EJMI

DOI: 10.14744/ejmi.2024.49044
EJMI 2024;8(2):137–143

Research Article

Correlation of HALP Score and Menopause Status with Treatment Response in Hormone Receptor-Positive Breast Cancer Patients Receiving Neoadjuvant Chemotherapy

Demet Isik Bayraktar,[1] Recep Turkel,[2] Murat Alan,[2] Guzin Demirag,[2] Leman Tomak,[3] Engin Yola[4]

[1]Department of Medical Oncology, Sabuncuoglu Serefeddin Training and Research Hospital, Amasya University, Amasya, Türkiye
[2]Department of Medical Oncology, Ondokuz Mayıs University, Faculty of Medicine, Samsun, Türkiye
[3]Department of Biostatistics and Medical Informatics, Ondokuz Mayis University, Faculty of Medicine, Samsun, Türkiye
[4]Department of Internal Medicine, Ondokuz Mayıs University, Faculty of Medicine, Samsun, Türkiye

Abstract

Objectives: We aimed to investigate the relationship of neoadjuvant therapy with HALP score, menopausal status and pathological response in patients with luminal A and luminal B breast cancer.

Methods: In this retrospective study, the files of patients who applied to Ondokuz Mayıs University Medical Oncology department between January 2016 and January 2023 were scanned and a total of 150 patients, 60 premenopausal and 90 postmenopausal, who received neoadjuvant chemotherapy were included.

Results: The median age of premenopausal patients was 40.67±6.35 (min 25-max 50), and postmenopausal patients was 57.67±7.48 (min 43-max 78). There was no relationship between overall survival and menopausal status (p=0.33). HALP score was significant only in postmenopausal patients (p=0.008). There was a significant association with complete pathological response (Miller&Payne 5) and PFS in the entire population (p=0.003). HALP score was lower in patients with PR level below 50% (p=0.039). There was no statistical significant between Ki67 and cerbB2, menopausal status and HALP score (p=0.106, p=0.064, respectively).

Conclusion: As a result, we did not detect the relationship between HALP score and pathological response in Luminal A and B patients receiving neoadjuvant therapy.

Keywords: Postmenopause, premenopause, HALP Score, neoadjuvan, breast cancer

Cite This Article: *Isik Bayraktar D, Turkel R, Alan M, Demirag G, Tomak L, Yola E. Correlation of HALP Score and Menopause Status with Treatment Response in Hormone Receptor-Positive Breast Cancer Patients Receiving Neoadjuvant Chemotherapy. EJMI 2024;8(2):137–143.*

Breast cancer is the most commonly diagnosed cancer in women and among cancers causing most deaths.[1] Estrogen receptors (ER), progesterone receptor (PR) and c-erbB2 (HER2) amplification score are the main elements directing treatment. In addition to these receptors shaping adjuvant and neoadjuvant treatment, they have prognostic and predictive features. Neoadjuvant treatment, especially, comes to the fore in HER2 positive or triple negative disease. Neoadjuvant treatment increases breast-protective surgery rates, while the tumor response to chemotherapy given before surgery guides determination of prognosis. The presence of residual tumor after neoadjuvant treatment affects the choice of adjuvant treatment.[2] Every tumor type is different immunohistochemically and treatment for

Address for correspondence: Demet Isik Bayraktar, MD. Department of Medical Oncology, Sabuncuoglu Serefeddin Training and Research Hospital, Amasya University, Amasya, Türkiye
E-mail: demetdoruk82@gmail.com

Submitted Date: March 21, 2024 **Accepted Date:** July 03, 2024 **Available Online Date:** July 19, 2024

every disease should be personalized. Neoadjuvant treatment is especially at the forefront for triple negative and Her2 (+) breast cancer.[3] Luminal A and B disease being less sensitive to chemotherapy may lead to a search for other predictive routes in the evaluation of neoadjuvant treatment and response to this treatment.

