Lymphocyte-to-C-reactive protein ratio as a clinically feasible nutrition-inflammation marker for predicting outcomes in patients with gastric cancer

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Abstract. Gastric cancer (GC) remains a major global health challenge, with substantial heterogeneity in clinical outcomes even among patients sharing the same American Joint Committee on Cancer stage. Inflammation-based biomarkers have attracted interest for their prognostic value; however, the significance of the lymphocyte-to-C-reactive protein ratio (LCR) in GC has not been systematically evaluated. A comprehensive literature search was performed in the PubMed, EMBASE and Cochrane Library databases in accordance with PRISMA guidelines. Studies assessing dichotomized LCR in relation to overall survival (OS) or disease-free survival (DFS) were eligible. Hazard ratios (HRs) were estimated using fixed- or random-effect models based on heterogeneity. Sensitivity and publication bias analyses were performed to evaluate the robustness of the findings. A total of 9 studies involving 4,429 patients were included in OS analysis. Results revealed that a low LCR was strongly associated with reduced survival [HR=2.24; 95% confidence interval (CI), 1.97-2.55]. A total of 5 studies involving 2,987 patients provided DFS data, revealing a similar association (HR=2.11; 95% CI, 1.78-2.51). Subgroup analysis indicated consistent prognostic effects across analytical methods, geographic regions, and treatment strategies. Sensitivity testing and funnel plots indicated stable results with no significant publication bias. In conclusion, a low LCR is a robust predictor of worse OS and DFS in GC and may complement existing staging systems to improve prognostic stratification. Standardized prospective studies are needed to validate its clinical utility.

Introduction

Gastric cancer (GC) continues to impose a substantial burden on global health. Although notable advances have been made in elucidating the molecular and cellular events underlying its onset and progression, this malignancy remains among the top five causes of cancer-related deaths worldwide (1). Striking geographical disparities exist in its distribution, with particularly elevated rates in Eastern populations, where dietary patterns, chronic inflammation linked to *Helicobacter pylori* infection, and inherited genetic alterations exert major influences on disease development (2). Because early clinical manifestations are often absent or obscure, numerous individuals present with advanced disease (3,4).

Surgery remains the primary treatment approach for GC, supplemented with by chemotherapy or radiotherapy when necessary. However, even with standardized interventions, long-term prognosis is frequently unfavorable owing to substantial biological heterogeneity and high recurrence rates (5). Although the American Joint Committee on Cancer staging framework offers a widely adopted prognostic reference, marked variability in survival among patients classified within the same pathological stage highlights its limitations. This inconsistency underscores the need for additional prognostic metrics capable of refining risk assessment and supporting more personalized clinical decision-making.

Chronic systemic inflammation, now recognized as a defining hallmark of malignant disease, drives multiple aspects of tumor biology, including initiation, progression and metastatic spread, through intricate interactions between immune effector mechanisms and tumor-associated microenvironments (6). Building on this biological axis, numerous studies have emphasized the prognostic utility of inflammation-derived indices such as the neutrophil-to-lymphocyte ratio (NLR), the platelet-to-lymphocyte ratio (PLR) and the C-reactive protein-to-albumin ratio (CAR), in various human cancers, including GC (7-9). These markers are attracting increased attention because they can be readily obtained, are cost-effective, and integrate both immune and inflammatory states. Ideally, prognostic indicators should not only predict patient outcomes but also provide guidance for perioperative decisions, treatment stratification, and surveillance planning.

Within the category of inflammation-based indices, the lymphocyte-to-C-reactive protein ratio (LCR) has recently emerged as a promising candidate. Okugawa *et al* (6) reported that LCR mirrors both postoperative and oncological outcomes in colorectal malignancies, suggesting its broader relevance

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as a composite index reflecting immune status, nutritional condition and systemic inflammation (6). Because lymphocyte activity and CRP-driven inflammatory signaling are tightly related to tumor progression, this ratio may capture host-tumor dynamics more effectively than single-component biomarkers.

Despite these encouraging observations, no meta-analysis has consolidated the prognostic implications of LCR in GC. The absence of synthesized evidence hinders the clinical integration of LCR and limits consensus on the potential role across different treatment settings. Therefore, a systematic evaluation is essential to quantify the association of LCR with survival endpoints and determine whether it can serve as a standardized prognostic indicator in GC. This evaluation can strengthen risk stratification paradigms and support more refined therapeutic planning for this highly aggressive malignancy.

Guided by these considerations, a comprehensive meta-analysis was performed to investigate the prognostic significance of circulating LCR in patients with GC. The aim of the present study was to generate robust evidence that clarifies the practicality and clinical relevance of this easily obtainable biomarker and to assess whether it can enhance existing prognostic systems and facilitate individualized patient management.

