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Review

Research Progress on Peripheral Blood Inflammatory Markers for Prognostic Evaluation in Ovarian Cancer

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Abstract

Objective: In this review, we summarized recent progress in research on peripheral blood inflammatory markers, including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI), for prognostic evaluation in ovarian cancer (OC), and assessed their predictive value and clinical application potential. **Mechanism:** Chronic inflammation shapes the tumor microenvironment (TME) and drives the progression of OC. Neutrophils, platelets, and monocytes exert pro-tumor inflammatory effects, whereas lymphocytes exert antitumor immune effects. Peripheral blood inflammatory markers (NLR, PLR, LMR, SII, and SIRI) reflect the imbalance between inflammation and immune surveillance, thereby influencing tumor behavior and patient prognosis. **Findings in Brief:** Studies have found that high NLR, PLR, and SII are associated with advanced tumor stage, greater tumor burden, and poor prognosis, whereas high LMR predicts better prognosis. SIRI shows limited prognostic value for survival outcomes due to insufficient evidence and inconsistent results. **Conclusions:** This review demonstrated that NLR, PLR, LMR, and SII are promising, easily accessible, and noninvasive prognostic biomarkers for OC. Their application may assist in risk stratification and clinical decision-making. However, further large-scale, standardized studies are required to validate the clinical utility of SIRI and to establish unified cutoff values for these markers.

Keywords: ovarian cancer; inflammatory markers; prognosis

1. Introduction

Ovarian cancer (OC) is the most lethal malignancy among tumors of the female reproductive system, accounting for approximately 3.4% of all female cancers and 4.8% of cancer-related deaths in women globally [1]. Its incidence has been gradually increasing worldwide. According to the statistics from the American Cancer Society (ACS), there were approximately 313,959 new OC cases and 207,252 OC-related deaths worldwide in 2020. The 2022 updated data showed that the number of new cases increased to 324,398, with a slight decrease in death cases (206,839), which is speculated to be related to advances in surgical and chemotherapeutic techniques [2,3]. The ACS predicted 20,890 new OC cases and 12,730 OC-related deaths in the United States by 2025 [4], further highlighting the persistent threat of OC to women's health.

OC has a subtle onset, lacks specific early clinical manifestations, and does not have effective early screening strategies. Unlike cervical cancer and breast cancer, which can be accurately screened using methods such as the Pap smear and mammography, OC cannot be reliably detected at an early stage, as no widely accepted screening tools are currently available [5]. Therefore, more than 70% of patients with ovarian cancer are diagnosed at International Federation of Gynecology and Obstetrics (FIGO) stage III–IV, with a 5-year survival rate of approximately 40% [6]. Therefore, convenient, cost-effective, and repeatable auxiliary biomarkers are needed to improve prognostic assessment in OC patients. Patients with OC who have similar disease stage, tumor subtype, and identical treatment may still show differences in survival outcomes. Thus, novel prognostic biomarkers are urgently needed to accurately predict patient prognosis and identify novel therapeutic targets [7].

Chronic inflammation is closely associated with the initiation and progression of various chronic disorders, including cardiovascular diseases, diabetes mellitus, and autoimmune diseases [8]. Basic and clinical research have shown that inflammation is also closely associated with tumor initiation, progression, invasion, and metastasis, a phenomenon known as "cancer-related inflammation" [9]. Mantovani et al. [9] first proposed this concept in 2008 and stated that the tumor microenvironment (TME), composed of inflammatory cells (such as neutrophils, lymphocytes, monocytes, and macrophages), cytokines (such as interleukin-6 [IL-6], tumor necrosis factor-α [TNF-α]), and chemokines, promotes tumor angiogenesis, inhibits antitumor immune responses, and enhances tumor cell inva-

sion and metastasis [10]. Within the TME, tumor cells actively remodel surrounding stromal cells and elicit persistent inflammatory responses, accompanied by the proliferation and infiltration of diverse immune cell subsets, ultimately promoting tumor progression [11]. In this context, many researchers have focused on peripheral blood inflammatory markers derived from routine clinical blood tests, as they are convenient, cost-effective, noninvasive, and highly reproducible. These markers reflect the systemic immune-inflammatory status of the host, and their changes are closely associated with the progression and prognosis of OC [12].

