analysis of the association between LNR and OS **(A)**, PFS **(B)**, and DFS **(C)** in patients with gynecological cancer.

3.3.2 Subgroup and meta-regression analysis

As the outcome of OS shows high heterogeneity, both meta-regression and subgroup analyses were conducted to explore the factors contributing to the high heterogeneity. Subgroup analysis was carried out based on the type of cancer. The analysis revealed significant differences in the association between LNR and OS of CC (HR = 2.53, 95% CI: 1.94–3.31; I^2 = 72.6%, $p < 0.05$), OC (HR = 2.05, 95% CI: 1.66–2.54; I^2 = 76.7%, $p < 0.05$), EC (HR = 2.16, 95% CI: 1.48–3.16; I^2 = 53.6%, $p < 0.05$), and VC (HR = 8.13, 95% CI: 3.41–19.43; I^2 = 57.2%, $p < 0.05$) (Figure 3). Furthermore, meta-regression analysis was carried out to investigate possible sources of heterogeneity. Single covariate regression was performed using variables such as country, sample size, type of gynecological cancer, and publication year. The results indicated that sample size was the main factor contributing to the heterogeneity, with a p-value of 0.014 (Table 3).

We did not conduct meta-analyses, and subgroup analyses for PFS and DFS, as they c.

3.3.3 Sensitivity analysis

In order to assess the stability of the models, a sensitivity analysis was conducted by excluding each individual study and calculating new HRs. The results showed that the HRs were relatively stable, as illustrated in Figure 4.

3.3.4 Publication bias

Publication bias was assessed by Begg's funnel plots and Egger's test. For OS, the p-values for Egger's test (Figure 5A) and Begg's test (Figure 5B) were $p = 0.255$ and $p < 0.00$, respectively. Visual inspection of Begger's funnel plot (Figure 5C) was not symmetrical, suggesting evidence of publication bias. We did not conduct a publication bias analysis for PFS and DFS, as they did not include more than 10 studies.

4 Discussion

This meta-analysis revealed that higher LNR was significantly associated with poorer prognosis across multiple metrics. Specifically, it found that higher LNR was correlated with worse OS, PFS, and DFS, indicating that patients with higher LNR often have worse outcomes. Furthermore, the pooled HRs for OS across different types of cancers are 3.42 for CC, 2.05 for OC, 2.16 for EC, and 8.13 for VC, suggesting that higher LNR often correlates with worse survival outcomes in CC, OC, EC, and VC. These findings underscore the significant prognostic implications of LNR in gynecological cancer, highlighting its role as a critical factor in predicting patient outcomes.