Materials and methods

Literature search and study selection criteria. The present systematic review was undertaken in full alignment with the PRISMA guidelines for reporting meta-analyses and systematic syntheses (10). The protocol of the present meta-analysis was not prospectively registered in PROSPERO or any other registry. To capture all relevant evidence, a comprehensive search of PubMed (https://pubmed.ncbi.nlm.nih.gov/), EMBASE (https://www.embase.com/) and the Cochrane Library (https://www.cochrane.org/) was performed, encompassing studies published up to November 18, 2025. The retrieval strategy employed predetermined terms related to the LCR ratio. The PubMed search strategy was as follows: [Lymphocyte-to-C-reactive protein ratio(Title/Abstract)] OR [Lymphocyte-C-reactive protein ratio(Title/Abstract)] OR [Lymphocyte/C-reactive protein ratio(Title/Abstract)] OR [Lymphocyte-to-CRP ratio(Title/Abstract)] OR [Lymphocyte-CRP ratio(Title/Abstract)] OR [Lymphocyte/CRP ratio(Title/Abstract)]. This strategy was adapted appropriately for EMBASE and the Cochrane Library according to the syntax and indexing rules of each database. Furthermore, the reference lists of included articles were manually screened to identify any additional work not detected through database queries. To reduce selection bias, two reviewers independently evaluated the literature, and disagreements were adjudicated by consultation with a senior investigator.

Studies were included if they met the following criteria: i) Studies specifically investigating patients with GC, as defined according to the diagnostic criteria used in the original reports; ii) studies evaluating the prognostic significance of pretreatment LCR, with LCR analyzed as a dichotomized variable; iii) studies reporting survival outcomes, including overall survival (OS) and/or disease-free survival (DFS); and iv) studies providing hazard ratios (HRs) with corresponding 95% confidence intervals (CIs), or sufficient data from which these estimates could be obtained. No additional restriction was imposed regarding explicit histological confirmation beyond the diagnostic criteria reported in the original studies. In addition, no minimum follow-up duration was required, provided that extractable survival data were available.

Data extraction and quality evaluation. For each study that met the inclusion criteria, all pertinent information was systematically gathered, including the leading author, publication year, duration of the study period, geographical setting, therapeutic modalities applied, overall cohort size, and fundamental demographic variables such as age distribution and sex composition. The thresholds used to categorize LCR values in individual reports were also recorded. When available, HRs with corresponding 95% CIs were preferentially extracted from multivariate Cox regression models to minimize the influence of potential confounding. If multivariate estimates were not available, univariate HRs were extracted. When HRs and 95% CIs were not reported directly but Kaplan-Meier survival curves were available, the log HR and its standard error were estimated using the established methods described by Tierney *et al* (11). Survival probabilities, numbers at risk, total events and log-rank information were extracted when available to reconstruct the corresponding HR estimates. Multivariate estimates were prioritized over reconstructed or univariate estimates in the quantitative synthesis. When a single publication reported more than one independent and non-overlapping cohort with separately available survival estimates, each cohort was extracted and analyzed as an independent dataset. Specifically, Xiong *et al* (12) reported both a discovery cohort and a validation cohort, which were treated as two separate cohorts in the quantitative synthesis because they included distinct patient populations and provided separate prognostic data (12).

The methodological robustness of the included observational studies was appraised using the Newcastle-Ottawa Scale (NOS), a widely accepted instrument for evaluating potential bias in non-randomized cohort and case-control research (13,14). Investigations earning six or more points on this scale were regarded as having satisfactory methodological rigor. Data extraction and quality assessment were independently performed and cross-verified by two authors, with any discrepancies resolved by a senior investigator.

Statistical methods. All quantitative analyses were performed with Stata (version 18.0; StataCorp LP), and the pooled estimates were illustrated using forest diagrams. To evaluate variability across studies, Cochran's Q statistic was applied together with the I^2 metric; heterogeneity was regarded as meaningful when the I^2 value was greater than 50% or when the Q test yielded a P-value below 0.1 (15). When substantial divergence among studies was detected, the DerSimonian-Laird random-effects approach was adopted. By contrast, datasets exhibiting minimal heterogeneity were synthesized using a fixed-effects framework based on inverse-variance weighting. To evaluate whether variations in LCR thresholds influenced the pooled estimates, an exploratory subgroup analysis was performed according to the median cut-off value reported