Peripheral blood inflammatory markers are mainly categorized into single inflammatory markers and composite inflammatory markers. Single inflammatory markers (such as C-reactive protein, IL-6) often have low specificity and limited predictive performance, as they can be affected by various non-tumor factors, such as infection, inflammation, and autoimmune diseases. In contrast, composite inflammatory markers, constructed via the combination of multiple single inflammatory indicators or blood cell counts, can more comprehensively reflect the balance between systemic inflammatory response and immune function, and exhibit higher specificity and prognostic predictive value in OC [13,14]. Commonly used composite inflammatory markers include neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI). These composite markers integrate the effects of different inflammatory cells and immune cell populations on tumor progression. They can be used to more accurately evaluate the severity of cancer-related inflammation and the status of antitumor immunity; thus, they provide more reliable information for the prognostic evaluation of OC patients.

Herein, we reviewed recent progress on the role of peripheral inflammatory markers in prognostic evaluation of OC. We provided information for investigators and clinicians, aiming to encourage more collaborative research and the development of therapeutic approaches.

2. Methods

In this review, we summarized recent advances in peripheral blood inflammatory markers, including NLR, PLR, LMR, SII, and SIRI, for prognostic evaluation in OC. We aimed to determine the predictive value and clinical application potential of these markers. We integrated existing evidence rather than performing a quantitative pooled analysis. The literature was searched and screened using standardized procedures, as detailed below.

2.1 Data Sources and Search Strategy

A comprehensive literature search was performed in PubMed, Web of Science, and Wiley Online Library up to January 2026. The search was conducted using key terms related to OC, peripheral inflammatory indices, and prognosis.

The searched terms were as follows: (“ovarian cancer” OR “ovarian carcinoma” OR “ovarian malignancy”) AND (“NLR” OR “PLR” OR “LMR” OR “SII” OR “SIRI”) AND (“prognosis” OR “survival” OR “prognostic factor”).

References of included articles and related reviews were also manually screened to ensure that no eligible studies were missed.

2.2 Inclusion and Exclusion Criteria

2.2.1 Inclusion Criteria

The inclusion criteria were as follows: (1) clinical studies focused on the association of NLR, PLR, LMR, SII, or SIRI with prognosis in OC patients; (2) retrospective cohort studies, case-control studies, prospective studies, randomized controlled trials, and meta-analyses; (3) studies reporting associations between inflammatory markers and clinicopathological features, survival, or prognostic outcomes; and (4) retrospective studies including at least 50 participants.

2.2.2 Exclusion Criteria

The exclusion criteria were as follows: (1) studies that did not meet the inclusion criteria; (2) case reports, conference abstracts, editorials, letters, and short communications; (3) basic studies, including only *in vitro* experiments or animal studies without clinical prognostic data; (4) duplicate publications, studies with incomplete data, or those from which valid prognostic information could not be extracted; and (5) studies focusing on other gynecologic malignancies or non-inflammatory prognostic indicators.

2.3 Study Selection Process

To ensure methodological rigor, two independent reviewers (HJ and YW) initially screened all retrieved articles based on the titles and abstracts. Next, the full texts of potentially relevant studies were evaluated to determine final eligibility. Any disagreements between the reviewers during the screening process were resolved through discussion to ensure objectivity and minimize selection bias.

2.4 Summary of Literature Screening

The initial search yielded 2286 records. After removing duplicates, 1664 articles remained. After screening titles and abstracts, 206 irrelevant studies were excluded. The full text of the remaining 326 articles was assessed, and 292 studies were excluded as they did not meet the inclusion criteria. An additional 13 articles were deleted because they were irrelevant or had duplicate conclusions. Finally, 21 studies were included in this review (Fig. 1).

