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Association between alteration of neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, cancer antigen-125 and surgical outcomes in advanced stage ovarian cancer patient who received neoadjuvant chemotherapy

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ABSTRACT

Introduction: Optimal resection significantly influences the prognosis of advanced-stage epithelial ovarian cancer (EOC) patients undergoing debulking surgery. In patients who received neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS), the determination of the ideal timing for surgery remains a challenge. Inflammatory markers, including the neutrophil-to-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and CA-125 levels, have been recognized as potential predictive markers.

Objective: This study aims to evaluate the predictive value of changes in NLR, PLR, and CA-125 levels following NACT, specifically assessing their impact on surgical outcomes during IDS for advanced-stage EOC.

Methods: A retrospective cohort study enrolled advanced-stage EOC patients who underwent NACT followed by IDS at Vajira Hospital in Thailand from January 2009 to June 2023. Data on clinical, surgical, and inflammatory markers were collected, and the predictive value of these markers for suboptimal resection outcomes was assessed.

Results: Among the 65 patients, 98.5 % exhibited radiologic responses post-NACT, while 29.2 % experienced suboptimal resections. Univariate analysis did not reveal significant associations between suboptimal resection and NLR changes after the first NACT cycle or alterations in NLR, PLR, and CA-125 levels at the end of NACT. Subsequent analysis suggested that an NLR decrease exceeding 70 % after the first cycle and NACT completion might predict suboptimal resection, yet statistical analyses showed limited prognostic efficacy (AuROC = 0.608 and 0.597).

Conclusion: Our study does not support that changes in NLR, PLR, platelet count, and CA-125 levels after NACT reliably predict IDS outcomes. Additional prospective investigations using larger cohorts or a combination of evaluation methods, rather than relying solely on NLR, are recommended.

1. Introduction

Ovarian cancer ranks eighth among the most prevalent cancers worldwide, with a global incidence of 6.6 per 100,000 (Huang et al., 2022). Notably, two-thirds of patients received their diagnosis at an advanced stage, with a corresponding 5-year survival rate of only 30 % (Siegel et al., 2022). The standard treatment for advanced ovarian cancer includes primary debulking surgery followed by platinum-based chemotherapy. One of the most important factors in predicting the prognosis for advanced ovarian cancer is achieving optimal or complete resection after cytoreductive surgery (Bryant et al., 2022).

In certain patients with specific conditions, such as those with unresectable advanced-stage disease, an alternative approach could be considered. Neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS) may offer advantages, including enhanced surgical outcomes and the preservation of organs and function, without adversely affecting overall survival (Berek et al., 2021; Machida et al., 2020) .

A practice guideline, as per publication, suggests restricting NACT to a maximum of 4 cycles before IDS. This recommendation includes clinical assessments, routine measurement of cancer antigen-125 (CA-125) each cycle, and radiographic imaging, preferably performed after 3 cycles of chemotherapy (Wright et al., 2016). Contrary to this guidance, recent studies (Marchetti et al., 2021; Perrone et al., 2023) indicate that

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the number of NACT cycles, exceeding 4, does not significantly worsen surgical outcomes or patient prognosis. Consequently, determining the optimal timing for IDS remains a challenging aspect, especially when NACT requires more than three cycles.

Effectively predicting the achievement of an optimal resection following NACT is crucial to reducing the number of required cycles and avoiding premature exploratory laparotomies. This necessitates a comprehensive evaluation of various factors related to the patient, tumor characteristics, and treatment response. Various approaches have been utilized for this evaluation, encompassing the assessment of CA-125 levels before IDS (Furukawa et al., 2013), analysis of the change in CA-125 levels from the commencement of the first NACT cycle to the completion of the last cycle (Zhang et al., 2018), ultrasound evaluation (Testa et al., 2012), assessment of radiologic responses using the Response Evaluation Criteria in Solid Tumors (RECIST) criteria, and laparoscopic evaluation (Fagotti et al., 2010). However, it is important to note that there is currently no widely accepted standard guideline for this specific clinical scenario.