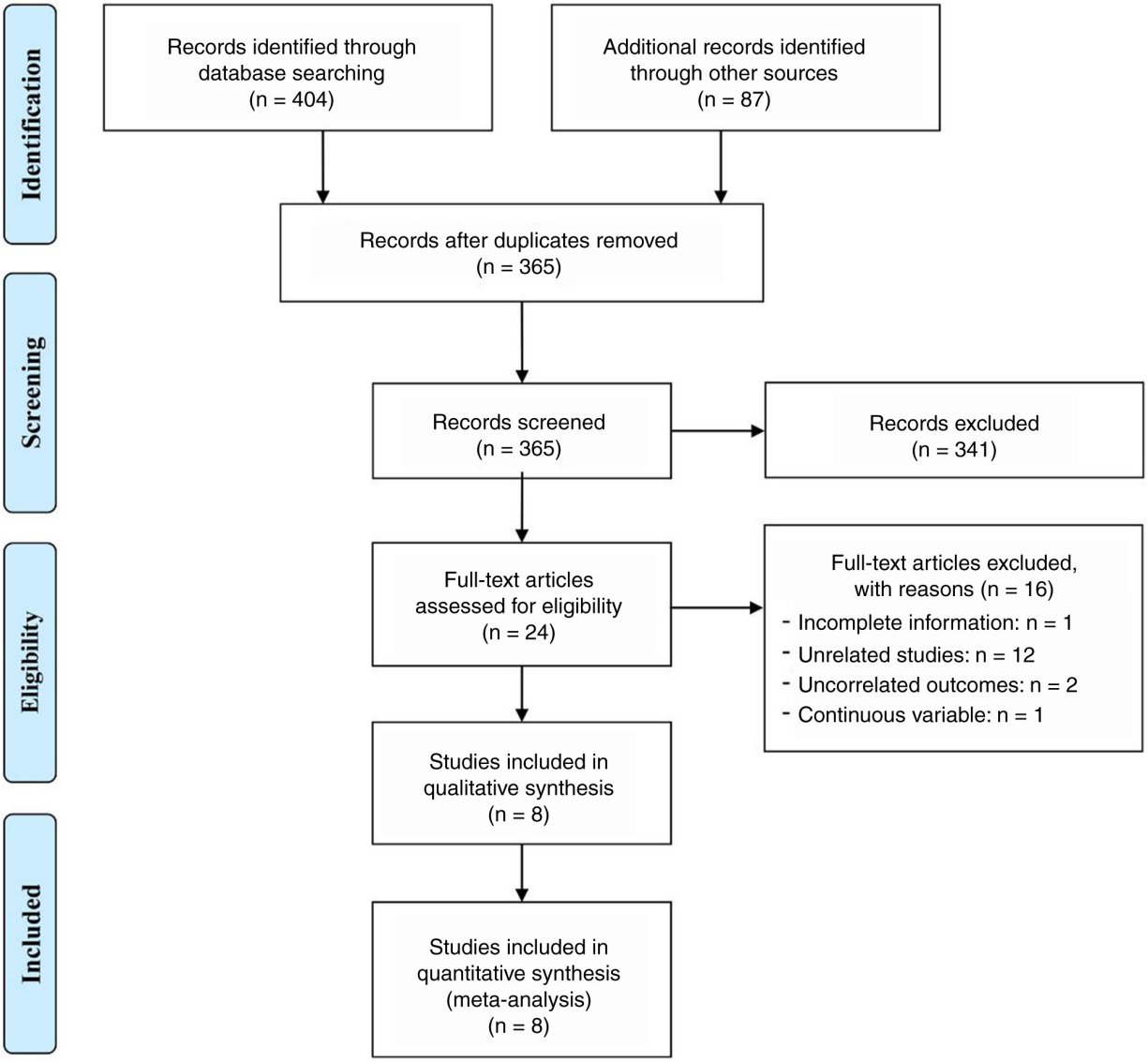

Figure 1. Flow diagram of identifying eligible studies.

by the included studies. Because no universally accepted LCR threshold has been established for GC, this analysis was considered exploratory.

Potential publication bias was assessed using Begg's rank-based test and Egger's regression methodology (15). To determine the stability of the synthesized effect estimates, sensitivity analyses were performed, in which each study was removed one at a time before recalculating the pooled HRs. Statistical significance was defined by a two-sided P-value of 0.05.

Results

Literature search results. A comprehensive literature search in multiple electronic databases, complemented by manual screening of reference lists, yielded 491 articles. After the elimination of 126 duplicates, the remaining articles were evaluated at the title and abstract levels, leading to the exclusion of 341 articles that did not fulfill the established selection criteria. Full-text review was subsequently performed for 24 articles, of which 15 were removed because they did not meet the eligibility requirements related to study design, participant characteristics, or reporting of survival endpoints. In total, eight publications comprising nine independent cohorts were included in the quantitative synthesis (12,16-22) (Fig. 1). Of note, Xiong *et al* (12) reported two independent cohorts, a discovery cohort and a validation cohort, which were analyzed separately because the patient populations were non-overlapping and survival estimates were reported independently.

Characteristics of the included studies. A comprehensive summary of the principal features of the included studies is presented in Table I. Altogether, the nine included studies contributed data from 4,429 patients with GC, with individual cohort sizes ranging between 123 and 774 participants. In terms of geographic distribution, four studies were performed in China, four in Japan, and one in Türkiye. This distribution highlights the regional pattern of currently available evidence.

Regarding treatment context, seven studies focused specifically on patients undergoing surgical treatment, whereas

Table I. Main characteristics of the studies included.

