

Research Article

Factors Affecting Survival in Hormone Receptor-Positive, HER2-Negative, Operated Breast Cancer Patients

 Gizem Bakır Kahveci,  Ümmügül Üyetürk

¹Department of Medical Oncology, Trakya University Faculty of Medicine, Edirne, Türkiye

²Department of Medical Oncology, Hisar Hospital Intercontinental, Istanbul, Türkiye

Abstract

Objectives: The aim of this study is to investigate the effects of demographic, clinical, histopathological features and treatment on prognosis in hormone receptor positive HER-2 negative operated breast cancer patients followed up in the oncology outpatient clinic.

Methods: Breast cancer patients with hormone receptor-positive, HER2-negative status who underwent surgery and presented to the medical oncology outpatient clinic between January 1, 2012, and December 31, 2018, were retrospectively evaluated. The patients' demographic characteristics at diagnosis, tumor type, number of lymph nodes, pathological tumor stage, and Ki-67 indices were analyzed. Statistical analysis was performed using SPSS version 15.0 software. Ethical approval for the study was obtained from the Bolu Abant İzzet Baysal University Non-Interventional Clinical Research Ethics Committee (Approval Date: 27.12.2018, Decision No: 2018/280).

Results: A total of 165 patients with hormone receptor-positive, HER2-negative breast cancer who underwent surgery were included in the study based on hospital data. The median age at diagnosis was 55 years (minimum 22 – maximum 85). Of the patients, 61 (37%) were premenopausal, and 104 (63%) were postmenopausal. The most common tumor type was invasive ductal carcinoma (75.2%). A statistically significant difference was observed between surviving and deceased patients regarding the number of lymph nodes ($p=0.003$), pathological tumor stage ($p=0.004$), and TNM stage ($p=0.004$).

Additionally, the proportion of patients with Ki-67 $\geq 20\%$ was significantly higher in those who experienced recurrence compared to those without recurrence ($p=0.002$).

Conclusion: Lymph node involvement and number, tumor size, hormone receptor status, and HER2 status are reliable prognostic markers. Consistent with previous studies, our findings indicate that increased tumor size, a higher number of involved lymph nodes, and elevated Ki-67 expression are associated with poorer survival outcomes.

Keywords: Hormone positivity, HER2 negativity, breast cancer, survival

Cite This Article: Bakır Kahveci G, Üyetürk Ü. Factors Affecting Survival in Hormone Receptor-Positive, HER2-Negative, Operated Breast Cancer Patients. EJMI 2025;9(2):89–96.

Breast cancer is the most common type of cancer among women worldwide, and survival rates vary depending on the biological characteristics of the disease as well as the response to treatment.^[1] Hormone receptor-positive, HER2-negative breast cancer is one of the most frequently

encountered subtypes in clinical practice and is generally linked to a more favorable prognosis.^[2] However, a variety of factors influence survival in these patients. This study aims to investigate the clinical, pathological, and molecular factors influencing survival in patients with hormone

Address for correspondence: Gizem Bakır Kahveci, MD. Department of Medical Oncology, Trakya University Faculty of Medicine, Edirne, Türkiye
Phone: +90 506 269 64 27 **E-mail:** bakirkahvecigizem@gmail.com

Submitted Date: March 21, 2025 **Revision Date:** April 16, 2025 **Accepted Date:** June 14, 2025 **Available Online Date:** July 11, 2025

©Copyright 2025 by Eurasian Journal of Medicine and Investigation - Available online at www.ejmi.org

OPEN ACCESS This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.



receptor-positive, HER2-negative, operable breast cancer, as well as to identify key predictors of patient prognosis. In this study, we investigated the impact of demographic, clinical, histopathological characteristics, and treatment on the prognosis of hormone receptor-positive, HER2-negative breast cancer patients.

