DOI: 10.4149/BLL_2023_009

Bratisl Med J 2023; 124 (1)

59 – 63

CLINICAL STUDY

The effect of the change in hemoglobin-albumin-lymphocyte-platelet scores occurring with neoadjuvant chemotherapy on clinical and pathological responses in breast cancer

Elif YUCE[1], Serdar KARAKULLUKCU[2], Hatice BULBUL[3], Celal ALANDAG[4], Ismail SAYGIN[5], Halil KAVGACI[6]

Karaman Training and Research Hospital, Medical Oncology Department, Turkey. **merevelif@gmail.com**

ABSTRACT

INTRODUCTION: Breast-cancer is a common-cause of death in women.(1) We investigated the effects of before/after-NACT on hemoglobin-albumin-lymphocyte-platelet (HALP) scores and of changes therein on clinical/pathological-responses.

MATERIALS AND METHODS: One-hundred-twenty-seven breast-cancer-patients receiving-NACT between December 2009 – January 2019 were investigated retrospectively.

RESULTS: The mean – age was 50.3±12.3 (min 27 – max 79), and 125 patients (98.4 %) were women. Fifty-four (42.5 %) were premenopausal and 71 (55.9 %) postmenopausal. Invasive-ductal-carcinoma was present in 111 patients (92.5 %). Eighty patients (70.2 %) were ≤ T2 and 34 (29.8 %) > T2. Lymph-node-status was positive in 99 patients (83.2 %) and negative in 20 (16.8 %). Ki-67 was ≤ 10 % in 22 (28.9 %), 11–20 % in 23 (30.3 %), and > 20 % in 31 (40.8 %). Complete clinical response was observed in 27 (21.3 %), partial-response in 76 (59.8 %), stable-disease in 21 (16.5 %), and progressive-disease in 3 patients (2.4 %). The objective-response-rate (ORR) was 103 (81.1 %). Pathological-complete-response (pCR) was observed in 24 patients (18.9 %). ORR was higher in Ki-67 > 20 % compared to ≤ 10 % and 10–20 % (90.3 % vs 59.0 % / 78.3 %, respectively, p: 0.027), but no difference occurred in pCR. Neutrophil-lymphocyte-ratio (NLR), platelet-lymphocyte-ratio (PLR), prognostic-nutritional-index (PNI), and HALP were measured before/after NACT. Associations with ORR and pCR were investigated via changes in these with NACT (excepting-PNI), but no-significant results emerged.

CONCLUSIONS: Higher ORR occurred post-NACT in patients with Ki-67 >20 %, while NLR, PLR, PNI, and HALP before/after-NACT and post-NACT-changes (excepting-PNI) had no-effect on ORR/pCR *(Tab. 5, Ref. 21)*. Text in PDF *www.elis.sk*

KEY WORDS: breast cancer, objective response rate (ORR), pathological complete response (pCR), hemoglobin-albumin-lymphocyte-platelet (HALP) score.

Introduction

Breast cancer is the second most prevalent cancer worldwide, and one of the most common cancer-related causes of death in women (1). Survival has been prolonged due to advances in the treatment of breast cancer and agents newly added to treatment at all stages, and it is therefore very important to preserve the quality of life of individuals who will live with this disease for many years. Neoadjuvant chemotherapy (NACT) allows patients to undergo less extensive surgery by means of tumor downstaging. This assists with the preservation of quality of life by preventing both, cosmetic and movement-restricting complications such as lymphedema (2). Another advantage of NACT, one not observed with adjuvant chemotherapy, is that it can evaluate the tumor's response to chemotherapy in vivo (3). Assessing the response to chemotherapy, particularly in the HER2-positive and triple-negative subtypes, is very important in terms of prognosis.

These advantages of NACT mean that it is becoming increasingly frequently employed, and is the standard treatment for locally advanced breast cancer. The parameter that best indicates the success of NACT is the pathological complete response (pCR). Overall survival (OS) results are better in breast cancers in which pCR is achieved, particularly in the HER2-positive and triple-negative subtypes. The contribution to survival of pCR is only unclear in luminal A tumors (4).