Efforts to find markers to direct treatment and predict prognosis still continue. Systemic inflammation and nutritional status have important places in progression of a variety of cancer types.[4,5] The efficacy of combined parameters like neutrophil lymphocyte ratio (NLR), prognostic nutritional index (PNI), platelet lymphocyte ratio (PLR), CRP/albumin ratio, and hemoglobin, albumin, lymphocyte, platelet (HALP) score has been researched in different cancer types in several studies.[6-11]

HALP score is a score created using 4 laboratory parameters that are indicators of nutrition and inflammation. The relationship of this score with prognosis has been investigated in many studies. To our knowledge, a limited number of studies have been conducted with neoadjuvant breast cancer.[12-16]

In this study, we aimed to research whether the efficacy of neoadjuvant treatment for luminal A and B breast cancer patients can be predicted by HALP score and whether there is a correlation between this response with menopause status in hormone-sensitive tumors.

Statistical Analysis

Statistical analyses were performed with SPSS 21.0 for windows. Data were presented as mean±standard deviation (SD), as median (min-max) as frequence (%). The Shapiro–Wilk test was used to analyze normal distribution assumption of the quantitative outcomes. Data were analysed by Mann–Whitney test for non-normal data. The frequencies were compared, using the Pearson Chi-square and Continuity Correction Chi-square. The area under the ROC curve (AUC) was evaluated as the measure of a diagnotic test's discriminatory power. Confidence intervals can be computed for AUC. In this article, both of sensitivity and specificity values were evaluated.

Kaplan-Meier method was used for survival analysis with the log-rank test used to statistical difference. A p value less than 0.05 was considered as statistically significant.

Method

This study is a single-center retrospective study. Patients attending the Medical Oncology Department of Samsun Ondokuz Mayıs University from 01 January 2016-01 January 2023 were retrospectively screened. Female patients aged over 18 years receiving neoadjuvant treatment and with pathology known after breast surgery were included in the study. Descriptive statistics were used to show clinicopathological characteristics. HALP score was calculated with the formula: hemoglobin (g/L) × albumin (g/L) × lymphocyte count (/L) / platelet count (/L). The cut-off value for the HALP score was accepted as 0,46 (0.871 sensitivity and 0.471 specificity). Among the biochemical parameters, those taken within 4 weeks of chemotherapy were evaluated.

Overall survival (OS) was calculated as the duration from date of diagnosis to death due to any cause. Follow-up time was calculated as the duration from date of diagnosis to final check-up. Patients not attending check-ups in recent times were called using the telephone numbers recorded in the hospital information system to learn their final status.

Pathological response was divided into two groups as Miller&Payne pathological response score 4,5 (90-100% tumor cell loss) and 1,2 and 3 (less than 90% tumor cell loss).[17]

Results

A total of 150 patients were included in the study. Patients were divided into two groups: premenopausal (n=60) and postmenopausal (n=90). The clinical and pathological characteristics of the patients are summarized in Table 1. The median age of premenopausal patients is 40.67 and the median age of postmenopausal patients is 57.67. Although ER was more common above 50% in both groups, PR was more common below 50% in postmenopause.

As expected, invasive ductal carcinoma was seen more frequently in both groups. There was no significant difference between the groups in terms of ER, PR, cerbB2, FISH, grade and Ki67 (Table 1). Additionally, luminal B was more common in both groups. Anthracycline treatments were used more frequently as chemotherapy regimens in both groups. The clinical stage was mostly evaluated as stage 2 and was found to be 76.7% and 77.8% in premenopausal and postmenopausal patients, respectively.

Women in the postmenopausal period had median survival duration of 84.21 months (95% CI, 3.07 (78.19-90.22)) and women in the premenopausal period had survival of 109.39 months (95% CI, 3.13 (103.26-115.52)). Survival was shorter in postmenopausal women; however, this was not statistically significant (p=0.139) (Fig. 1a).

Patients with Miller&Payne score 1-3 had mean median survival of 90.1 months (95% CI, 3.71 (82.82-97.36)), while patients with Miller&Payne score 4-5 had mean survival of 95.37 months (95% CI, 3.23 (89.03-101.7)). In the general group, patients with Miller&Payne 4-5 had higher survival and this was significant (p=0.031) (Fig. 1b).