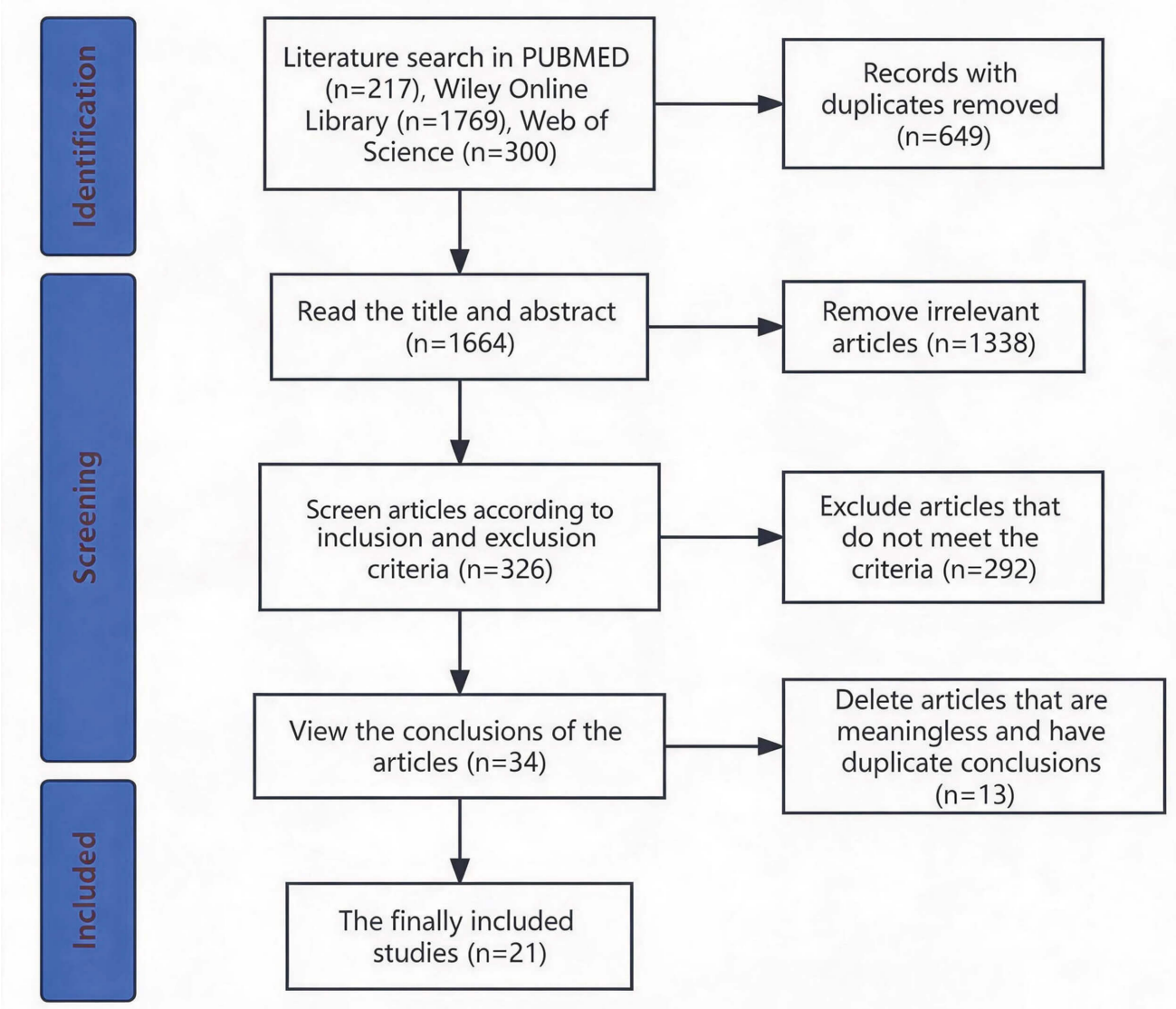

Fig. 1. Study selection process.

3. Associations Between Peripheral Blood Inflammatory Markers and OC

3.1 Neutrophil-to-Lymphocyte Ratio

The NLR is a widely used and comprehensively studied peripheral blood composite inflammatory marker. It is defined as the ratio of peripheral blood neutrophil count to lymphocyte count and reflects the balance between systemic inflammatory response and antitumor immune function. It is an easily accessible and cost-effective inflammatory biomarker. A high NLR is closely associated with tumor growth, invasion, and metastasis across various malignancies and carries significant prognostic implications in different types of cancer, such as gastric and colorectal carcinoma [15]. Although the mechanisms underlying the tumor-promoting effects of NLR remain incompletely elucidated, the tumor-promoting roles of neutrophils have been extensively studied. Neutrophils facilitate angiogenesis, induce chemoresistance, and directly promote tumor metastasis by releasing neutrophil extracellular traps and secreting pro-tumorigenic cytokines, chemokines, and reactive oxygen species [16]. A high NLR often coincides with elevated levels of tumor markers, including carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9), and carbohydrate antigen 72-4 (CA72-4), and is associated with low infiltration of functional antitumor immune cells, such as $CD3^+$ and $CD8^+$ T lymphocytes, in the TME [17]. These findings suggest that NLR may modulate tumor progression through dual pathways involving pro-inflammatory and immunosuppressive effects, providing a theoretical rationale for its application as a prognostic indicator in malignancies.