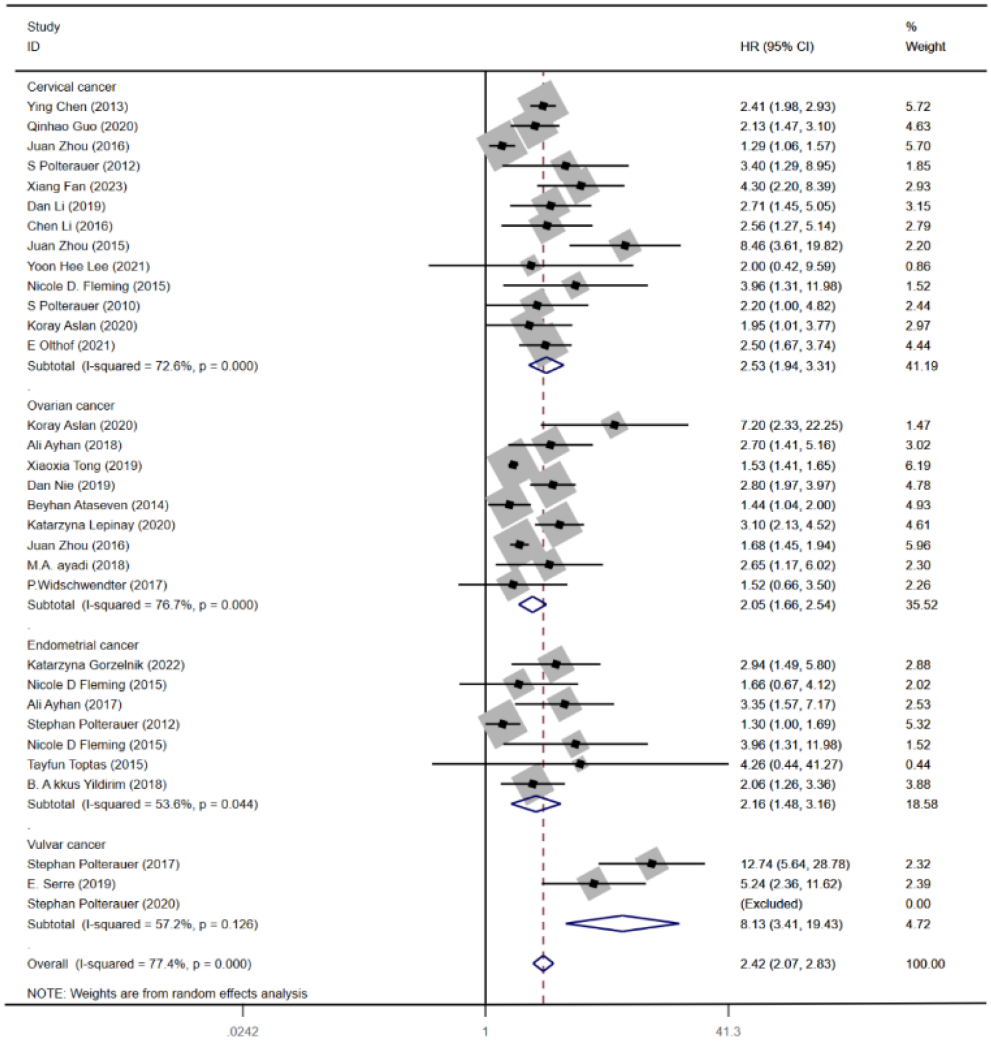

FIGURE 3
Forest plot for subgroup analysis for OS in gynecological cancer.

For CC, based on the results of previous studies, the cutoff value of LNR in patients with CC ranges from 5% to 30% (9–22), with higher LNR consistently associated with poorer prognosis. A meta-analysis (42) conducted in 2017, comprising eight articles with 3,325 patients diagnosed with CC, confirmed that higher LNR was an unfavorable prognostic factor for OS and DFS, which is consistent with our findings. In 2018, the FIGO Committee added IIICI (pelvic lymph node metastasis only) and IIIC2 (para-aortic lymph node metastasis) to the FIGO staging system for CC (43). Nevertheless, this was solely based on anatomic location and did not consider other lymph node characteristics. Researchers have looked for a reliable lymph node measure in CC, yielding conflicting results. Yoon et al. (19) showed that LNR was the most robust biomarker for predicting tumor recurrence, while Qinhao et al. (11) found that positive lymph nodes had the best prognostic performance for OS and PFS. Therefore, further studies are warranted to explore this aspect and establish the most reliable measure.

TABLE 3 Results of the meta-regression.

Co-factor	Coefficient	95% confidence interval	*p*-value
Year	0.055	(−0.003,0.114)	0.062
Type	0.193	(−0.063,0.449)	0.133
Country	−0.045	(−0.130,0.038)	0.274
Size	−0.00	(−0.00,−0.000)	0.014