Table 1. Clinicopathological features of patients

	Premenopausal status n(%)	Postmenopausal status n(%)
Age, year (min-max)	40.67±6.35 (min 25-max 50)	57.67±7.48 (min 43-max 78)
ER ve PR status		
ER <%50	11(%18.3)	13(%14.4)
ER >%50	49(%81.7)	77(%85.6)
PR <%50	27(%45.0)	49(%54.4)
PR >%50	33(%55.0)	41(%45.6)
cerbB2		
score 0	14(%23.3)	34 (%37.8)
score 1	9 (%15.0)	9 (%10)
score 2	16 (%26.7)	20 (%22.2)
score 3	21 (%35)	27 (%30)
FISH		
Negative	32 (%53.3)	56 (%62.2)
Positive	28 (%46.7)	34 (%37.8)
Grade		
Grade 1		1 (%1.1)
Grade 2	35 (%58.3)	44 (%48.9)
Grade 3	25 (%41.7)	45 (%50.0)
Ki67 % index		
≤ %20	23(%41.1)	33(%38.8)
>%20	33(%58.9)	52(%61.2)
Histological type		
invasive ductal	50 (%83.3)	81 (%90)
invasive lobular	2 (%3.3)	5 (%5.6)
other	8 (%13.4)	4 (%4.4)
Molecular subtype		
Luminal A	10 (%16.7)	22 (%24.4)
Luminal B	50 (%83.3)	68 (%75.6)
Chemotherapy		
anthracycline regimen	55 (%91.7)	86 (%95.6)
anthracycline-free regimen	5 (%8.3)	4 (%4.4)
Clinical stage		
1		1 (%1.1)
2	46 (%76.7)	70 (%77.8)
3	14 (%23.3)	19 (%21.1)
Pathologycal response		
No tumor	15 (%25.0)	17 (%18.9)
Stage I	10 (%16.7)	10 (%11.1)
Stage II	27 (%45.0)	47 (%52.2)
Stage III	8 (%13.3)	16 (%17.8)
Pathologycal yanıt		
Miller & Payne 1-2-3	28 (%46.7)	62 (%68.9)
Miller & Payne 4-5	31 (%51.7)	27 (%30.0)
Not evaluated	1 (%1.7)	1 (%1.1)
Latest status		
Dead	3 (%5)	12 (%13.3)
Alive	57 (%95)	78 (%86.7)

There was no correlation between menopause status with pathological response (p=0.055). Between pathological response and menopause status, there was no significant difference identified in terms of overall survival (p=0.33) (Fig. 1c-d).

Stage 2 patients had median survival of 102.52 months (95% CI, 3.56 (95.55-109.48)), while stage 3 patients had median survival of 82.2 months (95% CI, 3.71 (74.92-89.48)) (p=0.877).

When examined in terms of progression-free survival (PFS), in the general population, cases in stage 2 had median PFS of 96 months (95% CI 3.91 (88.31-103.65)), while cases in stage 3 had median PFS of 62.34 months (95% CI 6.21 (50.17-74.50)) (p=0.012) (Fig. 2a).

As expected, cases in stage 2 had significantly higher PFS compared to stage 3 (p=0.012). In the comparison made in terms of menopause and PFS, the average survival time in the premenopausal period was statistically higher in stage 2 than in stage 3 (p=0.001). However, there was no statistical difference in terms of PFS between stage 3 and stage 2 in the postmenopausal period (p=0.838).

In premenopausal patients, median PFS was 92.34 months (95% CI 5.76 (81.05-013.62)), while it was 77.72 months in postmenopausal patients (95% CI 3.63 (70.61-84.83)) (p=0.98) (Fig. 2b).

Cases with Miller&Payne score 1-3 had median PFS of 79.71 months (95% CI 4.41 (71.1-88.34)), while those with Miller-Payne score 4-5 had median PFS of 88.37 months (95% CI 4.04 (80.44-96.3)) (p=0.044) and this was significant. No difference was found in the comparison of Miller&Payne groups in terms of PFS in the premenopausal and postmenopausal periods; p value respectively; p=0.252 and p=0.097 (Fig. 2b-c).

When all patients were evaluated, the HALP score had a significant relationship with pathological complete response (Miller &Payne 5) and PFS. AUC=0.676; 0.580-0.771 (95% CI); p=0.003. HALP score was found to be lower in patients with low PFS. However, in the separate evaluation of pre- and postmenopausal women, the AUC value of the HALP score was significant only in postmenopause (p=0.008).

The pathological response in pre- and postmenopausal patients was evaluated by HALP score ROC analysis in the discrimination of Miller&Payne 1-3 and Miller&Payne 4-5. The value of AUC=0.416 for premenopause; 0.269-0.563 (95% CI); p=0.268 and AUC=0.548 for postmenopause; 0.420-0.677 (95% CI); p=0.470.