Studies have established the prognostic value of NLR in OC. Marchetti et al. [18] conducted a retrospective study involving 397 patients with OC and found that a high preoperative NLR was an independent adverse prognostic factor for progression-free survival (PFS) and overall survival (OS) in patients with primary advanced high-grade

Table 1. Characteristics of studies investigating NLR.

Author, year	Study design	Population	Patient characteristics	Cutoff values	Endpoints	Main results
Marchetti et al., 2021 [18]	Retrospective	397 patients	HGSOC, FIGO IIIC–IV	4.02	PFS, OS	High NLR predicts heavier disease burden and poor prognosis.
Zhang et al., 2024 [19]	Meta-analysis	20 retrospective studies	OC	2.30–5.25	PFS, OS	High NLR is associated with shorter survival.
Sowannakul et al., 2023 [20]	Retrospective	56 patients	PS-ROC Patients	2.45	PFS, OS	Prognostic value in PS-ROC remains uncertain.
Kovács et al., 2023 [21]	Retrospective	150 patients	EOC underwent PDS	3.362	Surgical outcomes	High NLR may predict poor surgical outcome.

NLR, neutrophil-to-lymphocyte ratio; HGSOC, high-grade serous ovarian cancer; FIGO, International Federation of Gynecology and Obstetrics; PFS, progression-free survival; OS, overall survival; PS-ROC, platinum sensitive recurrent ovarian cancer; OC, ovarian cancer; EOC, epithelial ovarian cancer; PDS, primary debulking surgery.

serous ovarian cancer (HGSOC). This marker was reliable and independent of the BRCA mutation status. They also found that a high preoperative NLR (≥4.02) in patients with primary advanced OC predicted a greater tumor burden (higher LPS-PIV score) and a higher likelihood of receiving neoadjuvant chemotherapy (NACT) rather than primary cytoreductive surgery (CRS) [18]. Similarly, Zhang et al. [19] conducted a meta-analysis and found that NLR was negatively correlated with PFS and OS in patients with OC. The association was highly significant in studies conducted in Asian populations, young patients (<55 years), small sample sizes (<200), and higher NLR cutoff values (≥3) ($p < 0.01$). However, the underlying causes of these differences require further investigation [19]. In contrast, in patients with platinum-sensitive recurrent ovarian cancer (PS-ROC), Sowannakul et al. [20] found no significant association between NLR and either PFS or OS. As the study sample size was small (only 56 patients), the prognostic role of NLR in PS-ROC should be further validated in larger cohorts. To predict surgical outcomes, Kovács et al. [21] conducted a study involving 150 OC patients and found that a high preoperative NLR (≥3.362) was associated with suboptimal outcomes of primary debulking surgery (PDS) in OC patients ($p < 0.001$), indicating incomplete tumor resection. This finding is consistent with the findings of Zhang et al. [19]. The extent of postoperative residual disease was directly associated with PFS and OS [22], suggesting that preoperative NLR may help guide treatment selection prior to therapy (Table 1, Ref.[18,19,20,21]).

The above evidence strongly indicates that preoperative NLR serves as a readily available and promising prognostic biomarker in OC. It not only predicts poor survival outcomes in primary advanced disease but also is correlated with unfavorable surgical outcomes and a greater tumor burden. However, its prognostic performance varies across different populations, cutoff values, and disease states, with particularly limited evidence in PS-ROC. Future studies are needed to determine the optimal NLR cutoff value, assess its prognostic role in heterogeneous subgroups, and evaluate its value in individualized risk stratification and clinical decision-making.

3.2 Platelet-to-Lymphocyte Ratio

As PLR is a composite index integrating the inflammatory effects of platelets and lymphocytes, it has attracted considerable attention for its prognostic value in OC. Its clinical significance arises from the functional imbalance between platelets and lymphocytes. Platelets can aggregate to form a protective shield that allows tumor cells to evade immune surveillance by natural killer cells and promotes tumor cell adhesion to vascular endothelium, thereby facilitating distant metastasis [23]. Moreover, activated platelets release cytokines, including transforming growth factor-β (TGF-β) and vascular endothelial growth factor (VEGF), which directly stimulate tumor cell proliferation, enhance tumor angiogenesis, and support the formation of a protumorigenic microenvironment [24]. In contrast, lymphocytes represent the core effector cells of antitumor immunity. A high PLR generally reflects a relative reduction in lymphocyte count, indicating impaired antitumor immune function. Such an imbalance between platelet-mediated tumor promotion and lymphocyte-mediated tumor suppression creates a microenvironment that favors OC growth and metastasis.