Several inflammatory markers have been investigated in their role to predict optimally resection in advanced stage ovarian cancer including neutrophil–lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), eosinophil-lymphocyte ratio (ELR), monocyte-lymphocyte ratio (ELR), systemic immune inflammation index (SII—platelet × neutrophil–lymphocyte ratio), ENL (eosinophil × neutrophil)/lymphocyte, fibrinogen-albumin ratio(FAR) (Bizzarri et al., 2023; Yang et al., 2020) .

In 1863, Rudolf Virchow observed leukocyte infiltration in neoplastic tissues and hypothesized a correlation between the origins of cancer and sites of chronic inflammation (Balkwill and Mantovani, 2001). Subsequently, numerous researchers have identified various types of leukocyte infiltrates present in nearly all tumors, demonstrating their potential to influence oncogenesis, tumor growth, and metastasis (Coussens and Werb, 2002; Balkwill and Mantovani, 2012). Furthermore, immune responses to cancer can stimulate local non-specific inflammation that extends to the systemic level and modifies metabolism to control cancer growth (Maccio and Madeddu, 2012; Medzhitov et al., 2012).

Various inflammatory markers have been examined as predictors of prognosis in different cancers. High neutrophil counts, elevated platelet counts, and a high NLR have been identified as predictors of shorter survival in renal cell carcinoma and lung cancer (Fox et al., 2013; Winther-Larsen et al., 2022). Additionally, increase in NLR and PLR at initial diagnosis is associated with the aggressiveness and extent of metastasis in ovarian cancer patients, and lower NLR are associated with better overall survival and progression-free survival (Ethier et al., 2017; Zhang et al., 2023; Chen et al., 2018; Manrriquez et al., 2020).

When assessing patients with advanced ovarian cancer who underwent NACT followed by IDS, prior research indicates that the pretreatment NLR value cannot reliably predict the response to NACT. However, the change in NLR after three NACT cycles serves as a predictive indicator for NACT response (Sanna et al., 2021). In a separate retrospective study involving 214 patients, it was found that a change in NLR exceeding 17 % and the resolution of thrombocytosis could predict optimal resection outcomes at the time of IDS (Gulseren et al., 2020).

The principal objective of this research is to explore the correlation between variations NLR levels before and after the completion of NACT and the suboptimal surgical outcome of IDS within the Thai population. This study takes into consideration disparities in demographic characteristics and the extent of surgery, distinguishing itself from previous research. Furthermore, the secondary objective is to probe into the potential associations between changes in NLR after one cycle of NACT and variations oin PLR and CA-125 levels following NACT, as well as their respective impacts on IDS outcomes.

2. Materials and methods

Following the approval of the proposal by the university's ethics committee, a retrospective cohort study was carried out. The medical records of patients diagnosed with International Federation of Gynecology and Obstetrics (FIGO) stage IIIC or IV EOC who received NACT followed by IDS at Vajira Hospital, Thailand, between January 1, 1997, and June 31, 2023, were reviewed. Inclusion criteria encompassed patients who received a minimum of 2 cycles of carboplatin-paclitaxel NACT, had their blood tests conducted at Vajira Hospital, and possessed complete clinical information. Conversely, individuals with other synchronous or metachronous cancers, as well as those afflicted with conditions known to impact NLR, such as recent administration of G-CSF, connective tissue diseases, endometriosis, HIV infection, acute myocardial infarction, sepsis, or acute trauma, were excluded from the study.

Data extraction involved the retrieval of information from patients' medical records, including age, tumor histology, FIGO stage, the number of NACT cycles administered, radiologic response evaluated in accordance with the RECIST criteria, the duration between the final NACT cycle and IDS, the location of metastasis at the time of IDS, and the surgical outcome, which encompassed both the size and extent of residual tumor following IDS.

The surgical outcomes were subsequently categorized into two groups: optimal resection, defined as the absence of any residual tumor or the presence of residual tumor measuring 1 cm or less in size at the time of IDS; and suboptimal resection, characterized by the presence of residual tumor exceeding 1 cm in size at the time of IDS.

Inflammatory and biochemical markers, including NLR (calculated by dividing the absolute neutrophil count by the absolute lymphocyte count), PLR (calculated by dividing the absolute platelet count by the absolute lymphocyte count), platelet count, and CA-125, were documented at three specific time points: before the first cycle of NACT (T0), within two days before the initiation of the second cycle of NACT (T1), and 21–30 days after completion of NACT, before IDS (T3). The changes in NLR from T0 to T1 were computed using the formula (NLR T0 - NLR T1)/NLR T0, while changes in NLR, PLR, platelet count, and CA-125 from T0 to T3 were determined using the formula (Marker T0 - Marker T3)/Marker T0.

