Baseline neutrophil-to-lymphocyte ratio is not associated with chemotherapy-induced nausea and vomiting in patients with breast cancer: A single-center retrospective cohort study

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Abstract. Chemotherapy-induced nausea and vomiting (CINV) remains one of the most distressing adverse effects of highly emetogenic chemotherapy despite advances in antiemetic prophylaxis. Systemic inflammatory markers have previously been investigated as potential predictors of treatment-associated toxicities in oncology. The present study aimed to evaluate the association between baseline neutrophil-to-lymphocyte ratio (NLR) and the risk of CINV in patients with breast cancer receiving anthracycline-based chemotherapy. The present retrospective cohort included 280 female patients with histologically determined breast cancer who received anthracycline and cyclophosphamide chemotherapy at a single tertiary oncology center. Baseline neutrophil and lymphocyte counts obtained prior to chemotherapy initiation were used to calculate the NLR. Patients were categorized into two groups according to NLR values: Low NLR (<3) and high NLR (≥3). The primary endpoint was complete response (CR), defined as the absence of vomiting and no need for rescue antiemetic therapy. CR rates were evaluated in the acute (0-24 h), delayed (24-120 h) and overall (0-120 h) phases following chemotherapy. Associations between NLR and clinical outcomes were assessed using χ^2 tests and multivariate logistic regression analyses adjusting for age, menopausal status, motion sickness history, antiemetic regimen and treatment setting. Among the 280 patients included in the present analysis, 162 (57.9%) exhibited low NLR and 118 (42.1%) exhibited high NLR. Baseline demographic and clinical characteristics were comparable between the two groups. CR rates did not differ significantly between patients with low and high NLR in the overall phase (75.3 vs. 70.3%; P=0.429), acute phase (87.7 vs. 86.4%; P=0.905) or delayed phase (82.1 vs. 76.3%; P=0.296). In multivariate logistic regression analyses, NLR was found not to be an independent predictor of CINV outcomes. However, a history of motion sickness and the type of antiemetic regimen were notably associated with the likelihood of failure to achieve CR, particularly in the overall and delayed phases. Baseline NLR was found not to be independently associated with the risk of CINV in patients with breast cancer receiving highly emetogenic chemotherapy. Overall, patient-associated susceptibility factors and antiemetic regimen selection appear to have a greater influence on CINV control compared with systemic inflammatory status as measured by NLR. Further prospective studies are warranted to explore the potential role of inflammatory biomarkers in predicting CINV.

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Abbreviations: CINV, chemotherapy-induced nausea and vomiting; NLR, neutrophil-to-lymphocyte ratio; AC, anthracycline and cyclophosphamide; CR, complete response; NK1, neurokinin-1; OR, odds ratio; QoL, quality of life; LSCC, lung squamous cell carcinoma

Key words: chemotherapy-induced nausea and vomiting, breast cancer, neutrophil-to-lymphocyte ratio, systemic inflammation, antiemetic therapy, anthracycline chemotherapy

Introduction

Breast cancer remains the most frequently diagnosed malignancy among women in Turkey and globally, accounting for a notable proportion of cancer-associated morbidity (1-3). Despite the rapid diversification and evolution of systemic therapies, including targeted agents and dose-dense regimens, chemotherapy-induced nausea and vomiting (CINV) continues to be among the most distressing and feared side effects reported by patients (4). Even with the advent of modern antiemetic guidelines, a marked number of patients experience breakthrough or delayed nausea, which notably impairs health-associated quality of life (QoL), leads to psychological distress and may result in dose reductions or treatment non-compliance (5,6).

The pathophysiology of CINV is a complex process involving both peripheral and central pathways (7). Primarily, highly emetogenic chemotherapy agents trigger the release of serotonin from enterochromaffin cells in the gastrointestinal

tract, stimulating the vagus nerve. Concurrently, the activation of neurokinin-1 (NK1) receptors by substance P in the area postrema, the chemoreceptor trigger zone in the brain, serves a key role, especially in the delayed phase of emesis (7,8). However, previous evidence has suggested that neurotransmitter release alone does not fully account for the inter-individual variability in CINV severity, pointing toward the involvement of systemic inflammatory responses in modulating the emetic threshold (9).