Genc et al. [25] conducted a retrospective analysis and found that a higher PLR value (≥183.5) was a significant predictor of advanced OC ($p = 0.005$). These findings support PLR as an independent indicator of pathological staging and assessment of disease progression in OC [25]. However, the abovementioned study had several limitations, including a relatively small sample size and the absence of FIGO stage IV patients, which limited the generalizability of the conclusions. Bizon et al. [26] reported similar findings and demonstrated significant differences in PLR between benign and malignant ovarian tumors (163.74 vs. 206.86; $p < 0.001$). The authors suggested that PLR

Table 2. Characteristics of studies investigating PLR.

Author, year	Study design	Population	Patient characteristics	Cutoff values	Endpoints	Main results
Genc et al., 2025 [25]	Retrospective	96 patients	Stage I–III OC underwent PDS	183.50	Staging	High PLR is associated with advanced stage.
Bizon et al., 2025 [26]	Meta-analysis	22 studies (5740 patients)	OC	Benign: 163.74; Malignant: 206.86	Diagnosis, staging	High PLR is related to malignancy and advanced stage.
Akyol et al., 2025 [27]	Retrospective	188 patients	OC underwent CRS	145.30	Postoperative complications	High PLR correlates with higher complication rate.
Winata et al., 2024 [28]	Meta-analysis	16 studies (3862 patients)	OC	Not mentioned	PFS, OS	High PLR is associated with poorer PFS and OS.
El Bairi et al., 2021 [29]	Meta-analysis	6 retrospective studies	EOC	Not mentioned	PFS, OS	High PLR is associated with poorer PFS and OS.

PLR, platelet-to-lymphocyte ratio; CRS, cytoreductive surgery.

combined with transvaginal ultrasound or the ROMA index can improve the prediction concerning the diagnosis and prognosis of OC, especially in premenopausal women, and may facilitate preoperative tumor assessment and risk stratification to optimize patient prognosis [26].

Akyol et al. [27] analyzed patients undergoing CRS for OC and found that most patients with a high PLR (≥145.3) did not receive preoperative NACT. These patients had significantly lower preoperative Hb, Hct, and lymphocyte counts ($p < 0.05$), significantly higher neutrophil, platelet, and CA-125 levels ($p < 0.05$), and significantly higher postoperative platelet counts ($p < 0.01$). A high PLR was associated with prolonged hospital stay and an increased risk of postoperative complications ($p < 0.05$). However, the study only included patients who underwent CRS, which limits the generalizability of the findings to the overall population [27]. Several meta-analyses revealed that a high preoperative PLR is associated with shorter PFS and OS in patients with OC [28,29], suggesting that PLR may serve as a promising prognostic biomarker for OC. However, these meta-analyses did not indicate specific cutoff values (Table 2, Ref. [25,26,27,28,29]).

In summary, PLR represents a promising and readily available biomarker for OC, with potential value in staging, differential diagnosis, prediction of surgical outcomes and postoperative complications, and prognosis. However, the existing evidence is limited by small sample sizes, highly selective patient populations, lack of standardized cutoff values, and insufficient adjustment for confounding factors, including age, comorbidities, and smoking. Further large-scale, well-designed studies are therefore warranted.

3.3 Lymphocyte-to-Monocyte Ratio

The LMR is defined as the ratio of lymphocytes to monocytes in peripheral blood, and its dynamic changes reflect the homeostatic balance of systemic immune function, which is closely associated with the development and progression of OC. Lymphocytes serve as key mediators of antitumor immunity by recognizing abnormal signals (tumor antigens) on the surface of malignant cells, initiating specific immune responses, and ultimately inducing tumor cell death, clearance, or growth inhibition [30]. In contrast, monocytes exhibit a dual role in tumor biology. In the TME, stimulation with pro-inflammatory signals, such as interferon-γ drives the differentiation of monocytes into M1-type macrophages and dendritic cells, which exert direct antitumor effects or enhance antitumor immunity indirectly through cytokine secretion. However, tumor cells can also secrete TGF-β, VEGF, IL-10, and other factors to redirect monocyte differentiation toward anti-inflammatory M2-type macrophages, which promote angiogenesis, enhance tumor invasion and metastasis, and suppress antitumor immunity. In chronic inflammation, sustained tumor growth decreases the secretion of pro-inflammatory mediators such as IL-1β and TNF-α by M1-polarized macrophages, promoting macrophage differentiation toward an M2-like phenotype. Therefore, monocyte count may provide insights into tumor burden in patients with cancer [31,32].