[1]Karaman Training and Research Hospital, Medical Oncology Department, Turkey, [2]Rize Provincial Health Department, Public Health Specialist, Turkey, [3]Karadeniz Technical University – Internal Medicine Department, Trabzon, Turkey, [4]Sivas Numune Hospital – Medical Oncology Department, Sivas, Turkey, [5]Karadeniz Technical University – Pathology Department, Trabzon, Turkey, and [6]Medical Park Hospital – Medical Oncology Department, Trabzon, Turkey

Address for correspondence: Elif YÜCE Dr, Karaman Training and Research Hospital, Medical Oncology Department, 70100 Turkey.
Phone: +90 507 873 64 69

Inflammation has long been known to promote the proliferation, angiogenesis, and metastasis of malignant cells in the tumor microenvironment and to reduce the response to chemotherapy. At the same time, cancer-related inflammation has also been shown to precipitate genetic instability in cancer cells (5). Studies in recent years have therefore investigated the prognostic significance in various cancers of systemic inflammatory response (SIR) parameters such as the neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) (3, 6–8). In addition to systemic inflammation, the prognostic nutritional index (PNI) is also employed to indicate nutritional status, another host prognostic factor. The prognostic significance of the PNI has been shown in several cancers (9, 10). Due to the frequent general presence of malnutrition it is recommended that the PNI be evaluated in cancer in order to prevent this being overlooked (11).

The hemoglobin-albumin-lymphocyte-platelet (HALP) score consists of four laboratory parameters including both nutritional and inflammatory status. Its association with prognosis has been investigated in several cancers (9, 12–16). However, to the best of our knowledge only limited numbers of studies have investigated the relationship between the HALP score and clinical and pathological responses in breast cancer. Due to this deficiency in the literature, the purpose of this study was to investigate whether NLR, PLR, and PNI values and HALP scores before and after preoperative chemotherapy in patients receiving NACT and changes between them (except for PNI) after NACT are useful in predicting the clinical response and pCR rates in breast cancer.

Materials and methods

One hundred twenty-seven patients diagnosed with breast cancer and receiving NACT at the Karadeniz Technical University Medical Faculty, Turkey, between December 2009 and January 2019 were included in the study. Breast magnetic resonance imaging (MRI) results before and after NACT were compared in order to evaluate clinical response rates, and use was made of the Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 criteria. Patients' pathological response rates were evaluated by the faculty's pathology department. NLR values were calculated by dividing neutrophils and lymphocytes, and PLR values by dividing platelets and lymphocytes. The formula 0.005*lymphocyte/mm3 +10*albumin (gr/dl) was applied to calculate PNI values, while the hemoglobin(g/L)*albumin(g/L)*lymphocyte(/L):platelet/L formula was applied for HALP scores. The relationship between patients' NLR, PLR, PNI, and HALP scores calculated before and after NACT, and the change in NLR, PLR, and HALP scores following NACT (delta-NLR, delta-PLR, and delta-HALP) and clinical and pathological response rates were also investigated. Since all patients were in the < 0 group, the relationship between delta-PNI and clinical and pathological response rates was not investigated. Data analysis was performed on SPSS version 22.0 statistical software. Descriptive statistics were expressed as number and percentage for categorical variables and as mean, standard deviation, median, and interquartile range (IQR) for numerical variables. The third quartile was employed to determine cut-off values for NLR, PLR, PNİ, and HALP. The cut-off value for delta-NLR, delta-PLR, and delta-HALP scores was regarded zero. p values < 0.05 were regarded as statistically significant.

Results

The patients' clinical and pathological characteristics are summarized in Table 1. The median age of the patients was 50.3±12.3 years (min 27, max 79). Eighty-two (77.4 %) of the 106 patients whose hormone receptor status was known were positive and 24 (22.6 %) were negative. Thirty-six (33.6 %) of the 107 patients whose immunohistochemistry records were accessible were HER2-

Tab. 1. Patients' clinicopathological features.