Methods

In this study, patients with hormone receptor-positive, HER2-negative, operable breast cancer who presented to the medical oncology clinic between January 1, 2012, and December 31, 2018, were retrospectively evaluated. Patient information was obtained from patient records and the KARMED system used in our hospital. Patients under the age of 18, those who received neoadjuvant therapy, those with metastatic disease, and those with hormone-negative or HER2-positive breast cancer were excluded from the study. The patients' medical history, family history, menopausal status, surgical history, diagnosis date, tumor location in the breast, type of surgery, surgery date, pathological diagnosis, tumor size, grade, Ki-67, luminal subtype, ER, PR, p53 status, number of dissected lymph nodes, diagnosis date, surgical date, chemotherapy date, adjuvant radiotherapy date, patients' current status, and last follow-up dates were reviewed through clinic files and computer records. Median values were calculated by ordering the data in ascending order and selecting the middle value. For continuous variables with skewed distributions, median values were used as they provide a more robust measure of central tendency that is less affected by outliers compared to arithmetic means.

The primary endpoint of this study was disease recurrence, while overall survival was evaluated as a secondary endpoint. Disease recurrence was defined as local or distant metastasis confirmed by clinical, radiological, or pathological assessment. Overall survival was measured from the date of diagnosis to the date of death from any cause or last follow-up.

Ethical approval for the study was obtained from the Ethics Committee of Abant İzzet Baysal University Faculty of Medicine on December 27, 2018 (decision no: 2018/280).

Statistical Analysis

Statistical analysis was performed using the SPSS 15.0 for Windows program. Descriptive statistics were presented as frequencies and percentages for categorical variables, and as mean, standard deviation, minimum, and maximum values for numerical variables. Independent group comparisons for numerical variables were conducted using the Student's t-test when the data met the assumption of nor-

mal distribution, and the Mann-Whitney U test when the normality assumption was not met. Proportions in independent groups were compared using the Chi-square test. Survival analyses were conducted using the Kaplan-Meier method. Disease-free survival was defined as the time from surgery to the first evidence of recurrence or death from any cause. Overall survival was calculated from the date of diagnosis to the date of death or last follow-up. Determinant factors were examined using Cox regression analysis. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 165 women with breast cancer were included in the study. The median age of the study group was 59 years (range: 29–86 years). Of the patients, 50.9% (n=84) had no significant medical history, 21.2% (n=35) had a family history of malignancy, and 7.9% (n=13) had a family member with a history of breast cancer. Thirty-seven percent (n=61) of the patients were premenopausal, while 63% (n=104) were postmenopausal. The median age at diagnosis was 55 years (range: 22–85 years). Tumor sizes ranged from 0.6 cm to 13 cm, with a median tumor size of 2.4 cm. The number of lymph nodes removed ranged from 0 to 53, with a median of 17.5 nodes removed and a median of 4.6 metastatic lymph nodes. The most common type of surgery was mastectomy with axillary lymph node dissection, performed in 110 patients (66.7%). The pathological diagnoses of the patients were determined either after biopsy or surgery. Of the patients, 75.2% (n=124) were diagnosed with invasive ductal carcinoma (IDC), and 12.7% (n=21) were diagnosed with invasive lobular carcinoma (ILC). When evaluating pathological grading, 57.2% (n=83) were classified as grade 2. According to the TNM staging of the patients, 55.2% (n=91) were in pT2, and 35.2% (n=58) were in pT1 (Table 1).

Biomarker Profiles and Hormone Receptor Status

The CEA levels of the patients included in the study ranged from 0.5 to 89.9 ng/mL, while CA 15-3 levels varied between 4.8 and 255.9 ng/mL. The Ki-67 proliferation index was found to be less than 20% in 54.3% of the patients, while 45.7% had a Ki-67 value of 20% or higher, indicating a heterogeneous distribution in tumor proliferation rates. A p53 mutation was not detected in the vast majority of patients (95.2%), with only 4.8% showing positive p53 expression. Estrogen receptor (ER) positivity was observed in 99.3% of patients, and progesterone receptor (PR) positivity was found in 87.3%. PR negativity was noted in only 12.7% of the group. When both ER and PR receptors were assessed together, 81.2% of patients exhibited co-positivity greater than 10%, whereas in 18.8% of patients, both re-

Table 1. Age at diagnosis, tumor size, number of lymph nodes, cancer location, type of surgery, pathological diagnosis, grade, pathological stage, and TNM stages.