Complete pathological response for the entire group was evaluated by HALP score ROC analysis in the distinction of Miller&Payne 1-4 and Miller&Payne 5. AUC=0.439; 0.332-0.547 (95% CI); p=0.292. The pathological response

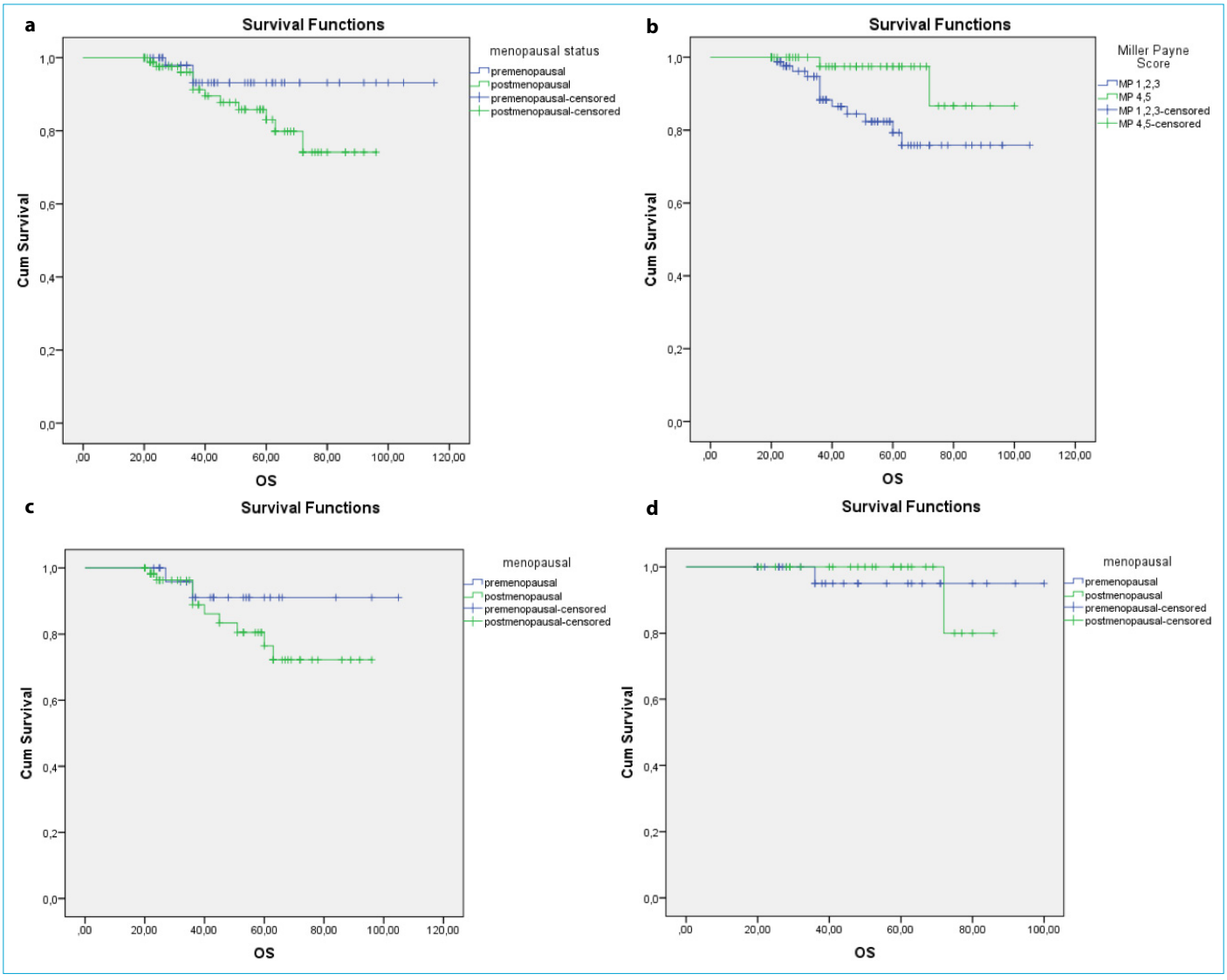

Figure 1. (a) Association of menopausal status with overall survival. **(b)** Association pathologycal response with overall survival in all patients. **(c)** Association of menopausal status with Miller& Payne 1,2,3 and overall survival. **(d)** Association of menopausal status with Miller& Payne 4,5 and overall survival.

in pre- and postmenopausal women was evaluated by HALP score ROC analysis in distinguishing Miller&Payne1-4 and Miller&Payne 5. The value of AUC=0.384 for premenopause; 0.216-0.552 (95% CI); p=0.173 and AUC=0.492 for postmenopause; 0.356-0.628 (95% CI); p=0.923.