First author, year	Country	Number	Age, years	Male/female, n	Stage information	Treatments	During the study	Cut-off	NOS score	(Refs.)
Matsunaga *et al*, 2023	Japan	101	65.1±11.0	79/22	-	Chemotherapy	01/2017-04/2022	13895	7	(19)
Aoyama *et al*, 2022	Japan	480	68 (32-90)[b]	318/162	-	Gastrectomy	2013-2017	7000	8	(17)
Wang *et al*, 2025	China	763	59.1±11.9	534/229	TNM stage I/II/III/IV: 64/149/274/276	NA	04/2013-12/2022	6452	6	(22)
Xiong *et al*, 2022 (Discovery cohort)	China	774	62.3 (57-70)[a]	639/135	TNM stage I/II/III: 157/243/374	Gastrectomy	04/2011-02/2016	6000	7	(12)
Xiong *et al*, 2022 (Validation cohort)	China	575	≥65/<65: 274/301	439/136	TNM stage I-III	Gastrectomy	03/2016-09/2019	6000	7	(12)
Miyatani *et al*, 2022	Japan	455	≥75/<75: 157/298	332/123	Stage I/II-III: 307/148	Gastrectomy	2005-2018	23800	7	(20)
Angin *et al*, 2021	Türkiye	123	65.4±10.2	83/40	-	Gastrectomy	01/2010-12/2015	1931	6	(16)
Okugawa *et al*, 2019	Japan	551	65.4 (18-90)[b]	387/164	TNM stage I/II/III/IV: 296/86/87/82	Gastrectomy	2001-2011	8350	7	(21)
Cheng *et al*, 2020	China	607	-	196/411	T1-T4	Gastrectomy	01/2013-06/2019	6300	7	(18)

[a]Median (first quartile-third quartile); [b]median (range). Xiong *et al* (12) reported two independent cohorts, namely a discovery cohort and a validation cohort. These two cohorts were listed separately because they included non-overlapping patient populations and provided separate survival estimates. NOS, Newcastle-Ottawa Scale.

the remaining two studies included individuals receiving multimodal therapy. All studies adopted a retrospective observational framework, a design that, despite certain inherent constraints, enabled the extraction of detailed clinical information and laboratory parameters.

Quality assessment based on the NOS yielded scores ranging from 6 to 8, suggesting a generally low risk of bias and reinforcing confidence in the robustness of the synthesized findings. Overall, these study characteristics reflect high methodological quality and provide essential context for interpreting subsequent meta-analysis results.

Pooled analysis of the association between LCR and OS. A total of nine studies fulfilled the eligibility criteria, contributing data from 4,429 individuals diagnosed with GC. In each dataset, patients were categorized into high- and low-LCR groups based on the cut-off values specified in the respective studies. When these data were synthesized, a pronounced survival disadvantage emerged for individuals with reduced LCR values. The pooled hazard ratio for OS was 2.24 (95% CI, 1.97-2.55; P<0.001), indicating that the mortality risk in low-LCR patients was more than twice that in high-LCR patients (Fig. 2).

To assess the consistency of these findings across studies, heterogeneity was examined using both Cochran's Q statistic and the I^2 index. Neither metric suggested meaningful variability: The Q test showed no statistical significance, and the I^2 value was 0% (P=0.453). This absence of detectable heterogeneity suggested that the effect estimates were highly concordant among included analyses. Consequently, a fixed-effects modeling approach was selected as the most appropriate framework for deriving the final pooled results.

Sensitivity analysis and publication bias of the association between LCR and OS. To evaluate the robustness of the pooled effect, a leave-one-out sensitivity analysis was conducted, in which each study was removed sequentially and the overall HR recalculated. This procedure tested whether any single dataset disproportionately affected the combined estimate. The results showed that the exclusion of individual studies produced negligible changes in both effect size and direction, indicating strong internal consistency across the included analyses (Fig. 3A). Although minor fluctuations were observed, the overall pattern remained stable. Removing the study by Miyatani *et al* (20) produced the lowest risk estimate (HR=2.16; 95% CI: 1.89-2.50; P<0.001), whereas omission of the dataset from Wang *et al* (22) resulted in the highest estimate (HR=2.33; 95% CI: 2.01-2.69; P<0.001). Importantly, all recalculated values were directionally aligned and statistically significant, demonstrating that no single investigation materially shaped the final outcome. Collectively, these findings confirm that the observed association between low LCR levels and unfavorable OS in GC is highly robust and not driven by outlier studies. This reinforces the methodological reliability of the quantitative synthesis.

To further evaluate potential distortions arising from selective publication, Begg's rank correlation and Egger's regression tests were applied. Neither test identified significant evidence of bias, with P-values of 0.466 and 0.350, respectively. This conclusion was supported by the symmetrical appearance

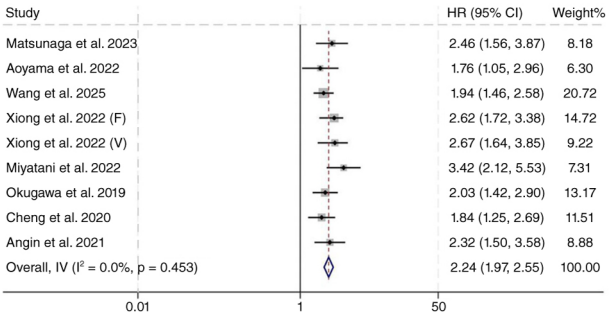

Figure 2. Forest plot illustrating the pooled effect estimates evaluating the relationship between pretreatment lymphocyte-to-C-reactive protein ratio and overall survival in individuals with gastric cancer. HR, hazard ratio; CI, confidence interval.