3. Statistical analysis

The sample size was determined, requiring a minimum of 64 patients. The data were summarized using descriptive statistical methods. Qualitative variables include histology, FIGO stage, outcomes of IDS, intraoperative site of metastasis, regimen and number of cycles of NACT, radiologic response, and residual tumor were presented using frequency and percentage, and comparisons between the suboptimal and optimal resection groups were made using the Chi-squared test or Fisher's test, as appropriate. Quantitative variables include age, time to surgery, NLR, PLR, CA-125, platelet count, change in NLR, change in PLR, and change in CA-125 were represented using mean, median and standard deviation, and comparisons between the optimal and suboptimal resection groups were conducted using the student's *t*-test or Mann-Whitney *U* test, as appropriate. Significance was denoted by a p-value of <0.05.

The association between inflammatory markers (NLR, PLR, CA-125, changes in NLR, changes in PLR, and changes in CA-125) and surgical outcomes was assessed through multiple logistic regression analysis, presenting results as Odds ratios (OR) with corresponding 95 % confidence intervals (95 % CI), and p-values with a threshold of <0.05. The accuracy in predicting the surgical outcome of IDS was evaluated using Receiver Operating Characteristic (ROC) analysis, including the area under the curve (AUC). The optimal cut-off point was determined using the Yoden's index, which provided sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV), along with the AUC of the ROC curve and its 95 % CI. All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 28.0 (IBM Corp., Armonk, NY, USA) and Stata version 13.0 (StataCorp, College Station, TX, USA).

4. Result

Ninety patients diagnosed with advanced ovarian cancer initially met the inclusion criteria. However, 25 patients were subsequently excluded from the analysis. The reasons for exclusion included 12 patients with incomplete medical record data, 2 patients with synchronous breast cancer, 1 patient with rheumatoid arthritis, and 1 patient with non-epithelial ovarian cancer. Additionally, nine patients were excluded from the study due to modifications in their chemotherapy regimens. Of these, six patients exhibited intolerance to chemotherapy toxicity, while three patients experienced disease progression during NACT (Fig. 1).

Among the 65 patients, the average age was 56.82 years, with a standard deviation of 10.39. Approximately two-thirds of them had high-grade serous carcinoma(HGSC) histology. All patients were administered a carboplatin regimen at an area under the curve (AUC) of 5–6, combined with paclitaxel at a dose of 175 mg/m2, given every 3–4 weeks, with a median cycle of 3 (ranging from 3 to 4). Following the final NACT cycle, nearly all patients (98.5 %) demonstrated either complete or partial responses as assessed by computer tomography, following the RECIST criteria. The median duration between the last NACT cycle and IDS was 33 days (ranging from 28.5 to 40.5). During surgery, the predominant presence of cancer was observed in the omentum, ascites, and peritoneal surfaces.

When comparing surgical outcomes, 46 of the patients (70.8 %) achieved optimal resection, while 19 of them (29.2 %) had suboptimal resection. The two groups were similar in terms of age, stage, histology, the number of NACT cycles, radiologic response, and the time to surgery. However, peritoneal implantation was significantly more prevalent in the suboptimal resection group (p-value 0.031) (Table 1).

The results of the inflammatory and biochemical markers, which include NLR, PLR, platelet count, and CA-125 at three distinct time points - before NACT (T0), after the first cycle of NACT (T1), and after completion of NACT (T3), are presented in Table 2. Upon conducting crude analysis, it was observed that there were no statistically significant variations between the optimal and suboptimal resection groups at all three time points. Furthermore, the changes in NLR after the first NACT cycle and after completion of NACT, the changes in PLR after completion of NACT, and the changes in CA-125 after completion of NACT also displayed no significant disparities between the two groups.