There was no statistically significant between the HALP score for ER being below or above 50%, but the HALP score was found to be lower in patients with PR below 50% (p=0.039). When HALP score and its relationship with menopause were compared between patients with Ki 67 ≤20 and >20, no significant difference was detected (p=0.106). In terms of c-erbB2, no significant difference was found between scores 0, 1, 2 and score 3, as well as FISH positivity and menopausal status (respectively p=0.064, p=0.27).

Discussion

There are a limited number of studies assessing the relationship between HALP score and treatment response in breast cancer patients receiving neoadjuvant treatment. [11-20] As neoadjuvant treatment response is more limited in luminal breast cancer patients compared to other groups, it may not be considered an appropriate choice for study. However, in our study, we researched how both treatment response and menopause status affect these patients. From this perspective, our study may be a first.

ER and PR positivity are important for the initiation of hormonal treatment. HER2 status is identified with scores of 0, 1+, 2+ and 3+ and a score of 2+ is clarified with in situ hybridization (FISH). Based on these three receptors, breast

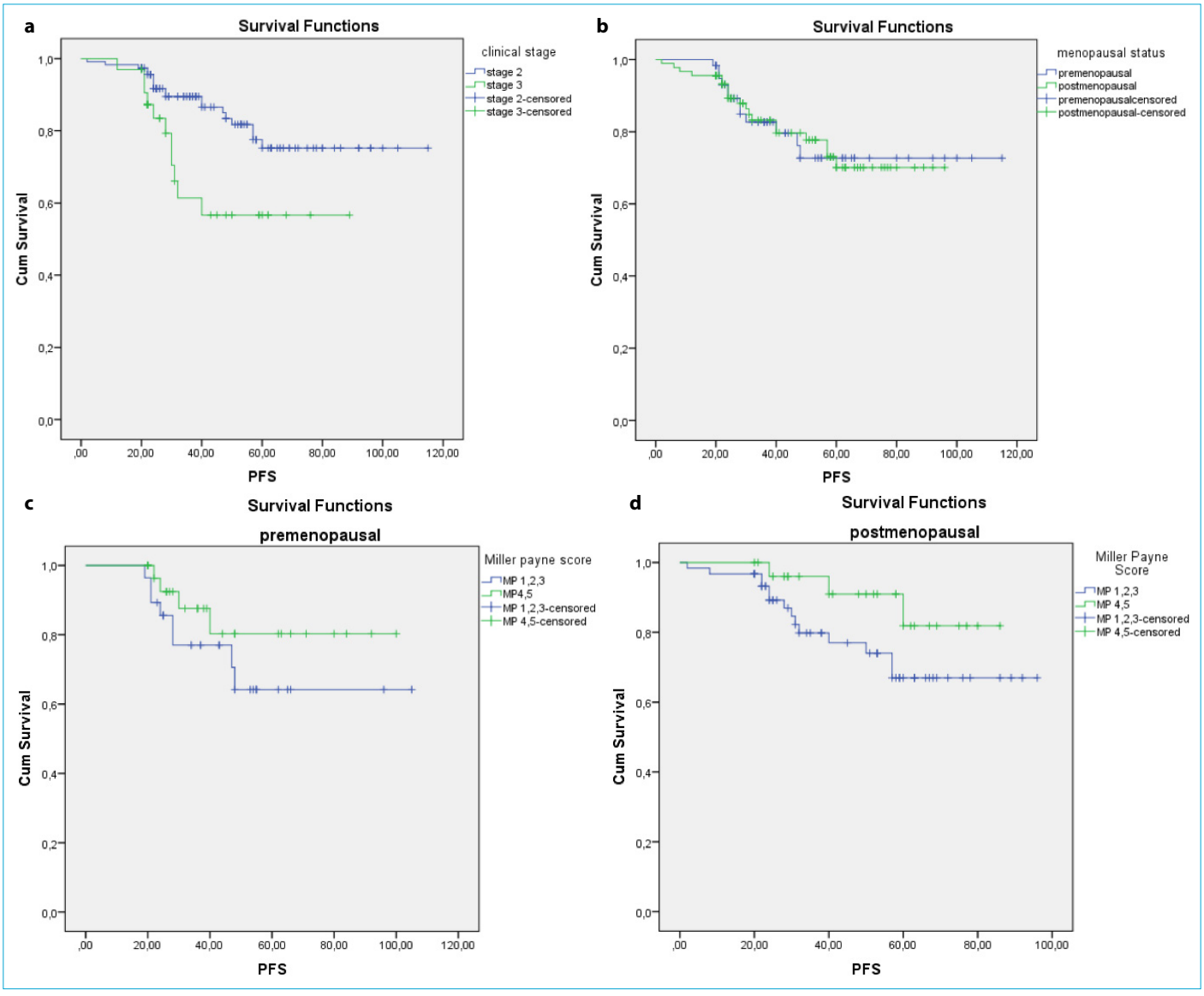

Figure 1. (a) Association of clinical stage 2 and 3 with PFS. **(b)** Association of menopausal status wiht PFS. **(c)** Association of Miller&Payne score 1-3 with PFS. **(d)** Association of Miller&Payne score 4-5 with PFS.

cancer may be divided into molecular subtypes as hormone positive luminal A and luminal B, HER2-enriched, basal-like and normal-like.[21]

In hormone positive (HR+) breast cancer, there is ER and PR expression. HR+ tumors comprise 70-80% of all breast cancer cases.[2] When selecting endocrine treatment, menopausal status is important. Premenopausal patients with active ovaries are directed toward a treatment modality including ovarian ablation. For treatment, tamoxifen, LHRH analogs and combined tamoxifen or aromatase inhibitors are each choices.

As shown in previous studies, systemic inflammation is effective in cancer formation, progression and prognosis.[22, 23] Because systemic inflammatory factors are closely related to the tumor microenvironment.[24] HALP score is also considered to be a good prognostic indicator that includes the parameters of this inflammation. For this purpose, its prognostic properties have been investigated in many types of cancer.[6-11]