Recent evidence has suggested that inflammatory pathways may contribute to the development of CINV in addition to the well-established serotonin- and substance P-mediated mechanisms (10,11). Chemotherapy-induced tissue injury can trigger the release of pro-inflammatory cytokines, including IL-1β, IL-6 and TNF-α. These cytokines may activate vagal afferents and sensitize central emetic circuits within the dorsal vagal complex, particularly the area postrema and nucleus tractus solitarius, thereby facilitating serotonin- and substance P-mediated emetic signaling (12). These observations have led to increasing interest in systemic inflammatory markers as potential predictors of CINV susceptibility (12,13). As a simple and widely available marker of systemic inflammation, the neutrophil-to-lymphocyte ratio (NLR) may reflect the inflammatory milieu that could modulate individual responses to emetogenic chemotherapy (10,11).

The NLR has emerged as a reliable and easily accessible systemic inflammatory marker, reflecting the balance between the innate immune response (neutrophils) and adaptive immunity (lymphocytes) (14). Systemic inflammation is characterized by the release of pro-inflammatory cytokines. These cytokines are known to interact with the central nervous system through the blood-brain barrier and the vagal afferents, potentially sensitizing the vomiting centers (15). High NLR levels, as a proxy for this inflammatory milieu, have been associated with increased symptom burden and worse tolerability of cytotoxic treatments in a number of oncological settings, including breast cancer (16,17). As a readily available marker of systemic inflammation, the NLR has been widely investigated in patients with solid tumors and has been associated with treatment outcomes and symptom burden across multiple cancer types, including breast, colorectal, lung and gastrointestinal cancers (18,19).

The present study aimed to investigate the association between systemic inflammatory status, represented by the pre-treatment NLR and the occurrence of CINV in Turkish female patients with breast cancer receiving highly emetogenic chemotherapy. Patients were stratified according to an NLR cut-off value of 3.0 to evaluate whether elevated baseline inflammatory status was associated with reduced antiemetic treatment efficacy. The primary objective was to assess the association between NLR levels and the rate of complete response (CR), defined as the absence of vomiting and no use of rescue antiemetic medication, during the acute (0-24 h), delayed (24-120 h) and overall (0-120 h) phases following chemotherapy.

Materials and methods

Study design and ethical approval. As a retrospective single-center cohort study, the present analysis was conducted at the Department of Oncology of the University of Health Sciences, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital (Istanbul, Turkey) between June 2024 and December 2025. The present study was approved by the Ethics Committee of the University of Health Sciences, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital (Istanbul, Turkey; approval no. 2024/253; approval date: 15 May 2024). Owing to the retrospective design of the present study and the use of anonymized patient data, the requirement for study-specific informed consent was waived by the ethics committee. In accordance with institutional policy, all patients had previously provided written general consent at hospital admission permitting the anonymized use of their medical data for scientific and research purposes. All procedures involving data collection and analysis were conducted in accordance with the ethical principles of the Declaration of Helsinki and the Personal Data Protection Law of Turkey (law no. 6698) (20), ensuring the confidentiality and protection of patient information.

Patient selection and study population. Female patients aged 18-90 years with histopathologically confirmed breast cancer who received anthracycline-cyclophosphamide (AC)-based chemotherapy at the University of Health Sciences, Sancaktepe Şehit Prof. Dr. Ilhan Varank Training and Research Hospital, Istanbul, Türkiye, between June 2024 and December 2025 were retrospectively identified through the hospital's electronic medical record system. Patients were screened for study eligibility, and only those with complete clinical, laboratory and follow-up data for the first chemotherapy cycle were included. Medical records were reviewed to obtain demographic characteristics, treatment information, antiemetic prophylaxis details and CINV outcomes during the acute and delayed phases following chemotherapy. Patients were eligible for inclusion if they met the following criteria: i.) ≥18 years old, ii.) histologically determined breast cancer, iii.) treated with a highly emetogenic AC chemotherapy regimen and iv.) had complete available laboratory and follow-up data for the first chemotherapy cycle. Patients were excluded if they had: i.) Active infection or chronic inflammatory disease at the time of blood sampling, ii.) systemic corticosteroid use unrelated to antiemetic prophylaxis and iii.) incomplete medical records or missing follow-up data.