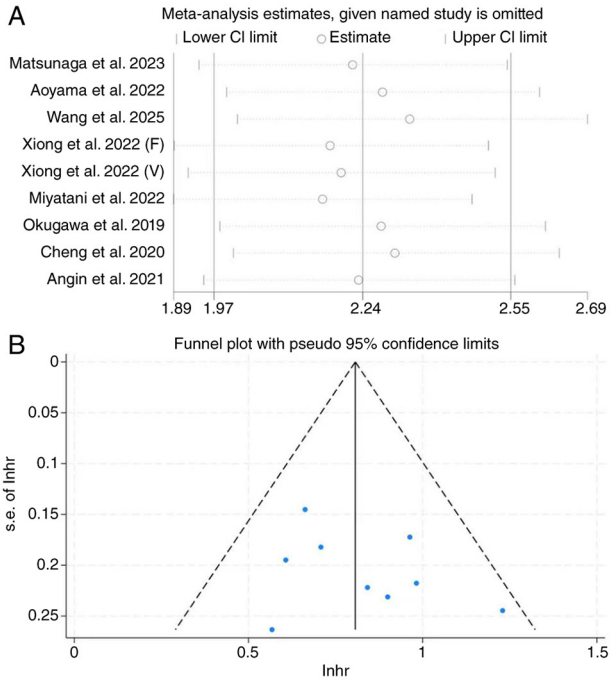

Figure 3. (A) Leave-one-out sensitivity assessment evaluating the stability of the association between the lymphocyte-to-C-reactive protein ratio and overall survival. (B) Funnel plot examining potential publication bias for studies reporting this association. CI, confidence interval.

of the funnel plot, which likewise indicated the absence of publication-related skewness (Fig. 3B).

Subgroup analyses of the association between LCR and OS. To determine whether the prognostic value of LCR was influenced by analytical approach, region, or treatment strategy, a series of predefined subgroup analyses were performed. When stratified by the source of effect estimates, the association between reduced LCR and adverse OS remained highly consistent. Effect sizes derived from univariate analyses indicated a substantial survival disadvantage for patients with low LCR levels (HR=2.66; 95% CI: 2.04-3.46; P<0.001), and this relationship persisted even after adjustment for confounding factors in multivariate models (HR=2.12; 95% CI: 1.83-2.46; P<0.001) (Fig. 4A). These findings suggest that the prognostic relevance of LCR is robust and not dependent on statistical modeling choices.

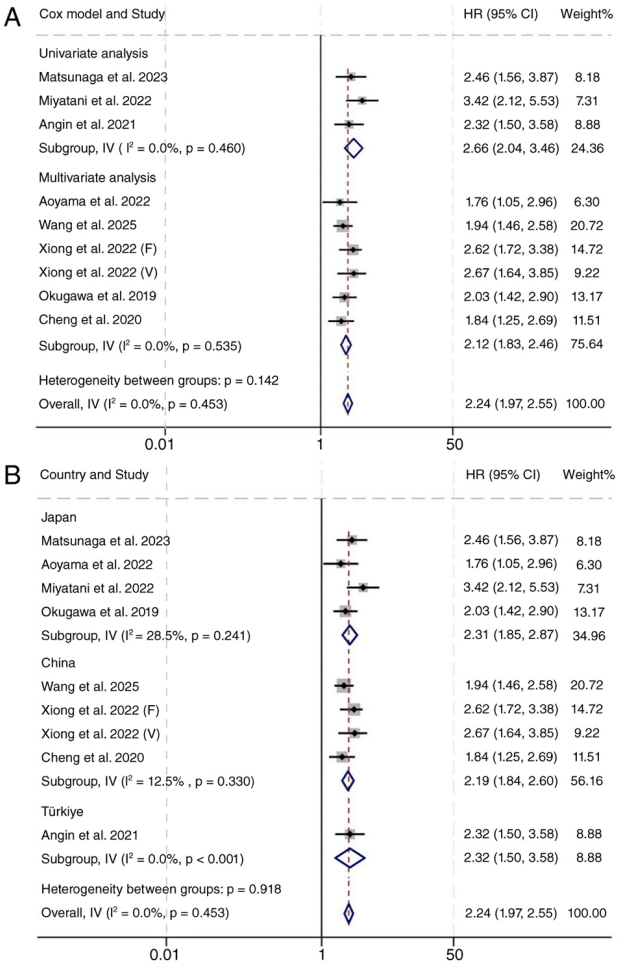

Figure 4. (A) Subgroup analysis based on the type of Cox regression model evaluating the relationship between the lymphocyte-to-C-reactive protein ratio and overall survival. (B) Subgroup analysis classified by study region assessing the same association. HR, hazard ratio; CI, confidence interval.