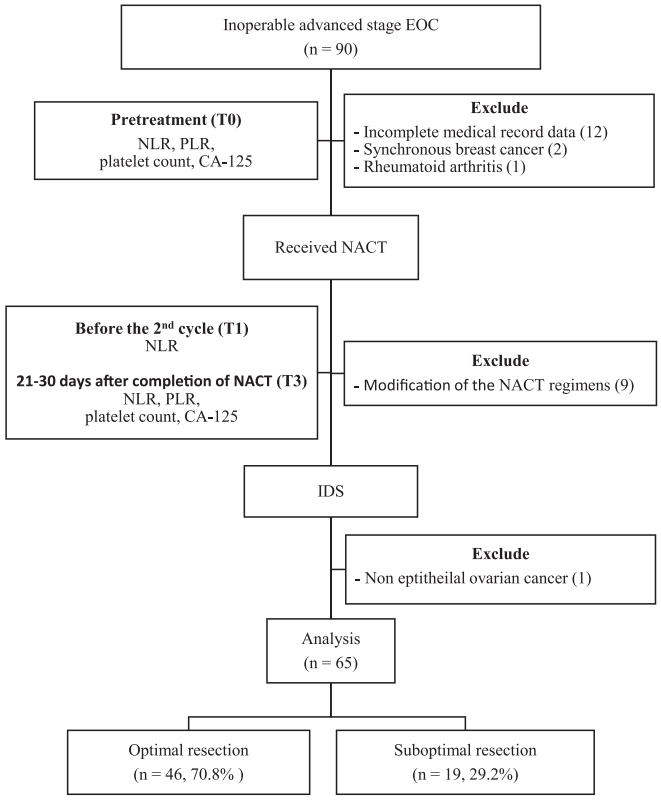

Fig. 1. The sequence of the study.

In order to forecast surgical outcomes, a univariate analysis was carried out to evaluate the predictive potential of variables, including the change in NLR following the first cycle of NACT, as well as the changes in NLR, PLR, and CA-125 at the final of NACT. Simple logistic regression analysis was employed for this purpose. The findings indicated that none of these variables – the changes in NLR, PLR, or CA-125 – associated with suboptimal resection result (Table 3).

Further analysis of the association between the change in NLR after the first cycle of NACT and changes in NLR, PLR, and CA-125 at the end of NACT in relation to the outcome of suboptimal resection was conducted using Receiver Operating Characteristic (ROC) analysis. The results indicated that the change in NLR after the first NACT cycle had an Area Under the Receiver Operating Characteristic (AUROC) of 0.608 (95 % CI: 0.456–0.759), while the changes in NLR, PLR, and CA-125 at the final NACT cycle had AUROCs of 0.597 (95 % CI: 0.447–0.747), 0.561 (95 % CI: 0.414–0.707), and 0.598 (95 % CI: 0.448–0.749), respectively (Supplementary Table 1, Supplementary Fig. 1). The Youden Index was utilized to identify the optimal threshold values for predicting suboptimal resection, resulting in values of 70 % for both the change in NLR after the first NACT cycle and the change in NLR after the final NACT cycle, while values of 50 % were determined for the changes in PLR, and CA-125 at the end of the final NACT cycle. The diagnostic performance of these factors was shown in Supplementary Table 2.

A univariate analysis using multiple logistic regression analysis was conducted using calculated cut-off values for changes in NLR, PLR, CA-125, and other clinical variables, including age, histologic subtype, FIGO stage, the extent of disease at the time of IDS, and the number of NACT cycles. No discernible factors were found to show potential associations with the suboptimal resection outcome.

Subsequently, a multivariate analysis was conducted, including variables that had a p-value < 0.2 in the univariable analysis. However, it was observed that there was multicollinearity between the change in NLR after the first cycle of NACT and after the end of NACT (Supplementary Fig. 1). Therefore, for further analyses, the change in NLR after the end of NACT was selected. Other factors considered in the analysis included the change in PLR exceeding 50 %, HGSC histology, and bowel and mesenteric metastasis. The findings from this analysis indicated that only HGSC histology displayed significant associations with the occurrence of suboptimal resection. However, it is noteworthy that the 95 % confidence intervals for these associations were wide, encompassing values that might not be deemed significant (Table 4).

The subgroup analysis of 48 patients with HGSC histologic subtype was then conducted, revealing that changes in NLR, PLR, and CA-125 were still not significantly associated with suboptimal outcomes.