Variable	Patients (%)
Age, year (min–max)	50.3±12.3 (min 27, max 79)
Gender	
Male:	2 (1.6)
Female:	125 (98.4)
Menopausal Status (n=125)	
Premenopausal	54 (42.5)
Postmenopausal	71 (55.9)
Histological type (n=120)	
Ductal carcinoma	111 (92.5)
Lobular carcinoma	6 (5)
Other	3 (2.5)
Clinical T Stage (n=114)	
T1	26 (22.8)
T2	54 (47.4)
T3	26 (22.8)
T4	8 (7)
Clinical Lymph Node Status (n=119)	
N+	99 (83.2)
N–	20 (16.8)
Molecular subtype (n=105)	
Luminal A	23 (21.9)
Luminal B	58 (55.2)
HER2 +	14 (13.3)
Triple -	10 (9.5)
Ki-67 index (n=76)	
≤%10	22 (28.9)
>%10 ≤%20	23 (30.3)
>%20	31 (40.8)
Operation Type (n=127)	
MRM (modified radical mastectomy)	116 (91.3)
BCS (breast conserving surgery)	11 (8.7)

Tab. 2. Response rates to the neoadjuvant chemotherapy.

Response	All patients, n=127 (%)
Clinical response	
CR	27 (21.3)
PR	76 (59.8)
SD	21 (16.5)
PD	3 (2.4)
Pathological Response	
pCR (breast+axilla)	24 (18.9)
Residual mass	103 (81.1)

CR – Complete response, pCR – Pathological complete response, PD – Progressive disease, PR – Partial response, SD – Stable disease

positive and 10 (9.3 %) were triple-negative. Fifty-six (44.1 %) had been started on NACT with an anthracycline + taxane combination, 30 (23.6 %) with a combination of anthracycline + cyclophosphamide, 26 with (20.5 %) an HER2-targeted regimen, seven (5.5 %) with a platinum + taxane regimen, and eight (6.3 %) with other regimens (FEC, TC, and taxane alone). Sixteen patients completed the first chemotherapy protocol and progressed to the second. Nine (56.3 %) of these received taxane alone, four (25 %) received a taxane + platinum combination, and three (18.8 %) received HER2-targeted regimens. Ninety-seven (76.4 %) of our patients did not complete six-month NACT. Our patients' clinical and pathological response rates are summarized in Table 2. Analysis of clinical responses revealed ORR (complete response + partial response) in 103 (81.1 %) patients, while evaluation of pathological response rates revealed pCR in the breast + axilla in 24 (18.9 %) patients.

Factors affecting clinical and pathological responses were also investigated. ORR was significantly higher in patients with Ki-67 > 20 % than in those with Ki-67 ≤ 10 % and 10–20 % (90.3 % vs 59.0 % and 78.3 %, respectively, p: 0.027). No significant difference was observed between the Ki-67 groups in terms of pCR (32.3 % vs 18.2 % and 17.4 %, respectively, p: 0.344). No difference was also determined in ORR and pCR between pre- and postmenopausal patients (81.5 % vs 81.7 % p: 1.0, 45.8 % vs 54.2 %, p: 0.952, respectively). There was no difference in terms of ORR and pCR between the ≤ T2 and > T2 patients (78.75 % vs 85.3 % p: 0.582, 18.75 % vs 20.6 % p: 1.0, respectively). No difference was also found in ORR and pCR between patients with and without lymph node involvement (78.9 % vs 85.0 % p: 0.761, 17.2 % vs 30.0 % p: 0.216, respectively). No difference in ORR and pCR was also determined between luminal A, luminal B, HER2-positive, and triple-negative patients (73.9 % vs 79.3 % vs 92.9 % vs 80 % p: 0.61, 8.7 % vs 22.4 % vs 28.6 % vs 30.0 %, p: 0.317, respectively).

The patients' pre- and post-NACT NLR, PLR, PNI, and HALP scores were measured, and the presence of any association between these and ORR and pCR was investigated (Tabs 3 and 4, respectively). The presence of any relationship between the changes in these values after NACT and ORR and pCR was also investigated (Tab. 5). No statistically significant difference was observed in terms of ORR and pCR between cut-off values below and above the area under the curve for HALP scores before and after preoperative NACT, and the change between these (delta-HALP) (delta-HALP: ORR: 83.1 % vs 73.3 %, p: 0.470 and pCR: 18.8 % vs 13.3 %, p: 1.0).