In a study, HALP score was identified to be lower in older patients.[1] In our study, the HALP score was found to be higher in the postmenopausal period; p=0.004.

Another study of triple negative breast cancer patients.[18] found 3-year survival rates were lower in patients with low HALP score compared to patients with high HALP score ($p<0.05$). In the study, the correlation between menopause status and HALP score was not examined. According to criteria determined radiologically for treatment response,

the non-complete response (non-pCR) group had shorter 3-year survival compared to the PCR group (p<0.05). In our study, response evaluation used the Miller&Payne pathological score. The group with good response (Miller&Payne score 4-5) was compared with the group with low response (Miller&Payne score 1-3). Overal survival in the good response group was statistically higher than the low response group (p=0.031).

A study including breast cancer patients found the cut-off score was 29.01 (84% sensitivity and 26.1% specificity) and did not find that identification of axillary lymph nodes (LN) was a suitable determining factor. However, patients with low HALP score had higher axillary LN involvement compared to patients with high HALP score (p=0.38).[20] In a study conducted with tripple negative breast cancer (TNBC) patients, 3-year survival results were lower in the non-pCR group than in the pCR group (p>0.05).[19] In our study, PFS and OS in patients with pathological response were significantly longer than in the group without pathological response. However in our study, no statistical difference was detected in terms of pathologic response (Miller&Payne 4-5) and menopausal status when compared with the HALP score.

In several studies, low HALP score was shown to be correlated with increased risk of death and cancer-related death. In our study, no significant relationship was found between OS and HALP score.

For women in the premenopausal period, clinical stage 2 and 3 were statistically different in terms of PFS, while this difference was not present for women in the postmenopausal period.

The relationship between ER above and below 50% and PR above and below 50% with menopause and HALP was evaluated. Because as ER and PR decrease, chemotherapy response may increase. There was no significant difference between the HALP score for ER being below or above 50%, but the HALP score was found to be lower in patients with PR below 50% (p=0.039).