5. Discussion

This retrospective study analyzed 65 patients diagnosed with stage IIIC or IV EOC who underwent IDS following NACT, which included 3–4 cycles of carboplatin combined with paclitaxel. The primary objective was to evaluate whether alterations in NLR, PLR, platelet count, and CA-125 levels could function as predictive indicators for suboptimal resection outcomes after IDS.

Residual disease following cytoreductive surgery plays a pivotal role in the prognosis of advanced ovarian cancer (Bryant et al., 2022). Suboptimal surgical outcomes in patients undergoing IDS may exacerbate less favorable prognosis. When performing NACT followed by IDS, determining the optimal number of NACT cycles and the decision to proceed with IDS presents a challenge. Having reliable tools to predict suboptimal outcomes could offer significant benefits, allowing for the

Table 1
Demographic and clinical characteristics of advance stage ovarian cancer patients who received neoadjuvant chemotherapy.

Characteristics	Total (n = 65)		Optimal resection (n = 46)		Suboptimal resection (n = 19)		p-value
Age (years)	56.82 ± 10.39		57.15 ± 10.13		56 ± 11.26		0.688
Histology							
HGSC	48	(73.8)	31	(67.4)	17	(89.5)	0.118
Non HGSC	17	(26.2)	15	(32.6)	2	(10.5)	
FIGO stage							
IIIC	35	(53.8)	27	(58.7)	8	(42.1)	0.222
IV	30	(46.2)	19	(41.3)	11	(57.9)	
Intraoperative site of metastasis							
Carcinomatosis peritonei	57	(87.7)	39	(84.8)	18	(94.7)	0.420
Upper abdomen	26	(40.0)	17	(36.9)	9	(47.4)	0.579
Bowel and mesentery	29	(44.6)	18	(39.1)	11	(57.9)	0.183
Pleural effusion	18	(27.7)	11	(23.9)	7	(36.8)	0.289
Number of NACT cycles	3	(3 - 4)	3	(3 - 4)	3	(3 - 4)	0.626
Radiologic response							
Complete/ partial response	64	(98.5)	45	(97.8)	19	(100)	1.000
Stable disease	1	(1.5)	1	(2.2)	0	(0.0)	
Interval from last NACT to IDS (days)	33	(28 - 41)	33	(29 - 40)	31	(28 - 41)	0.593
Sites of residual tumors							
Diaphragm	12	(18.5)	6	(13.0)	6	(31.6)	0.156
Omentum	7	(10.8)	0	(0.0)	7	(36.8)	<0.001
Peritoneum	9	(13.8)	4	(8.7)	5	(26.3)	0.108
Upper abdomen	9	(13.8)	3	(6.5)	6	(31.6)	0.015
Lower abdomen	4	(6.2)	2	(4.3)	2	(10.5)	0.574
Pelvis	14	(21.5)	4	(8.7)	10	(52.6)	<0.001

Abbreviations: HGSC, high grade serous carcinoma; NHGSC, non-high grade serous carcinoma; FIGO, The International Federation of Gynecology and Obstetrics; NACT, neoadjuvant chemotherapy; IDS, interval debulking surgery.
Data are presented as number (%), mean ± standard deviation or median (interquartile range).
P-value corresponds to [t]Independent samples *t*-test, [m]Mann-Whitney *U* test, [c]Chi-square test or [f]Fisher's exact test.

Table 2
Inflammatory markers and CA-125 levels in patients with advanced-stage ovarian cancer who underwent neoadjuvant chemotherapy.