In OC, previous studies have identified varying cutoff values for LNR ranging from 9% to 50% (23–31). Consistently, higher LNR was linked to poorer prognosis, which is in line with our study findings. It is worth noting that OC is a heterogeneous group of diseases with varying histology, molecular genetic analysis, and prognosis (44); some researchers have begun to conduct more in-depth research on the classification of epithelial OC. The prognostic value of lymph node ratio has been confirmed in high-grade serous ovarian carcinoma (45), low-grade serous ovarian carcinoma (22), clear cell ovarian carcinoma (27), and borderline ovarian tumors (46). Especially in borderline ovarian tumors (46), David controlled for age, histology, stage, tumor size, and adequate

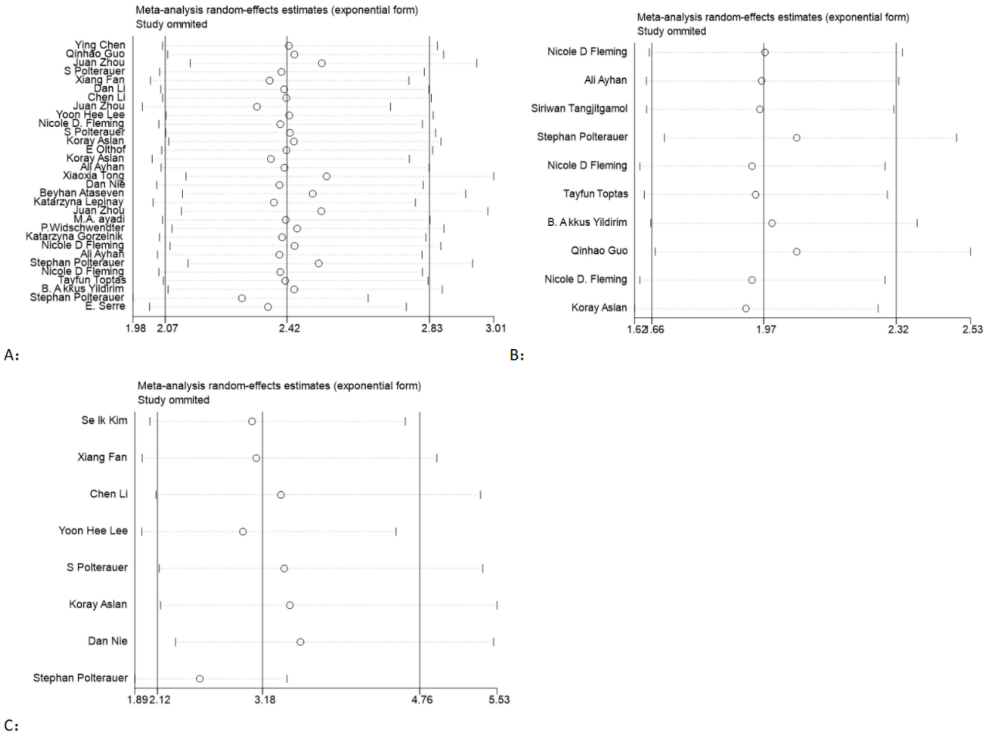

FIGURE 4
Sensitivity analysis of the association between LNR and OS **(A)**, PFS **(B)**, and DFS **(C)** in gynecological cancer.

lymphadenectomy status, and LNR remained an independent factor for survival; qualitative assessment of lymph node involvement is not a prognostic factor for survival. Another study (30) based on the Surveillance, Epidemiology, and End Results database showed that there is a significant and independent correlation between higher LNR and poorer OS, and its prognostic value is superior to removed lymph nodes and positive lymph node counts. Despite this, a study conducted by Xiao et al. (26) found that LNR did not reach statistical significance for discriminating OS in stage IV patients, although it showed better performance than the number of positive lymph nodes. Therefore, future research should emphasize the prognostic utility of LNR in various stages of OC.