Data collection and laboratory parameters. Demographic and clinical variables were extracted from the hospital database, including age, BMI, Eastern Cooperative Oncology Group performance status, smoking status, disease stage and family history of cancer.

Baseline laboratory values were obtained from complete blood count measurements performed within 24-48 h prior to the first cycle of chemotherapy. The NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. Based on the predefined study hypothesis and in accordance with a similar clinical framework evaluating the predictive value of baseline inflammatory ratios on emetic outcomes (21), a threshold value of 3.0 was selected to stratify patients into two groups: A low NLR group (<3.0) and a high NLR group (≥3.0).

Assessment of CINV. CINV was assessed during both the acute phase (0-24 h) and the delayed phase (24-120 h)

following the first chemotherapy cycle. The primary outcome measure was the CR rate, defined as the absence of vomiting episodes and no need for rescue antiemetic medication during the observation period. The secondary outcome was the evaluation of the association between baseline NLR levels and the occurrence of nausea and vomiting. Information regarding antiemetic prophylaxis, vomiting episodes and rescue antiemetic use was obtained from electronic medical records, including oncology physician notes, medication records and patient-reported symptoms documented during routine follow-up visits after the first chemotherapy cycle. Nausea severity was not systematically documented in the electronic medical records and therefore could not be evaluated separately in the present study.

Statistical analysis. All statistical analyses were performed using R statistical software (version 4.4.0; Posit Software, PBC). Continuous variables are expressed as the mean ± SD or median with interquartile range depending on the distribution of the data. Categorical variables are presented as frequencies and percentages. Comparisons between the low-NLR and high-NLR groups were performed using an unpaired Student's t-test for normally distributed continuous variables, the χ^2 test for categorical variables and Fisher's exact test when expected cell counts were small.

To evaluate independent predictors of CINV occurrence, multivariate logistic regression analysis was performed. Variables with clinical relevance or P<0.10 in univariate analyses were entered into the multivariate logistic regression model. Adjusted odds ratios (ORs) with 95% CIs were calculated. A two-sided P<0.05 was considered to indicate a statistically significant difference. For logistic regression analyses, failure to achieve CR (non-CR) was used as the dependent variable. Therefore, OR <1 indicated a lower likelihood of treatment failure and a higher probability of achieving CR. Comparisons of response outcomes between NLR groups were performed using Pearson's χ^2 test with Yates' continuity correction.

Results

Patient characteristics. A total of 280 female patients with histopathologically determined breast cancer who received AC-chemotherapy were included in the present analysis. Patients were stratified according to baseline NLR into low NLR (<3) and high NLR (≥3) groups. Baseline demographic and clinical characteristics are summarized in Table I. The mean age of the cohort was ~49 years, and the distribution of menopausal status included both premenopausal and postmenopausal patients. Motion sickness history and chemotherapy treatment setting (adjuvant vs. neoadjuvant) were also recorded.

No statistically significant differences were observed between the NLR groups with regard to age, menopausal status, stage, motion sickness history, antiemetic regimen, treatment setting or comorbidity (all, P>0.050). Despite not being statistically significant, patients in the low NLR group reported a higher prevalence of motion sickness compared with those in the high NLR group (44.4 vs. 33.1%; P=0.072).

CINV outcomes according to NLR status. The association between baseline NLR and CINV outcomes during the first chemotherapy cycle are presented in Table II. Patients with higher baseline NLR (≥3) tended to exhibit lower CR rates, defined as the absence of vomiting and no requirement for rescue antiemetic medication. However, no statistically significant differences were observed between the low- and high-NLR groups in univariate analyses of overall (P=0.429), acute (P=0.905) or delayed (P=0.296) complete response rates.

Table I. Baseline demographic and clinical characteristics in the low NLR (<3) and high NLR (≥3) groups.