Variables	Total (n = 65)		Optimal (n = 46)		Suboptimal (n = 19)		p-Value
NLR-T0	4.31	(2.73–5.39)	3.96	(2.59–5.05)	4.74	(3.43–6.41)	0.163
NLR-T1	2.34	(1.43–3.44)	2.42	(1.36–3.53)	2.02	(1.56–3.38)	0.795
NLR-T3	2.01	(1.42–2.78)	1.97	(1.43–2.64)	2.53	(1.29–2.97)	0.594
Change in NLR (%)							
after NACT 1st cycle	50.87	(31.73–69.34)	48.38	(29.28–64.32)	58.43	(37.33–76.37)	0.403
after end of NACT	56.90	(22.72–74.34)	53.87	(15.42–74.01)	70.72	(45.77–75.62)	0.665
pre-NACT CA-125	1555	(430–3037)	453	(295–957)	252	(240–1196)	0.695
post-NACT CA-125	49	(21–166)	37	(15–169)	64	(35–117)	0.241
pre-NACT Platelet count ($x10^3$)	475.35 ± 174.83		457.30 ± 163.41		519.05 ± 197.67		0.198
post-NACT Platelet count ($x10^3$)	249.18 ± 114.32		243.50 ± 114.19		262.95 ± 116.56		0.537
PLR-T0	357.15 ± 170.19		350.55 ± 176.25		374.01 ± 157.15		0.624
PLR-T3	165.81 ± 89.07		173.22 ± 97.35		146.88 ± 61.51		0.291
Change in PLR (%)	63.47	(46.70–76.88)	63.04	(38.13–75.11)	63.49	(54.67–77.84)	0.445
Change in CA-125 (%)	95.71	(84.99–98.38)	96.62	(87.97–98.50)	94.70	(73.15–97.81)	0.215

Abbreviations: NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; CA-125, cancer antigen-125; NACT, neoadjuvant chemotherapy; T0, before the first cycle of NACT; T1, within two days before the initiation of the second cycle of NACT; T3, within seven days prior to the IDS procedure.
Data are presented as mean ± standard deviation or median (interquartile range).
P-value corresponds to [t]Independent samples *t*-test or [m]Mann-Whitney *U* test.

Table 3
Univariate analysis of changes in inflammatory markers and CA-125 for predicting suboptimal resection in advanced stage ovarian cancer patients.

Factors	Crude OR (95 %CI)		p-value
Change in NLR after NACT 1st cycle	0.894	(0.350–2.282)	0.815
Change in NLR after end of NACT	1.006	(0.513–1.974)	0.985
Change in PLR (%)	1.003	(0.991–1.015)	0.660
Change in CA-125 (%)	0.986	(0.961–1.012)	0.291

Abbreviations: OR, Odds Ratio; CI, confident interval; NACT, neoadjuvant chemotherapy; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; CA-125, cancer antigen-125.

reduction of the optimal number of NACT cycles and preventing premature exploratory laparotomies. Utilizing white blood cell counts as an exploration of inflammatory markers before deciding on radiologic evaluation might be a cost-effective and easily accessible approach.

In this study, despite the majority of patients showing partial or complete radiologic responses, the rate of achieving optimal cytoreductive outcomes remained at only 70 %. Unfortunately, due to the limitation of retrospective design, the unavailability of detailed information about the extent of the disease, it was not possible to assess the accuracy of the imaging study. Moreover, neither the values of pretreatment NLR, PLR, platelet count, nor CA-125 could predict surgical outcomes, including their changes after the first or last cycle of NACT. According to ROC analysis with Youden index calculations, a decrease in NLR of over 70 % at the first and last cycle of NACT might be a significant predictor of suboptimal resection. Nevertheless, the AUROC for the NLR change registered only 0.608 after the initial NACT cycle and 0.597 upon the NACT cycle's completion. These outcomes indicate a modest prognostic efficacy, probably influenced by the limited sample size or the plausible situation where the alteration in NLR is not solely dictated

Table 4
Univariable and multivariate analysis using multiple logistic regression analysis of factors associated with suboptimal resection.

Factors	Univariate analysis			Multivariate analysis		
	Crude OR[1] (95 %CI)		p-value	Adjusted OR[2] (95 %CI)		p-value
Change in NLR after 1st cycle of NACT > 70 %	2.62	(0.83–8.26)	0.101			
Change in NLR after end of NACT > 70 %	2.35	(0.79–6.98)	0.125	3.01	(0.87–10.43)	0.082
Change in PLR > 50 %	2.84	(0.72–11.24)	0.136	1.65	(0.35–7.69)	0.526
Change in CA-125 < 50 %	1.69	(0.26–11.00)	0.585			
Age > 60 years	0.69	(0.23–2.08)	0.515			
HGSC histology	4.11	(0.84–20.16)	0.081	4.76	(1.04–21.77)	0.044
FIGO stage IV	1.95	(0.66–5.77)	0.226			
Site of metastasis						
Carcinomatosis	3.23	(0.37–28.25)	0.289			
Upper abdomen	1.53	(0.52–4.53)	0.437			
Bowel and mesentery	2.14	(0.72–6.34)	0.17	3.23	(0.93–11.26)	0.660
Pleural effusion	1.86	(0.59–5.88)	0.293			
Number of cycles	0.88	(0.52–1.51)	0.648			