In EC, according to prior research (20, 25, 32–37), the cutoff values for LNR in EC patients span from 6.5% to 50%. These studies consistently indicated that higher LNR is associated with a worse prognosis, a trend observed in our study. Previous multi-center retrospective studies (20, 25, 32–37) have found a correlation between LNR and worse OS and PFS. Xi-Lin et al. (47) found that the lymph node ratio had a better predictive performance for these patients than the number of removed lymph nodes, the number of positive lymph nodes, and the number of negative lymph nodes. However, a study conducted by Fleming et al. (34) did not find a statistically significant association between LNR and OS, probably due to the small patient cohort in this single-institution study and the low median count of retrieved lymph nodes. This suggests that the prognostic value of LNR may be limited to patients who have undergone a minimum threshold of lymph node removal. Nevertheless, this threshold has not been universally adopted as a clinical standard. Future research should focus on identifying optimal lymph node removal strategies to mitigate the morbidity associated with systemic lymphadenectomy.

In VC, Kunos et al. (48) initially described LNR for prognostic assessment in patients with VC, and they found that patients with LNR > 20% had an increased likelihood of contralateral positive

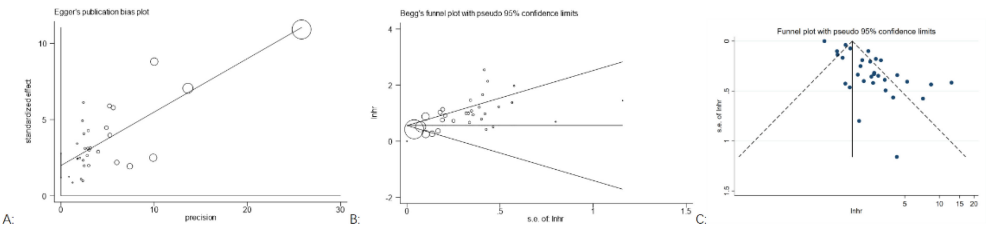

FIGURE 5
Egger's **(A)**, Begg's **(B)**, and funnel plots **(C)** show bias for OS.

lymph nodes, recurrence, and cancer-specific death compared with patients with LNR < 20%. Moreover, some studies (38–40) stratified patients into three groups (LNR = 0%, 0% < LNR < 20%, and LNR > 20%), and the LNR > 20% group had the highest risk for OS and recurrence, which is consistent with our study. According to a study conducted by Polterauer et al., LNR appears to be a consistent, independent prognostic parameter for both OS and PFS, and its predictive value is superior to positive lymph node number. These studies support the predictive value of the LNR for VC.

Our research has certain strengths. First, this is the first complete meta-analysis to quantify the role of LNR in the prognosis of gynecological cancer. Second, this meta-analysis included a large number of primary studies (34 papers) and patients (23,202 patients with positive lymph nodes), which allowed for a more robust statistical analysis. Finally, our findings have demonstrated the importance of LNR in the prognosis of gynecological cancer. Therefore, we recommend LNR as a prognostic parameter that should be included in a future gynecological cancer staging system.

While our study has shown that LNR is of significant prognostic value in gynecologic cancers, it also has limitations. First, literature-based meta-analyses rely on published data and may be biased toward positive results, and we found that it does have bias in our study. In addition, the absence of data on tumor size, pathological stages, number of examined lymph nodes, number of metastasized lymph nodes, and surgical methods limited further subgroup analysis. Furthermore, the LNR cutoff in different studies was inconsistent. Finally, all included studies were retrospective, and this study type has intrinsic limitations. Thus, more prospective data are required to further ascertain the prognostic value of LNR in specific populations.

5 Conclusion

Higher LNR is linked to lower OS, PFS, and DFS in patients diagnosed with gynecological cancer. The prognostic value of LNR for OS is consistent across different types of gynecological cancer, including CC, OC, EC, and VC. Further prospective studies are essential to establish the optimal LNR threshold, determine the minimum threshold of lymph node removal, and evaluate whether LNR can effectively guide the use of adjuvant therapies in gynecological cancer.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding authors.

Author contributions

MC: Writing – original draft. YW: Writing – original draft. YC: Writing – original draft. LH: Writing – review & editing. AZ: Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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