The LMR is correlated with tumor stage in OC patients and serves as an independent prognostic factor for PFS and OS. A lower preoperative LMR (<2.07) is associated with more advanced tumor stage and poorer prognosis, whereas patients with a higher LMR (≥2.07) show better response to chemotherapy [33]. Gong et al. [34] conducted a meta-analysis and validated these findings. They reported that low preoperative LMR was associated with high-grade (G2/G3) histology, high serum CA-125 levels, malignant ascites, and lymph node metastasis ($p < 0.05$), supporting its role as a potential biomarker of unfavorable prognosis in OC. However, the study did not find an association between LMR and patients' age or histological type, and the reported cutoff values remained inconsistent, ranging from 1.85 to 4.2 [34]. Song et al. [35] reported that preopera-

Table 3. Characteristics of studies examining LMR.

Author, year	Study design	Population	Patient characteristics	Cutoff values	Endpoints	Main results
Eo et al., 2016 [33]	Retrospective	234 patients	EOC	2.07	PFS, OS	Low LMR is an independent risk factor for poor OS.
Gong et al., 2019 [34]	Meta-analysis	8 studies (2259 patients)	OC	ranged from 1.85 to 4.20	PFS, OS, staging, lymph node metastasis	Low LMR is associated with advanced stage and poor survival.
Song et al., 2023 [35]	Retrospective	991 patients	OC	3.39	RFS, OS, staging	Low LMR indicates high tumor burden and short RFS.
Tang et al., 2020 [36]	Retrospective	214 patients	OC underwent PDS	3.80	PFS, OS	Low LMR predicts shorter PFS and OS.

LMR, lymphocyte-to-monocyte ratio; RFS, recurrence-free survival.

tive LMR serves as an independent prognostic predictor in OC. In their study, a low LMR (<3.39) was associated with advanced FIGO stage, lymph node metastasis, and higher CA-125 levels, suggesting a higher tumor burden, which is consistent with previous studies. The researchers also found that LMR had higher predictive efficacy for survival prognosis compared to NLR and PLR [35]. Moreover, to investigate the prognostic value of LMR in OC, Tang et al. [36] combined LMR with CA-125 (COLC) and found that COLC had greater predictive efficacy for PFS and OS in OC patients than LMR alone. However, the prognostic significance of LMR remains controversial across different histological subtypes of OC. For example, Qin [37] found that although low preoperative LMR predicted poor prognosis in serous ovarian adenocarcinoma, the correlation was not significant ($p > 0.05$), suggesting that LMR may not be suitable as a universal prognostic marker for serous OC (Table 3, Ref. [33,34,35,36]).

However, the above studies have several limitations. Most were retrospective in nature with relatively small sample sizes, and many studies were conducted exclusively in Asian populations. Additionally, unified and standardized cutoff values for LMR are lacking across studies. These limitations restrict the reliability and generalizability of the available evidence. To establish this convenient, simple, and inexpensive prognostic factor for risk stratification, large-scale, standardized studies are warranted.

3.4 Systemic Immune-Inflammation Index

The SII is a quantitative biomarker integrating neutrophil, platelet, and lymphocyte counts, enabling comprehensive evaluation of systemic immune and inflammatory status. A high SII may result from increased neutrophils, increased platelets, and/or decreased lymphocytes, and can be regarded as a composite index reflecting the integrated effects of NLR and PLR. Compared with NLR and PLR, SII uses the product of neutrophil and platelet counts as the numerator, making it more sensitive to fluctuations in systemic immune-inflammatory status. SII has the advantages of easy accessibility and high clinical applicability, and its three-component structure allows a more comprehensive reflection of systemic inflammation. Several studies have validated the prognostic value of SII in various malignancies, including gastric and breast cancer [38,39]. Additional studies have also confirmed its clinical utility in OC.