Tab. 3. The relationship between clinical and pathological responses and preoperative NLR, PLR, PNI and HALP scores before neoadjuvant chemotherapy.

	ORR (CR+PR) n (%)			pCR n (%)		
	+	–		+	–	
NLR:						
<2.495:	77 (77.8%)	15 (65.2%)	p:0.32	18 (81.8%)	74 (74%)	p:0.61
≥2.495:	22 (22.2%)	8 (34.8%)		4 (18.2%)	26 (26%)	
PLR:						
<144.25:	77 (77.8%)	15 (65.2%)	p:0.32	16 (72.7%)	76 (76%)	p:0.96
≥144.25:	22 (22.2%)	8 (34.8%)		6 (27.3%)	24 (24%)	
PNI:						
<57.72:	72 (75%)	16 (76.2%)	p:1.0	17 (77.3%)	71 (74.7%)	p:1.0
≥57.72:	24 (25%)	5 (23.8%)		5 (22.7%)	24 (25.3%)	
HALP:						
≤60.974:	68 (70.8%)	19 (90.5%)	p:0.11	15 (68.2%)	72 (75.8%)	p:0.64
>60.974:	28 (29.2%)	2 (9.5%)		7 (31.8%)	23 (24.2%)	

CR – Complete response, HALP – Hemoglobin albumin lymphocyte platelet, NLR – Neutrophil lymphocyte ratio, ORR – Objective response rate, pCR – Pathological complete response, PD – Progressive disease, PLR – Platelet lymphocyte ratio, PNI – Prognostic nutritional index, PR – Partial response, SD – Stable disease

Tab. 4. The relationship between clinical and pathological responses and preoperative NLR, PLR, PNI and HALP scores after neoadjuvant chemotherapy.

	ORR (CR+PR) n (%)			pCR n (%)		
	+	–		+	–	
NLR:						
<3.1711:	78 (76.5%)	16 (66.7%)	p:0.46	20 (87%)	74 (71.8%)	p:0.21
≥3.1711:	24 (23.5%)	8 (33.3%)		3 (13%)	29 (28.2%)	
PLR:						
<226.888:	80 (78.4%)	15 (62.5%)	p:0.17	18 (78.3%)	77 (74.8%)	p:0.93
≥226.888:	22 (21.6%)	9 (37.5%)		5 (21.7%)	26 (25.2%)	
PNI:						
<52.05:	76 (74.5%)	18 (75%)	p:1.0	17 (73.9%)	77 (74.8%)	p:1.0
≥52.05:	26 (25.5%)	6 (25%)		6 (26.1%)	26 (25.2%)	
HALP:						
≤45.506:	77 (75.5%)	18 (75%)	p:1.0	14 (60.9%)	81 (78.6%)	p:0.12
>45.506:	25 (24.5%)	6 (25%)		9 (39.1%)	22 (21.4%)	

CR – Complete response, HALP – Hemoglobin albumin lymphocyte platelet, NLR – Neutrophil lymphocyte ratio, ORR – Objective response rate, pCR – Pathological complete response, PD – Progressive disease, PLR – Platelet lymphocyte ratio, PNI – Prognostic nutritional index, PR – Partial response, SD – Stable disease

Discussion

NACT is the standard treatment in locally advanced breast cancer (17). Since the clinical and pathological responses obtained with NACT are significant in terms of prognosis in breast cancer, it is important to understand the factors affecting the response to NACT. The best known factors for predicting response in patients receiving NACT are the tumor molecular subtype and the Ki-67 percentage (18, 19). In agreement with the previous literature, ORR was also higher among patients with Ki-67 > 20 % in the present study (p: 0.027).