Variable	Low NLR (n=162)	High NLR (n=118)	P-value
Age, mean ± SD	48.38±10.94	48.11±11.30	0.843
Menopausal status			0.878
Perimenopausal	14 (8.6)	10 (8.5)	
Postmenopausal	65 (40.1)	44 (37.3)	
Premenopausal	83 (51.2)	64 (54.2)	
Stage, mean ± SD	2.34±0.48	2.36±0.48	0.668
Motion sickness			0.072
No	90 (55.6)	79 (66.9)	
Yes	72 (44.4)	39 (33.1)	
Antiemetic regimen			0.148
Aprepitant	84 (51.9)	50 (42.4)	
Fosaprepitant	78 (48.1)	68 (57.6)	
Treatment setting			0.279
Adjuvant	25 (15.4)	25 (21.2)	
Neoadjuvant	137 (84.6)	93 (78.8)	
Comorbidity			0.661
No	123 (75.9)	86 (72.9)	
Yes	39 (24.1)	32 (27.1)	

All variables are presented as n (%) unless otherwise stated. Continuous variables were compared using the independent samples t-test, and categorical variables were compared using Pearson's χ^2 test. NLR, neutrophil-to-lymphocyte ratio.

Predictors of CR (overall phase). A multivariate logistic regression analysis was performed to identify factors associated with failure to achieve CR during the overall phase (0-120 h) following chemotherapy. The results are presented in Table III. Baseline NLR ≥3 was not significantly associated with failure to achieve CR (OR=0.77; 95% CI, 0.44-1.35; P=0.360). However, two variables were independently associated with failure to achieve CR. Patients with a history of motion sickness exhibited a significantly lower odds of failure to achieve CR (OR=0.42; 95% CI, 0.23-0.77; P=0.005). Patients receiving fosaprepitant-based antiemetic prophylaxis exhibited significantly lower odds of failure to achieve CR (OR=0.38; 95% CI, 0.20-0.68; P=0.001). Age, menopausal status and treatment setting were not significantly associated with CR.

Predictors of CR in the delayed phase. A second multivariate logistic regression model was constructed to evaluate predictors of CR during the delayed phase (24-120 h). The results are

Table II. Univariate analysis of the association between NLR and CR.

A, Overall CR

NLR group	Non-CR	CR	CR rate, %	P-value
Low NLR (<3)	40	122	75.3	0.429
High NLR (≥3)	35	83	70.3	

B, Acute CR

NLR group	Non-CR	CR	CR rate, %	P-value
Low NLR (<3)	20	142	87.7	0.905
High NLR (≥3)	16	102	86.4	

C, Delayed CR

NLR group	Non-CR	CR	CR rate, %	P-value
Low NLR (<3)	29	133	82.1	0.296
High NLR (≥3)	28	90	76.3	

Comparisons between NLR groups and response outcomes were performed using Pearson's χ^2 test with Yates' continuity correction. NLR, neutrophil-to-lymphocyte ratio; CR, complete response.

Table III. Multivariate logistic regression analysis for failure to achieve overall CR.

Variable	OR	95% CI	P-value
High NLR (≥3)	0.77	0.44-1.35	0.360
Age	1.03	0.99-1.07	0.200
Motion sickness	0.42	0.23-0.77	0.005
Fosaprepitant	0.38	0.20-0.68	0.001
Menopausal status	NS	-	-
Treatment setting	NS	-	-

Multivariate logistic regression analysis was performed to identify independent predictors of failure to achieve CR. Variables with clinical relevance were included in the model. Results are presented as ORs with 95% CIs. Statistical significance was defined as P<0.05. OR <1 indicates a lower likelihood of failure to achieve complete response. NLR, neutrophil-to-lymphocyte ratio; CR, complete response; OR, odds ratio.

presented in Table IV. Baseline NLR ≥3 was not significantly associated with failure to achieve delayed CR (OR=0.69; 95% CI, 0.37-1.28; P=0.230). Consistent with the overall-phase model, motion sickness was associated with significantly lower odds of failure to achieve delayed CR (OR=0.49; 95% CI, 0.25-0.94; P=0.033). In addition, fosaprepitant use was significantly associated with a lower likelihood of CINV-related treatment failure (OR=0.29; 95% CI, 0.15-0.57; P<0.001). Other variables, including age, menopausal status and treatment setting, were not statistically significant predictors (all, P>0.050).

Table IV. Multivariate logistic regression analysis for failure to achieve delayed CR.