Chen et al. [40] performed a retrospective study and reported that a high preoperative SII (≥998.87) was significantly associated with advanced FIGO stage, lymph node metastasis, bilateral ovarian involvement, positive resection margins, peritoneal metastatic lesions, ascites, and vascular invasion in OC patients ($p < 0.05$). Similarly, Mao et al. [41] conducted a meta-analysis and confirmed that a high SII (≥720) was an independent prognostic factor for shorter PFS and OS in patients with OC ($p < 0.001$), regardless of treatment regimen, including surgery, chemotherapy, radiotherapy, and targeted therapy. However, the meta-analysis was limited by a substantial imbalance in the number of patients across treatment groups; for example, 423 patients received platinum-based chemotherapy, whereas only 108 patients received bevacizumab. Additionally, patients who underwent NACT combined with surgery were not included, which may have introduced bias [41]. Other researchers have proposed SII as a predictive marker of chemotherapy response in OC: higher SII values (≥2223.15) were correlated with a greater reduction in the peritoneal cancer index, indicating enhanced chemosensitivity. SII also showed high accuracy in predicting resistance to platinum-based therapy. Therefore, pretreatment SII assessment may help identify patients with poor response to chemotherapy and facilitate the development of personalized therapeutic strategies, including those who may benefit from bevacizumab combination therapy [42]. Additionally, Farolfi et al. [43] analyzed patients with recurrent epithelial OC (EOC) who were administered platinum-based chemotherapy. They found

Table 4. Characteristics of studies investigating SII.

Author, year	Study design	Population	Patient characteristics	Cutoff values	Endpoints	Main results
Chen et al., 2025 [40]	Retrospective	154 patients	EOC underwent complete staging surgery	998.87	Clinicopathological features, OS	High SII correlates with advanced stage and poor prognosis.
Mao et al., 2023 [41]	Meta-analysis	6 studies, (1546 patients)	OC	720	PFS, OS	High SII predicts poorer OS and PFS.
Bektaş et al., 2025 [42]	Retrospective	79 patients	FIGO ≥IIIC EOC underwent IDS	2223.15	Chemotherapeutic efficacy, PCI reduction	High SII is correlated with increased chemosensitivity.
Farolfi et al., 2020 [43]	Retrospective	375 patients	FIGO III–IV EOC	730	PFS, OS, chemoresponse	High SII predicts poor prognosis in platinum-sensitive recurrent EOC.

SII, systemic immune-inflammation index; IDS, interval debulking surgery; PCI, peritoneal cancer index.

Table 5. Characteristics of studies examining SIRI.

Author, year	Study design	Population	Patient characteristics	Cutoff values	Endpoints	Main results
Salima et al., 2025 [44]	Retrospective	327 patients	Benign and malignant ovarian tumors	3.50 (malignant) vs. 2.97 (benign)	Diagnosis	SIRI is significantly higher in malignant tumors.
Ronsini et al., 2025 [45]	Multicenter prospective	94 patients	Benign, borderline and malignant ovarian tumors	0.76 (benign) vs. 1.36 (borderline) vs. 2.73 (malignant)	Diagnosis	SIRI increases with malignancy and shows better diagnostic efficacy than CA-125.
Huang et al., 2021 [46]	Retrospective	75 patients	OC	1.25 (stage I–II) vs. 1.81 (stage III–IV)	Tumor staging	SIRI is significantly higher in advanced-stage OC.
Köse et al., 2025 [47]	Retrospective cohort	139 patients	OC underwent surgery	Data not available	Postoperative complications (CDC ≥3)	Preoperative SIRI is associated with severe postoperative complications.

SIRI, systemic inflammation response index; CDC, Clavien–Dindo classification.

that SII was not associated with PFS or OS in patients with platinum-resistant recurrent EOC, but was significantly correlated with both survival endpoints in those with platinum-sensitive recurrent EOC. A higher SII (≥730) was associated with shorter PFS and OS (Table 4, Ref. [40,41,42,43]) [43].

These findings suggest that SII has adverse prognostic value in OC. However, SII cutoff values differ considerably across studies, and the sample selection processes were potentially biased. Therefore, larger, prospective, multicenter, and standardized studies are needed to establish a unified SII cutoff value and validate its clinical utility.

3.5 Systemic Inflammation Response Index

The SIRI is another important peripheral blood composite inflammatory marker, constructed based on the neutrophil, monocyte, and lymphocyte counts. It reflects the balance between the inflammatory response mediated by neutrophils and monocytes, and the immune response mediated by lymphocytes. It can be regarded as a comprehensive indicator of NLR and LMR. Both neutrophils and monocytes can promote tumor progression by secreting inflammatory factors, enhancing tumor angiogenesis, and inhibiting immune function, whereas lymphocytes inhibit tumor progression through cytotoxic activity against tumor cells. The interaction among these three cell types directly affects tumor behavior and patient prognosis.