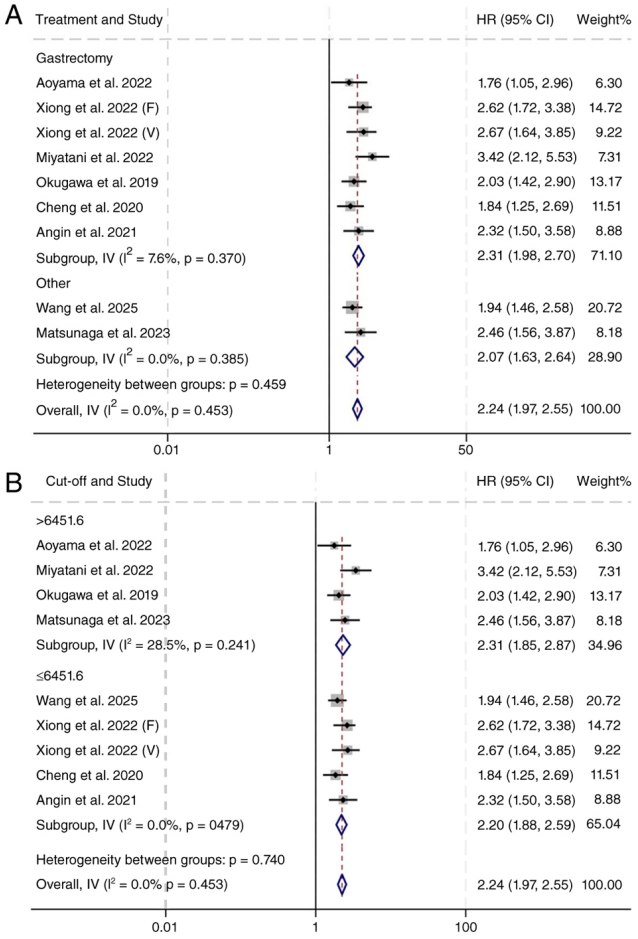

Figure 5. (A) Subgroup analysis stratified by treatment modality assessing the association between the lymphocyte-to-C-reactive protein ratio and overall survival. (B) Subgroup analysis classified by cut-off assessing the same association. HR, hazard ratio; CI, confidence interval.

Geographically stratified analyses further reinforced this conclusion. In studies conducted in Japan, low LCR values were strongly associated with inferior OS, with a pooled HR of 2.31 (95% CI: 1.85-2.87; P<0.001). A similar magnitude of risk was observed among cohorts from China, where low LCR remained a significant predictor of poor survival (HR=2.19; 95% CI: 1.84-2.60; P<0.001) (Fig. 4B). The consistent effect across regions suggests that the prognostic value of LCR transcends geographic and demographic variability.

It was further examined whether treatment modality and LCR cut-off value influenced the prognostic association between LCR and OS. In the treatment-based subgroup analysis, low LCR remained significantly associated with unfavorable OS both in patients undergoing gastrectomy (HR=2.31; 95% CI: 1.98-2.70; P<0.001) and in those receiving other treatment modalities (HR=2.07; 95% CI: 1.63-2.64; P<0.001; Fig. 5A). Similarly, when studies were stratified by the median LCR cut-off value, the association remained significant in both the high cut-off group (>6451.6: HR=2.31; 95% CI: 1.85-2.87; P<0.001) and the low cut-off group (≤6451.6: HR=2.20; 95% CI: 1.88-2.59; P<0.001; Fig. 5B).

Collectively, the subgroup analyses provide compelling evidence that the prognostic effect of low LCR is consistent across diverse analytical frameworks, geographic populations, cut-off and clinical management strategies. These findings highlight the potential of LCR as a broadly applicable biomarker for risk stratification in GC.

Pretreatment LCR and DFS. A total of five eligible studies, encompassing 2,987 individuals diagnosed with GC, were included to investigate the prognostic significance of pretreatment LCR in relation to DFS. In each cohort, patients were stratified into high- and low-LCR subgroups based on the cut-off values defined by the original studies. When these datasets were quantitatively synthesized, low pretreatment LCR was consistently associated with a markedly increased risk of earlier recurrence. The pooled HR for DFS was 2.11 (95% CI: 1.78-2.51; P<0.001), indicating that patients with reduced LCR levels experienced substantially shorter DFS compared with those with higher levels (Fig. 6A).

Between-study heterogeneity was minimal. Cochran's Q test did not reach statistical significance, and the I^2 statistic was 0% (P=0.301), demonstrating that the effect estimates were highly concordant across all included cohorts. Owing to this strong consistency, a fixed-effect model was adopted to generate the final summary estimate. These findings collectively suggest that LCR may serve as a simple and clinically