Variable	OR	95% CI	P-value
High NLR (≥3)	0.69	0.37-1.28	0.230
Age	1.00	0.96-1.05	0.970
Motion sickness	0.49	0.25-0.94	0.033
Fosaprepitant	0.29	0.15-0.57	<0.001
Menopausal status	NS	-	-
Treatment setting	NS	-	-

Multivariate logistic regression analysis was performed to identify independent predictors of failure to achieve delayed CR. Variables with clinical relevance were included in the model. Results are presented as ORs with 95% CIs. Statistical significance was defined as P<0.05. OR<1 indicate a lower likelihood of failure to achieve delayed CR. NLR, neutrophil-to-lymphocyte ratio; CR, complete response; ORs, odds ratio; NS, not statistically significant.

Discussion

In the present study, the association between pre-treatment NLR, as a marker of systemic inflammatory status, and the risk of CINV in patients with breast cancer receiving highly emetogenic chemotherapy was investigated. Specifically, the present study evaluated whether an elevated NLR (≥3) could predict the likelihood of achieving CR, defined as the absence of vomiting and no need for rescue antiemetic medication, during the acute, delayed and overall phases following chemotherapy. Based on the present findings, baseline NLR was not notably associated with CR outcomes in any of the evaluated phases. However, analyses revealed that certain clinical factors were associated with the likelihood of failure to achieve CR. In particular, a history of motion sickness and the type of antiemetic regimen appeared to influence treatment response, suggesting that patient-related susceptibility and pharmacologic prophylaxis may serve a more notable role in determining antiemetic efficacy compared with baseline inflammatory status in the patient population. Despite systemic inflammation theoretically being able to influence emetic sensitivity, the findings of the present study suggest that NLR has limited clinical utility in predicting CINV in patients receiving contemporary antiemetic prophylaxis.

The importance of identifying high-risk individuals in the breast cancer population is further underscored by a recent retrospective study by Jiang *et al* (22), which evaluated CINV risk factors specifically in patients undergoing chemotherapy. The findings of this study indicated that a history of nausea and vomiting, along with advanced age (>65 years) and a higher number of chemotherapy cycles, were notable predictors of emetic episodes. In partial agreement with these results, the present study further determined the importance of prior emetic sensitivity, as evidenced by the marked association between motion sickness and a higher likelihood of failure to

achieve CR. However, a distinct contrast arises regarding the role of age; while the aforementioned study identified older age as a risk factor, the analysis in the present study did not find age to be a notable determinant, aligning more closely with classical literature that often suggests younger patients are at higher risk (23). Despite the focus on clinical risk factors in both studies, neither Jiang *et al* (22) nor the present study established NLR as a primary predictor for CINV in this specific oncological setting. This suggests that in patients with breast cancer receiving highly emetogenic regimens, the emetic response is more likely driven by individual neuro-susceptibility and treatment-associated cumulative toxicity rather than baseline systemic inflammatory status.

A key point of divergence in previous literature is a study by Naito *et al* (24), which suggested that a high baseline NLR could indeed serve as a predictor for CINV in patients with breast cancer receiving anthracycline-based regimens. The findings of this study indicated that patients with elevated systemic inflammation may be more susceptible to emetic episodes, contrasting with the results of the present study where no notable association was found between NLR and CR rates across any phase. This discrepancy may stem from differences in the defined NLR cut-off values or the specific antiemetic protocols employed; while both studies focused on highly emetogenic chemotherapy, variations in the administration of newer-generation NK1 receptor antagonists, such as the fosaprepitant used in the present cohort, might have mitigated the inflammatory-driven emetic response more effectively. When the authors examined the multivariate factors, the present analysis highlighted that pharmacological intervention and personal history, specifically motion sickness, exerted a more notable influence on outcomes compared with baseline hematological ratios. Consequently, while Naito *et al* (24) underscored the potential of the NLR as a biological marker, the findings of the present study suggest that its clinical utility may be diminished when patients are managed with optimized, contemporary antiemetic prophylaxis. The variability in findings across studies may be explained by a number of methodological and clinical factors. Differences in cancer types, chemotherapy regimens, antiemetic protocols, NLR cut-off values and outcome definitions may markedly influence the observed association between systemic inflammatory markers and CINV. Moreover, the limited number of studies specifically evaluating NLR in patients with breast cancer receiving highly emetogenic chemotherapy makes direct comparisons challenging and highlights the need for further prospective research in this area.