Inflammation is regarded as the seventh hallmark of cancer. It has long been known to lead to malignant cell proliferation, angiogenesis, and metastasis, and to lower the response to chemotherapy and hormonotherapy (5). Since high NLR and PLR values have been shown to be correlated with increased cancer-related SIR, its prognostic significance has been investigated in several types of cancer, and better prognosis has been observed in patients with low NLR and PLR values (6, 8, 20). Whether these

Tab. 5. The relationship between clinical and pathological responses with delta-NLR, delta-PLR and delta-HALP scores after neoadjuvant chemotherapy.

	ORR (CR+PR) n (%)			pCR n (%)		
	+	–		+	–	
Delta-NLR:						
<0:	53 (81.5%)	12 (18.5%)	p:1.0	14 (21.5%)	51 (78.5%)	p:0.285
>0:	45 (80.4%)	11 (19.6%)		7 (12.5%)	49 (87.5%)	
Delta-PLR:						
<0:	26 (86.7%)	4 (13.3%)	p:0.519	8 (26.7%)	22 (73.3%)	p:0.202
>0:	72 (79.1%)	19 (20.9%)		13 (14.3%)	78 (85.7%)	
Delta-HALP:						
<0:	84 (83.1%)	17 (16.9%)	p:0.470	19 (18.8%)	82 (81.2%)	p:1.0
>0:	11 (73.3%)	4 (26.7%)		2 (%13.3)	13 (86.7%)	

CR – Complete response, HALP – Hemoglobin albumin lymphocyte platelet, NLR – Neutrophil lymphocyte ratio, ORR – Objective response rate, pCR – Pathological complete response, PD – Progressive disease, PLR – Platelet lymphocyte ratio, PNI – Prognostic nutritional index, PR – Partial response, SD – Stable disease

ratios are also predictive in determining the response to neoadjuvant therapy in breast cancer has also been investigated. Graziano et al's study published in 2018 considered the effects on achieving pCR of pre-NACT NLR and PLR and combinations thereof in 373 breast cancer patients receiving NACT. While no significant association was observed between NLR or PLR values alone, significantly higher pCR was achieved in patients in the low-NLR/low-PLR combination group (p 0.009) (7).

NLR, PLR, and HALP score are known to be of prognostic significance in several cancers. The principal limitation of studies showing that significance is the absence of standardized cut-off values. Since statistically significant cannot be obtained with ROC analysis, particularly in studies with low numbers of patients, statistical analysis is performed based on the cut-off values from previous studies. Since studies' patient profiles are not exactly identical, we do not think that statistical analysis using cut-off values from other studies will yield healthy results. Studies in the literature support this view (3, 21). Dan et al suggested that, theoretically, delta-NLR was more predictive than pre- and post-NACT NLR in evaluating the effectiveness of NACT in breast cancer. While no significant association was observed between pre-and post- preoperative NLR and pCR, they achieved significantly higher pCR in patients with delta-NLR < 0 ($p < 0.001$). The authors attributed this result to the study having focused on delta-NLR, a change variable, rather than an absolute value (3). In support of that idea, Wang et al. also showed that low delta-NLR and delta-PLR after chemotherapy in unresectable stomach cancer were associated with better overall survival (OS) and progression free survival (PFS) (21).

Since the HALP score shows both systemic inflammatory response and nutritional status, it is known to be a practical option in prognosis evaluation in several cancers (12, 13). To the best of our knowledge, only limited studies have investigated the effect of the change in HALP scores after NACT on clinical and pathological responses in breast cancer. In the light of this information, this study was intended to investigate the effect on clinical and pathological responses of pre- and post- preoperative HALP scores, systemic inflammatory response markers (NLR and PLR), and PNI values and the changes occurring in these in breast cancer patients receiving NACT. Although better numerical results were achieved in obtaining ORR and pCR in patients with delta-NLR, delta-PLR, and delta-HALP scores < 0, these results were not statistically significant (delta-HALP: ORR: 83.1 % vs 73.3 %, p: 0.470 and pCR: 18.8 % vs 13.3 %, p: 1.0).