Abbreviations: OR, Odds Ratio; OR_{adj}, Adjusted Odds Ratio; CI, confident interval; NACT, neoadjuvant chemotherapy; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; HGSC, high grade serous adenocarcinoma; FIGO, The International Federation of Gynecology and Obstetrics.
Variable was included in multivariable model due to have p-value < 0.2 in univariable analysis.
[1] Crude Odds Ratio estimated by Binary logistic regression.
[2] Adjusted Odds Ratio estimated by Multiple logistic regression.

by the tumor's response to NACT. It is essential to highlight that NLR, as an inflammation marker, lacks specificity, and its interpretation could potentially be affected by chemotherapy, even when the blood sample was collected more than 21 days after NACT administration (Drug name: Paclitaxel - BC Cancer, n.d.; Drug name: Carboplatin - BC Cancer, n.d.-a).

In the context of the Asian population, particularly in Thailand, where there is a notable prevalence of non-HGSC histology (Matz et al., 2017), this study was found to have the highest ratio of non-HGSC subtype compared to previous studies. Although there are no reports specific to ovarian cancer, evidence suggests that high-grade cancer has a higher NLR compared to low-grade cancers (Ashwath et al., 2019; Hassan et al., 2023) . However, addressing this concern, this study was designed to calculate the change in NLR before and after NACT for each individual patient. Despite the small number of patients in the analysis, the subgroup study of 48 patients with HGSC histologic subtype also showed no predictive value of change in NLR for predicting suboptimal resection outcome. Further investigation is needed to explore the differences in NLR between low-grade and high-grade ovarian cancer, as well as different histologic subtypes.

Compared to this study, Gulseren and colleagues reported different findings. They observed higher NLR and PLR values in the suboptimal outcome group, along with an increased change in NLR and PLR in that group. They also identified a significant relationship between a change in NLR exceeding 17 % and suboptimal outcomes, with an Odds ratio of 0.1 (95 % CI: 0.1–0.2, p-value < 0.001) and better prognostic performance presented by high AUROC (Gulseren et al., 2020). This variation in findings may be attributed to differences in study design, including variations in demographic factors such as ethnicity and the aforementioned proportion of non-HGSC histology. Additionally, their study incorporated 11 patients experiencing disease progression during NACT who did not undergo IDS, classifying them into the suboptimal resection group. In contrast, our study exclusively enrolled patients who underwent IDS.

This study, the first of its kind conducted in the Thai population, does have certain limitations. Firstly, it employs a retrospective design, resulting in an unexpected exclusion rate and a relatively small population for analysis. Secondly, despite efforts to minimize biases by coordinating blood sample collection with chemotherapy and ensuring consistent laboratory analysis, variations occurred in the interval between the last cycle of NACT and the date of laboratory collection. The 10-year duration of data gathering might also impact the quality of laboratory technology. Furthermore, the absence of a consensus on the precise NLR cutoff point poses a challenge. Similar to the approach of Gulseren and colleagues, we determined the NLR cutoff point using ROC analysis.

In conclusion, our study does not provide support for alterations in NLR, PLR, platelet count, and CA-125 following NACT in advanced-stage EOC as reliably predictive markers for IDS surgical outcomes. Instead, we recommend evaluating cancer response to NACT using a combination of clinical evaluation and other inflammatory markers, rather than relying solely on NLR. We suggest conducting further prospective studies with larger cohorts to gain a deeper understanding of this matter.

6. Declaration of Generative AI and AU-Assisted Technologies in the Writing Process

During the preparation of this work the authors used ChatGPT language model, developed by OpenAI in order to improve readability and language. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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CRediT authorship contribution statement

Ponganun Tuntinarawat: Methodology, Investigation, Writing – original draft. **Ratnapat Tangmanomana:** Data curation. **Thannaporn Kittisiam:** Writing – review & editing, Supervision, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.gore.2024.101347.

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