The absence of a notable association between NLR and CINV outcomes may reflect the multifactorial nature of CINV. Although systemic inflammation has been implicated in emetic pathways through cytokine-mediated signaling, established patient-associated risk factors and the effectiveness of antiemetic prophylaxis may exert a greater influence on clinical outcomes (7,9). Furthermore, the widespread use of contemporary NK1 receptor antagonist-based regimens in the present cohort may have reduced the potential impact of baseline inflammatory status on CINV susceptibility.

The multifactorial nature of CINV is further illustrated by the prediction model developed by Hu *et al* (25) which emphasizes the importance of patient-associated risk factors such as age and history of morning sickness in determining emetic susceptibility. In the present study, the identification of motion sickness as a notable independent predictor of failing to achieve CR in both the overall and delayed phases aligns with the emphasis on clinical phenotyping. However, while Hu *et al* (25) identified younger age as a primary risk determinant, the present analysis showed no such association, likely due to the demographic homogeneity of the breast cancer population receiving standardized highly emetogenic chemotherapy. Ultimately, the fact that established clinical triggers such as motion sickness remained predictive while the NLR did not reach statistical significance suggests that, in the context of modern antiemetic prophylaxis, individual neurobiological sensitivity may supersede baseline systemic inflammatory status in modulating the emetic threshold.

The influence of systemic inflammation on emetic pathways is not limited to oncology, as shown by previous research in the surgical setting (21,15,26). This evidence has suggested that in specific populations such as lung squamous cell carcinoma, physiological parameters, particularly pulmonary function and cardiovascular comorbidities, markedly influence CINV severity (26). The findings of Wang (26) indicated that lower oxygen partial pressure and compromised respiratory function (low forced expiratory volume in 1 sec) were associated with heightened emetic risk, likely due to the exacerbated systemic stress and impaired metabolic clearance in these patients. By contrast, the present study focused on a breast cancer cohort receiving AC regimens, where respiratory parameters were not a primary variable. However, a parallel can be drawn regarding inflammatory markers; while Wang (26) observed that elevated IL-6 levels had a protective effect against severe CINV in patients with lung squamous cell carcinoma (LSCC), data from the present study on NLR showed no such predictive value. This discrepancy highlights that the association between systemic inflammation and the emetic reflex may be highly tumor-specific and dependent on the primary organ affected. While LSCC-related CINV is influenced by respiratory-driven physiological stress, CINV in the breast cancer population in the present study appears more closely associated with individualized neuro-susceptibility, represented by motion sickness and the pharmacological potency of the antiemetic regimen (such as fosaprepitant).

Research regarding the association between systemic inflammation and emetic outcomes has also been reported in surgical settings. For instance, elevated preoperative NLR has been associated with an increased risk of postoperative nausea and vomiting in patients undergoing procedures such as rhinoplasty and breast reduction surgery (21,27). These findings support the hypothesis that baseline inflammatory status may influence the susceptibility of an individual to emetic stimuli. However, the present results in patients with breast cancer receiving highly emetogenic chemotherapy did not demonstrate a similar predictive value for NLR. This discrepancy may reflect fundamental differences in the mechanisms underlying postoperative nausea and vomiting and chemotherapy-induced nausea and vomiting. While surgical emesis is largely driven by perioperative inflammatory responses and anesthetic exposure, CINV involves complex neurochemical pathways activated by highly emetogenic cytotoxic agents, such as anthracyclines (e.g., doxorubicin or epirubicin) and cyclophosphamide. In

addition, the routine use of modern antiemetic prophylaxis, particularly NK1 receptor antagonists such as fosaprepitant, may attenuate the potential contribution of baseline inflammatory markers in the oncology setting. Beyond baseline hematological ratios, the present findings suggest that emetic risk stratification in the era of modern antiemetic prophylaxis may depend more upon patient-associated susceptibility factors than on baseline inflammatory status. While NLR did not reach statistical significance in any phase of the present study, a history of motion sickness was consistently associated with lower odds of failure to achieve CR. In addition, fosaprepitant use was associated with improved CINV control, particularly during the delayed phase. We hypothesize that effective NK1 receptor antagonist-based prophylaxis may reduce the clinical impact of subtle neuro-inflammatory mechanisms involved in CINV. However, due to the retrospective and non-randomized nature of the present study, this finding should be interpreted as an association rather than evidence of a causal benefit, as antiemetic regimen selection may have been influenced by physician preference and other unmeasured clinical factors.