We think that our inability to show any statistically significant effect on clinical and pathological responses of NLR, PLR, PNI, and HALP score values before and after preoperative NACT and the differences in these (with the exception of PNI) poses a limitation on this study. The principal limitations of this study are the low patient number and the differing ages, genders, and menopausal states, and therefore immune responses, of our patients. In addition, it should be remembered that the patients' stages at the time of diagnosis, and the histological and molecular subtypes differed, and that the responses to NACT may also be different. The types and durations of chemotherapy that our patients received in NACT also varied. It should not be forgotten that all these can affect clinical and pathological responses. Further studies with larger numbers are now needed to support the hypothesis in this study.

Conclusions

A higher ORR is achieved with NACT in breast cancer in patients with Ki-67 > 20 %. However, this study does not support the idea that preoperative NLR, PLR, PNI, and HALP scores measured before and after NACT and the changes in these after NACT (with the exception of PNI) are of prognostic significance in patients with breast cancer. Further, more extensive studies on the subject are now needed.

References

1. Ferlay J, Colombet M, Soerjomataram I, Mathers C, Parkin DM, Piñeros M et al. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. Int J Cancer 2019; 144 (8): 1941–1953. https: //onlinelibrary.wiley.com/doi/abs/10.1002/ijc.31937

2. Mamtani A, Barrio A V., King TA, Van Zee KJ, Plitas G, Pilewskie M et al. How Often Does Neoadjuvant Chemotherapy Avoid Axillary Dissection in Patients With Histologically Confirmed Nodal Metastases? Results of a Prospective Study. Ann Surg Oncol 2016; 23 (11): 3467–3474. https: //pubmed.ncbi.nlm.nih.gov/27160528/

3. Dan J, Tan J, Huang J, Zhang · Xiaoli, Yao Guo ·, Huang Y et al. The dynamic change of neutrophil to lymphocyte ratio is predictive of pathological complete response after neoadjuvant chemotherapy in breast cancer patients. Breast Cancer 1234; 27: 982–988. https: //doi.org/10.1007/s12282-020-01096-x

4. Untch M, Konecny GE, Paepke S, von Minckwitz G. Current and future role of neoadjuvant therapy for breast cancer. Breast 2014; 23 (5): 526–537. https: //pubmed.ncbi.nlm.nih.gov/25034931/

5. Colotta F, Allavena P, Sica A, Garlanda C, Mantovani A. Cancer-related inflammation, the seventh hallmark of cancer: links to genetic instability. Carcinogenesis 2009; 30 (7): 1073–1081. https: //pubmed.ncbi.nlm.nih.gov/19468060/

6. Seo HK, Hwang DW, Lee JH, Song KB, Shin SH, Kwon J et al. Role of systemic inflammation in predicting the prognosis of ampulla of Vater carcinoma. Surg Oncol 2019; 29: 33–40. https: //pubmed.ncbi.nlm.nih.gov/31196491/

7. Graziano V, Grassadonia A, Iezzi L, Vici P, Pizzuti L, Barba M et al. Combination of peripheral neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio is predictive of pathological complete response after neoadjuvant chemotherapy in breast cancer patients. Breast 2019; 44: 33–38. https: //pubmed.ncbi.nlm.nih.gov/30611095/

8. Mazaki J, Katsumata K, Kasahara K, Tago T, Wada T, Kuwabara H et al. Neutrophil-to-lymphocyte ratio is a prognostic factor for colon cancer: a propensity score analysis. BMC Cancer 2020; 20 (1). https: //pubmed.ncbi.nlm.nih.gov/32977767/

9. Zhai B, Chen J, Wu J, Yang L, Guo X, Shao J et al. Predictive value of the hemoglobin, albumin, lymphocyte, and platelet (HALP) score and lymphocyte-to-monocyte ratio (LMR) in patients with non-small cell lung cancer after radical lung cancer surgery. Ann Transl Med 2021; 9 (12): 976–976. https: //atm.amegroups.com/article/view/73135/html