Only a few research groups have investigated the relationship between SIRI and OC. Studies have confirmed that the cutoff value of SIRI is significantly higher in malignant ovarian tumors than in benign OC (3.50 vs. 2.97; $p = 0.042$) [44]. Ronsini et al. [45] also reported that SIRI levels increase from benign and borderline ovarian tumors to malignant tumors (0.76 vs. 1.36 vs. 2.73; $p < 0.001$), with diagnostic performance for OC exceeding that of CA-125. Huang et al. [46] conducted a retrospective analysis of 75 patients with OC and found that SIRI levels were significantly higher in patients with advanced-stage (III–IV)

disease than in those with early-stage (I–II) disease (1.81 vs. 1.25; $p < 0.001$). A positive correlation was also found between SIRI and CA-125 ($p < 0.05$) [46], which may help clinicians assess tumor malignancy, invasive and metastatic potential, and risk of disease progression in ovarian tumors, providing a reliable auxiliary reference for clinically evaluating disease severity and prognosis in patients with advanced OC. In a retrospective study involving 139 patients with OC, postoperative complications were graded using the Clavien–Dindo classification (CDC). The results revealed a significant association between preoperative SIRI and the occurrence of severe complications (CDC grade ≥ 3; $p = 0.022$), suggesting potential utility in optimizing perioperative management and reducing the risk of postoperative complications (Table 5, Ref. [44,45,46,47]) [47].

Direct evidence confirming the association between SIRI and PFS or OS in patients with OC is lacking. Therefore, large-sample, multicenter clinical studies are needed to clarify the prognostic value of SIRI in patients with OC.

4. Discussion

A complex pathophysiological interaction exists between inflammation and OC. In this review, we included multiple inflammatory markers with standardized methodology, focused content, and clear clinical relevance. We found that preoperative NLR, PLR, and SII are negatively correlated with the prognosis of OC, whereas LMR is positively correlated with prognosis. However, the association between SIRI and PFS or OS in patients with OC remains incompletely established, and thus further research is warranted.

Although peripheral blood composite inflammatory markers have promising clinical potential in the prognostic evaluation of OC, existing studies have several limitations. First, unified cutoff criteria for most composite inflammatory markers are lacking. The cutoff values used in different studies vary considerably, which is related to factors such as study population, detection methods, statistical approaches, ethnic differences, and clinical characteristic [19]. Second, most studies are retrospective, with selection bias, small sample sizes, and short follow-up; therefore, they do not adequately validate long-term prognostic value. Third, non-neoplastic factors, such as infection, menstruation, immune system diseases, medication history, or other comorbidities, may also affect systemic inflammatory marker values. Therefore, clinical interpretation should consider patient medical history and physiological status of improve the accuracy of prognostic evaluation. Fourth, the utility of composite inflammatory markers in patients with OC across different pathological subtypes and treatment stages requires further evaluation.

Further research into cancer-related inflammation and the pathogenesis of OC will broaden the potential application of peripheral blood composite inflammatory markers in prognostic evaluation of OC. In the future, large-sample, multicenter, prospective studies with long-term follow-up are needed to establish unified cutoff criteria for composite inflammatory markers and enhance their clinical application value. A combined multi-indicator prognostic model can be constructed by integrating tumor markers, imaging indicators, and clinicopathological features, thereby further improving the accuracy and reliability of prognostic evaluation for OC.

5. Conclusions

In this review, we preliminarily demonstrated that higher NLR, PLR, and SII, as well as lower LMR are associated with a higher disease burden and poorer prognosis in OC patients. Additionally, PLR may be used for the diagnosis of OC. Higher SIRI is mainly associated with the diagnosis, staging, and complications of OC, whereas its relationship with patient survival remains unclear.

Abbreviations

OC, ovarian cancer; ACS, American Cancer Society; FIGO, International Federation of Gynecology and Obstetrics; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; SII, systemic immune-inflammation index; SIRI, systemic inflammation response index; PFS, progression-free survival; OS, overall survival; CDC, Clavien–Dindo classification; IL-6, interleukin-6; TNF-α, tumor necrosis factor-α; TGF-β, transforming growth factor-β; VEGF, vascular endothelial growth factor; HGSOC, high-grade serous ovarian cancer; PS-ROC, platinum-sensitive recurrent ovarian cancer; TME, tumor microenvironment; NACT, neoadjuvant chemotherapy; CRS, cytoreductive surgery; PDS, primary debulking surgery; RFS, recurrence-free survival.

Author Contributions

HJ, JW, and YW designed the research study. HJ wrote the manuscript. YZ performed literature retrieval and sorting. XX and YS participated in data acquisition and analysis. JW performed manuscript review. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

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Conflicts of Interest

The authors declare no conflicts of interest.

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