In another study conducted with luminal breast cancer patients, patients were classified according to Ki67 and a worse recurrence-free survival and overall survival was found in luminal B and HER2 positive patients.[25] In our study, we evaluated patients separately as pre- and postmenopausal according to Ki67 and HER2 status. However, we did not detect a relationship between Ki67 and HER2 and HALP score. The limitations of this study are that it is single-center and the number of patients is limited. Multicenter prospective studies with more patients are needed.

In conclusion, we did not determine the effectiveness of the HALP score in determining prognosis in our study. We found a higher HALP score in postmenopausal patients, but this was not associated with OS, PFS and pathological response. ER, Ki67 and c-erbB2 were also not associated with HALP score. We found a significantly lower HALP score only in the patient group with PR <50%. As expected, PFS and OS were higher in patients with Miller&Payne scores 4 and 5, regardless of the HALP score. No relationship was detected between pathological response and menopausal status.

Disclosures

Ethics Committee Approval: Ethic committee approval was obtained from Ondokuz Mayıs University Ethics Committee.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – D.I.B.; Design – D.I.B.; Supervision – G.D.; Materials – E.Y., R.T.; Data collection &/or processing – E.Y., M.A.; Analysis and/or interpretation – L.T.; Literature serach – D.I.B.; Writing – D.I.B.; Critical review – G.D.

References

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. CA Cancer J Clin. 2021 Jan;71(1):7-33. doi: 10.3322/caac.21654. Epub 2021 Jan 12. Erratum in: CA Cancer J Clin. 2021 Jul;71(4):359.
2. Sun MM, Jiang YN, Song GX, Zhuo SS, Zhang ZH. [Changes of immunohistochemical biomarkers before and after neoadjuvant chemotherapy in breast cancer and their prognosis]. Zhonghua Bing Li Xue Za Zhi. 2021 May 8;50(5):482-487.
3. Kohler BA, Sherman RL, Howlader N, Jemal A, Ryerson AB, Henry KA, Boscoe FP, Cronin KA, Lake A, Noone AM, Henley SJ, Eheman CR, Anderson RN, Penberthy L. Annual Report to the Nation on the Status of Cancer, 1975-2011, Featuring Incidence of Breast Cancer Subtypes by Race/Ethnicity, Poverty, and State. J Natl Cancer Inst. 2015 Mar 30;107(6):djv048.
4. McMillan DC. Systemic inflammation, nutritional status and survival in patients with cancer. Curr Opin Clin Nutr Metab Care. 2009 May;12(3):223-6.
5. Lu H, Ouyang W, Huang C. Inflammation, a key event in cancer development. Mol Cancer Res. 2006 Apr;4(4):221-33.
6. Templeton AJ, McNamara MG, Šeruga B, Vera-Badillo FE, Aneja P, Ocaña A, Leibowitz-Amit R, Sonpavde G, Knox JJ, Tran B, Tannock IF, Amir E. Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: a systematic review and meta-analysis. J Natl Cancer Inst. 2014 May 29;106(6):dju124.
7. Sun K, Chen S, Xu J, Li G, He Y. The prognostic significance of the prognostic nutritional index in cancer: a systematic review and meta-analysis. J Cancer Res Clin Oncol. 2014 Sep;140(9):1537-49.
8. Templeton AJ, Ace O, McNamara MG, Al-Mubarak M, Vera-Badillo FE, Hermanns T, Seruga B, Ocaña A, Tannock IF, Amir E.