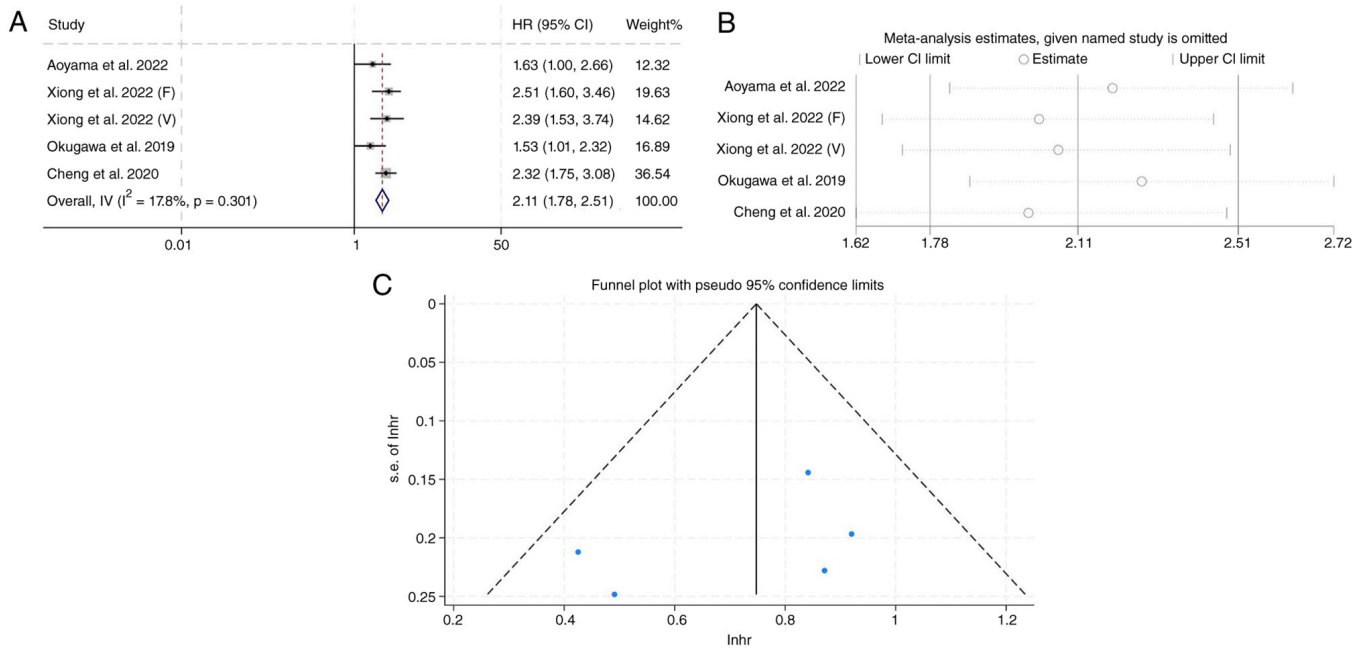

Figure 6. (A) Forest plot presenting the combined hazard ratios for the association between baseline lymphocyte-to-C-reactive protein ratio and disease-free survival in gastric cancer. (B) Leave-one-out sensitivity evaluation demonstrating the robustness of this relationship. (C) Funnel plot assessing potential publication bias among the included studies. HR, hazard ratio; CI, confidence interval.

accessible biomarker capable of identifying patients at elevated risk for early relapse.

Sensitivity analyses further supported the robustness of the pooled results. Sequential omission of individual studies revealed no material changes in the magnitude or direction of the hazard ratio, confirming that the association between reduced LCR and inferior DFS was not driven by any single dataset (Fig. 6B).

Evaluation of publication bias using Begg's rank correlation and Egger's regression also demonstrated no statistically significant evidence of small-study effects (Begg's P=0.462; Egger's P=0.391). The symmetrical appearance of the funnel plot provided additional reassurance that the synthesized results were unlikely to be influenced by selective reporting practices (Fig. 6C). Geographically stratified analyses further reinforced this conclusion (Fig. 7).

Overall, these findings reinforce the prognostic value of pretreatment LCR for predicting disease recurrence in GC and highlight its potential role as a readily applicable tool for risk stratification.

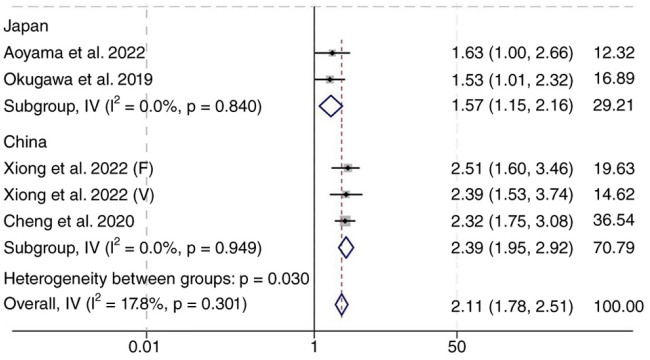

Figure 7. Subgroup analysis stratified by geographic region examining the association between the lymphocyte-to-C-reactive protein ratio and overall survival. HR, hazard ratio; CI, confidence interval.

Discussion

The present meta-analysis is the first to comprehensively assess the prognostic significance of LCR in GC. It was found that lower LCR values consistently indicated poorer survival. Because LCR is derived from routine laboratory measurements, it provides a readily obtainable, reproducible, and economical metric that can complement current prognostic frameworks. Individuals with lower LCR values tended to exhibit a higher risk of postoperative relapse or rapid tumor progression, indicating the potential of this index to refine risk stratification and support more personalized therapeutic decision-making.