10. Gao QL, Shi JG, Huang YD. Prognostic Significance of Pretreatment Prognostic Nutritional Index (PNI) in Patients with Nasopharyngeal Carcinoma: A Meta-Analysis. Nutr Cancer 2021; 73 (9): 1657–1667. https: //pubmed.ncbi.nlm.nih.gov/32924631/

11. Yuce E, Alandag C, Cakir E, Fidan E. Prognostic Factors in Gastrointestinal Stromal Tumors (GIST): Could Prognostic Nutritional Index (PNI) be a New Prognostic Factor? J Coll Physicians Surg Pak 2022; 32 (1): 81–85. https: //pubmed.ncbi.nlm.nih.gov/34983153/

12. Hu SJ, Zhao XK, Song X, Lei LL, Han WL, Xu RH et al. Preoperative maximal voluntary ventilation, hemoglobin, albumin, lymphocytes and platelets predict postoperative survival in esophageal squamous cell carcinoma. World J Gastroenterol 2021; 27 (4): 321–335. https: //pubmed.ncbi.nlm.nih.gov/33584065/

13. Yang N, Han X, Yu J, Shu W, Qiu F, Han J. Hemoglobin, albumin, lymphocyte, and platelet score and neutrophil-to-lymphocyte ratio are novel significant prognostic factors for patients with small-cell lung cancer undergoing chemotherapy. J Cancer Res Ther 2020; 16 (5): 1134–1139. https: //pubmed.ncbi.nlm.nih.gov/33004760/

14. Jiang H, Li H, Li A, Tang E, Xu D, Chen Y et al. Preoperative combined hemoglobin, albumin, lymphocyte and platelet levels predict survival in patients with locally advanced colorectal cancer Vol. 7. www.impactjournals.com/oncotarget

15. Guo Y, Shi D, Zhang J, Mao S, Wang L, Zhang W et al. The hemoglobin, albumin, lymphocyte, and Platelet (HALP) score is a novel significant prognostic facto for patients with metastatic prostate cancer undergoing cytoreductive radical prostatectomy. J Cancer 2019; 10 (1): 81–91.

16. Feng JF, Wang L, Yang X. The preoperative hemoglobin, albumin, lymphocyte and platelet (HALP) score is a useful predictor in patients with resectable esophageal squamous cell carcinoma. Bosn J basic Med Sci 2021; 21 (6): 773–780. https: //pubmed.ncbi.nlm.nih.gov/33974528/

17. Provenzano E. Neoadjuvant Chemotherapy for Breast Cancer: Moving Beyond Pathological Complete Response in the Molecular Age. Acta Med Acad 2021; 50 (1): 88–109. https: //pubmed.ncbi.nlm.nih.gov/34075766/

18. Samiei S, Simons JM, Engelen SME, Beets-Tan RGH, Classe JM, Smidt ML. Axillary Pathologic Complete Response After Neoadjuvant Systemic Therapy by Breast Cancer Subtype in Patients With Initially Clinically Node-Positive Disease: A Systematic Review and Meta-analysis. JAMA Surg 2021; 156 (6). https: //pubmed.ncbi.nlm.nih.gov/33881478/

19. Chen X, He C, Han D, Zhou M, Wang Q, Tian J et al. The predictive value of Ki-67 before neoadjuvant chemotherapy for breast cancer: a systematic review and meta-analysis. Future Oncol 2017; 13 (9): 843–857. https: //pubmed.ncbi.nlm.nih.gov/28075166/

20. Azab B, Bhatt VR, Phookan J, Murukutla S, Kohn N, Terjanian T et al. Usefulness of the neutrophil-to-lymphocyte ratio in predicting short- and long-term mortality in breast cancer patients. Ann Surg Oncol 2012; 19 (1): 217–224. https: //pubmed.ncbi.nlm.nih.gov/21638095/

21. Wang F, Liu ZY, Xia YY, Zhou C, Shen XM, Li XL et al. Changes in neutrophil/lymphocyte and platelet/lymphocyte ratios after chemotherapy correlate with chemotherapy response and prediction of prognosis in patients with unresectable gastric cancer. Oncol Lett 2015; 10 (6): 3411–3418.

Received July 26, 2022.
Accepted August 24, 2022.