Prognostic role of platelet to lymphocyte ratio in solid tumors: a systematic review and meta-analysis. Cancer Epidemiol Biomarkers Prev. 2014 Jul;23(7):1204-12.
9. Xu HJ, Ma Y, Deng F, Ju WB, Sun XY, Wang H. The prognostic value of C-reactive protein/albumin ratio in human malignancies: an updated meta-analysis. Onco Targets Ther. 2017 Jun 19;10:3059-3070.
10. Jiang H, Li H, Li A, Tang E, Xu D, Chen Y, Zhang Y, Tang M, Zhang Z, Deng X, Lin M. Preoperative combined hemoglobin, albumin, lymphocyte and platelet levels predict survival in patients with locally advanced colorectal cancer. Oncotarget. 2016 Nov 1;7(44):72076-72083.
11. Shen XB, Zhang YX, Wang W, Pan YY. The Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) Score in Patients with Small Cell Lung Cancer Before First-Line Treatment with Etoposide and Progression-Free Survival. Med Sci Monit. 2019 Jul 29;25:5630-5639.
12. Graziano V, Grassadonia A, Iezzi L, Vici P, Pizzuti L, Barba M, Quinzii A, Camplese A, Di Marino P, Peri M, Veschi S, Alberti S, Gamucci T, Di Gioacchino M, De Tursi M, Natoli C, Tinari N. 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 Apr;44:33-38.
13. Seo HK, Hwang DW, Lee JH, Song KB, Shin SH, Kwon J, Lee YJ, Kim SC. Role of systemic inflammation in predicting the prognosis of ampulla of Vater carcinoma. Surg Oncol. 2019 Jun;29:33-40.
14. Zhai B, Chen J, Wu J, Yang L, Guo X, Shao J, Xu H, Shen A. 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 Jun;9(12):976.
15. Mazaki J, Katsumata K, Kasahara K, Tago T, Wada T, Kuwabara H, Enomoto M, Ishizaki T, Nagakawa Y, Tsuchida A. Neutrophil-to-lymphocyte ratio is a prognostic factor for colon cancer: a propensity score analysis. BMC Cancer. 2020 Sep 25;20(1):922.
16. 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.
17. de Groot S, Lugtenberg RT, Cohen D, Welters MJP, Ehsan I, Vreeswijk MPG, Smit VTHBM, de Graaf H, Heijns JB, Portielje JEA, van de Wouw AJ, Imholz ALT, Kessels LW, Vrijaldenhoven S, Baars A, Kranenbarg EM, Carpentier MD, Putter H, van der Hoeven JJM, Nortier JWR, Longo VD, Pijl H, Kroep JR; Dutch Breast Cancer Research Group (BOOG). Fasting mimicking diet as an adjunct to neoadjuvant chemotherapy for breast cancer in the multicentre randomized phase 2 DIRECT trial. Nat Commun. 2020 Jun 23;11(1):3083.
18. Alandag C, Yilmaz M, Ucar M, Demir N, Erdis E, Yucel B. Prognostic Significance of HALP Score in Early Stage Triple-Negative Breast Cancer. EJMI 2022;6(4):409-416.
19. Lou C, Jin F, Zhao Q, Qi H. Correlation of serum NLR, PLR and HALP with efficacy of neoadjuvant chemotherapy and prognosis of triple-negative breast cancer. Am J Transl Res. 2022 May 15;14(5):3240-3246.
20. Duran A, Pulat H, Cay F, Topal U. Importance of HALP Score in Breast Cancer and its Diagnostic Value in Predicting Axillary Lymph Node Status. J Coll Physicians Surg Pak. 2022 Jun;32(6):734-739.
21. Vaz-Luis I, Ottesen RA, Hughes ME, Mamet R, Burstein HJ, Edge SB, Gonzalez-Angulo AM, Moy B, Rugo HS, Theriault RL, Weeks JC, Winer EP, Lin NU. Outcomes by tumor subtype and treatment pattern in women with small, node-negative breast cancer: a multi-institutional study. J Clin Oncol. 2014 Jul 10;32(20):2142-50.
22. Kinoshita T, Goto T. Links between Inflammation and Postoperative Cancer Recurrence. J Clin Med. 2021 Jan 10;10(2):228.
23. Cao X, Xu J. Insights into inflammasome and its research advances in cancer. Tumori. 2019 Dec;105(6):456-464.
24. Cruceriu D, Baldasici O, Balacescu O, Berindan-Neagoe I. The dual role of tumor necrosis factor-alpha (TNF-α) in breast cancer: molecular insights and therapeutic approaches. Cell Oncol (Dordr). 2020 Feb;43(1):1-18.
25. Cheang MC, Chia SK, Voduc D, Gao D, Leung S, Snider J, Watson M, Davies S, Bernard PS, Parker JS, Perou CM, Ellis MJ, Nielsen TO. Ki67 index, HER2 status, and prognosis of patients with luminal B breast cancer. J Natl Cancer Inst. 2009 May 20;101(10):736-50.