The biological significance of LCR as a prognostic indicator is reinforced by evidence highlighting the combined roles of lymphocyte-driven immune activity and CRP-mediated inflammatory signaling in oncogenesis. Lymphocyte abundance has been recognized as a prognostic marker in multiple cancers, including breast, colorectal and pancreatic malignancies (23,24). In addition, specific lymphocyte subsets infiltrating the tumor, such as $CD8^+$ cytotoxic cells and memory T-cell populations, have been associated with more favorable clinical outcomes (25), highlighting the importance of cellular immunity in maintaining antitumor surveillance.

CRP, by contrast, is a classical acute-phase reactant synthesized by hepatocytes under interleukin-2-dependent regulation (26). Compared with other inflammatory markers, CRP exhibits more stable kinetic behavior during inflammation (26). Its elevation, frequently observed in colorectal,

pulmonary and GCs (27), has been associated with adverse pathological features, such as nodal involvement, deeper gastric wall invasion and distant metastasis. Since Virchow first elucidated the conceptual link between inflammation and neoplasia in the nineteenth century (28), the complexity of tumor-host inflammatory interactions remains incompletely defined.

Inflammation within the tumor microenvironment promotes leukocyte apoptosis and margination, resulting in lymphopenia (29). Reduced lymphocyte counts have been associated with poor outcomes in various malignancies (30,31), consistent with the hypothesis that weakened immunosurveillance accelerates tumor evolution and metastatic dissemination. Elevated levels of proinflammatory mediators further promote angiogenesis and metastatic capability. Consequently, systemic inflammation in cancer is usually marked by increased neutrophil and monocyte counts accompanied by decreased lymphocyte counts, indicating enhanced inflammatory activity alongside compromised adaptive immunity.

These mechanistic findings align with the findings of studies investigating inflammation-based biomarkers. Among these biomarkers, the NLR has been thoroughly examined in GC, with elevated preoperative levels consistently associated with shortened survival and more advanced disease (32,33). Similarly, other inflammation-based indices, such as PLR, LMR and CAR, have shown prognostic value in multiple tumor types (34-37). Notably, emerging evidence suggests that markers integrating both inflammatory burden and lymphocyte status can outperform traditional single-parameter indices. Studies on colorectal cancer have reported that LCR provides superior prognostic discrimination compared with other inflammation-based indices (6,38,39). The results of the present study are consistent with these findings.

From a clinical perspective, LCR has several practical advantages. It can be calculated easily from routine blood tests, is inexpensive, and does not require specialized equipment or additional invasive procedures. Therefore, LCR may be useful as an adjunct to existing prognostic systems, such as tumor stage, pathological features and treatment-related factors. Patients with low pretreatment LCR may represent a higher-risk population who require closer surveillance, more individualized perioperative management, or more intensive follow-up strategies. However, LCR should not be considered a replacement for established staging systems. Instead, it may provide complementary prognostic information and help refine risk assessment when used together with conventional clinicopathological parameters.

Several limitations should be considered when interpreting the current findings. First, all included studies were retrospective, which may increase the risk of selection bias and unmeasured confounding. Although multivariate estimates were preferentially extracted when available, residual confounding could not be completely excluded. Second, the protocol of the present meta-analysis was not prospectively registered, which should be acknowledged when considering the methodological transparency of the present systematic review. Third, most included cohorts were derived from East Asian populations, particularly China and Japan. Ethnicity-related differences, dietary habits, *Helicobacter pylori* prevalence, screening practices, baseline nutritional and inflammatory status, stage distribution at diagnosis, and regional treatment strategies may influence both LCR levels and survival outcomes. Differences in lymphadenectomy extent, perioperative or adjuvant chemotherapy, postoperative surveillance, and supportive care may also affect the prognostic performance of LCR. Therefore, extrapolation of these findings to Western and other non-East Asian populations should be made cautiously.

Another important limitation is the lack of a standardized LCR cut-off value among the included studies. Although our exploratory subgroup analysis showed that the association between low LCR and unfavorable OS remained significant across different cut-off subgroups, the optimal threshold for clinical use remains undetermined. Variation in cut-off values may affect clinical interpretation and limit direct application in routine practice. Future prospective multicenter studies with standardized measurement methods and predefined LCR thresholds are needed to validate the present findings and establish an appropriate cut-off value for patients with GC. In addition, some studies provided HRs from different statistical models, and reconstructed estimates from Kaplan-Meier curves may introduce measurement uncertainty when directly reported HRs were unavailable.

In conclusion, the present meta-analysis indicated that a reduced LCR was consistently associated with poor survival outcomes, including both overall and DFS, in GC. As an inexpensive and readily obtainable biomarker, LCR offers robust prognostic value across diverse analytical methods, clinical settings and geographic regions. Its strong and stable predictive performance suggests that LCR may serve as a valuable adjunct to current staging systems, aiding in more precise risk stratification and individualized patient management. Nonetheless, prospective multicenter studies with standardized LCR thresholds are warranted to validate these findings and facilitate its broader clinical application.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

KL and LC conceived and designed the study, performed data collection, statistical analysis and interpretation, drafted the manuscript, and critically revised the manuscript. Both authors have read and approved the final version of the manuscript. KL and LC confirm the authenticity of all the raw data.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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