The clinical relevance of effective emetic control has been demonstrated by Pirri *et al* (28) who emphasized that despite advances in antiemetic therapy, ~50% of patients with cancer still suffer from nausea, which severely impairs their QoL and psychological adjustment. This research highlighted that persistent nausea, often more pervasive compared with vomiting, notably disrupts physical, social and role functioning. Although the present study did not find a significant predictive association between the NLR and CINV outcomes, the present findings may contribute a valuable perspective to the current, yet insufficient, body of knowledge regarding emetic risk stratification. While systemic inflammatory markers such as NLR may not serve as primary predictors in the context of highly emetogenic chemotherapy, identifying alternative markers such as motion sickness remains key for preserving the QoL. Therefore, despite the negative results regarding NLR, the present study provides an important contribution to the literature by refining the boundaries of biological predictors and underscoring the necessity of a personalized, phenotype-based approach to antiemetic prophylaxis.

The primary strength of the present study lies in its methodological focus on a highly homogeneous cohort of patients with breast cancer receiving a standardized AC regimen, which notably minimized treatment-associated confounding variables and supported the internal validity of the present findings. By conducting a granular temporal analysis across the acute, delayed and overall phases and utilizing multivariate models to adjust for critical covariates, the present study provided a robust assessment of the NLR as a potential biomarker. Additionally, the inclusion of real-world comparative data between fosaprepitant and oral aprepitant adds a layer of practical clinical relevance to the current literature. However, specific limitations must be acknowledged. While the present retrospective design imposed inherent limits on subjective symptom tracking, the reliance on hard clinical endpoints, including rescue medication use, provided a concrete measure of antiemetic failure. In addition, being a single-center study, the generalizability of the present results may be limited by institutional practices. In addition, CINV assessment was limited to the first chemotherapy cycle, and cumulative effects across multiple cycles were not evaluated. The reliance on a single baseline NLR measurement, without longitudinal tracking of inflammatory cytokines or post-chemotherapy fluctuations, may not fully capture the dynamic neuro-inflammatory environment triggered by cytotoxicity. Only baseline NLR values were evaluated in the present study; therefore, the findings do not exclude the possibility that other inflammatory biomarkers or dynamic changes in inflammatory status during chemotherapy may contribute to CINV susceptibility. Finally, nausea severity was not systematically recorded and therefore could not be analyzed independently from vomiting outcomes. As nausea is often reported as one of the most severe CINV symptoms, this may have limited the comprehensive assessment of treatment-associated symptom burden. Despite this, the present findings contribute to the growing body of evidence regarding CINV risk stratification and highlight the importance of individualized patient-associated risk factors when planning antiemetic prophylaxis.

Overall, in the present retrospective cohort of patients with breast cancer receiving highly emetogenic chemotherapy, baseline NLR was not associated with the risk of CINV. By contrast, a history of motion sickness and antiemetic regimen were markedly associated with CINV outcomes. These findings suggest that baseline NLR has limited utility as a predictor of CINV in this clinical setting. However, the present results do not exclude a potential role for other inflammatory biomarkers or dynamic changes in inflammatory status during treatment. Prospective studies incorporating longitudinal assessments of inflammatory markers are warranted to further clarify the association between inflammation and CINV.

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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

RC was responsible for software (R-based statistical analyses), validation, formal analysis, investigation (patient identification, medical record review and clinical data acquisition), data curation and writing the original draft. RC and AD contributed to conceptualization, methodology, resources (provision of patient data and institutional clinical resources) and writing, review and editing. RC and AD confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The present study was approved by the Scientific Committee of the University of Health Sciences, Sancaktepe Şehit Prof.

Dr. İlhan Varank Training and Research Hospital, Istanbul, Turkey (approval no. 2024/253; approval date: 15 May 2024). The requirement for informed consent was waived due to the retrospective nature of the study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Use of artificial intelligence (AI) tools

During the preparation of this manuscript, the authors used ChatGPT (OpenAI; GPT-5.5; https://chatgpt.com/) solely to improve the readability and language of the text. No AI tool was used for data analysis, interpretation of the results or generation of scientific conclusions. All AI-assisted outputs were carefully reviewed, revised and verified by the authors, who take full responsibility for the final content of the manuscript.

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