	(Min-Max)	
Age at diagnosis, years	28-85	
Tumor Size (cm)	2,4 / (0,6-13)	
Dissected LN	17,5 / (1-53)	
Metastatic LN	4/(1-51)	
	n	%
Type of Surgery		
Mastectomy + SLND	13	7,9
Mastectomy + ALND	110	66,7
BCS+SLND	16	9,7
BSC+ALND	21	12,7
BSC	4	2,4
Simple mastectomy	1	0,6
Grade (%)		
1	29	20,1
2	83	57,6
3	32	22,2
Unknown	21	14,5
T Stage		
T1	58	35,2
T2	91	55,2
T3	10	6,1
T4	6	3,6
N Stage		
N1	38	23,2
N2	24	14,6
N3	23	14,0
N0	78	47,6
Nx	1	0,6
Pathological Prognostic Stage		
1A	68	43,0
1B	44	27,8
2A	10	6,3
2B	4	2,5
3A	18	11,4
3B	8	5,1
3C	6	3,8
TNM Stage		
1	38	23,3
2A	44	27,0
2B	29	17,8
3A	23	14,1
3B	4	2,5
3C	25	15,3
Pathological Diagnosis		
Invasive Ductal Carcinoma	124	75,2
Invasive Lobular Carcinoma	21	12,7
Tubular Carcinoma	2	1,2
Mucinous Carcinoma	6	3,6
Papillary Carcinoma	8	4,8
Cribriform Carcinoma	4	2,4

Lymph Node (LN), Breast-Conserving Surgery (BCS), Sentinel Lymph Node Biopsy (SLNB), Axillary Lymph Node Biopsy (ALNB), Tumor-Nodes-Metastasis (TNM).

ceptors were under 10%. The high rate of hormone receptor positivity (99.3% for ER and 87.3% for PR) observed in our patient cohort indicates that the majority of these patients are candidates for endocrine therapy. This suggests that hormone-based treatments should be considered as a fundamental component in the therapeutic management of these patients, as supported by current clinical guidelines (Table 2).

Cumulative Survival Rates

No statistically significant difference was found in the mean ages, medical history, family history characteristics, family history of breast cancer, and surgical history between the surviving and deceased patients. Similarly, no significant differences were observed in the mean age at diagnosis, tumor size, number of excised and metastatic lymph

Table 2. Tumor Markers, Hormone Receptors, Proliferation Status

	(Min-Max)	
CEA	(0,5-89,9)	
CA 15-3	(4,8-255,9)	
Ki 67	(0-80)	
	n	%
Ki 67 n (%)		
<%20	51	54,3
>%20	43	45,7
p53 n (%)		
Negative	6	3,6
Positive	2	1,2
unknown	157	95,2
ER	90/ (1-100) 90/(1-100)	
Positive	149	99,3
ER n (%)		
<%10	5	3,0
>%10	159	97,0
PR	53,6±34,7 (0-100 / 60)	
PR n (%)		
Negative	21	12,7
Positive	144	87,3
PR n (%)		
<%10	31	18,8
>%10	134	81,2
ER&PR n (%)		
ER ve PR <%10	31	18,8
ER ve PR >%10	134	81,2
ER&PR n (%)		
ER + & PR < %20	38	23,2
ER + & PR > %20	126	76,8

Carcinoembryonic Antigen (CEA), Cancer Antigen 15-3 (CA 15-3), Protein 53 (p53), Estrogen Receptor (ER), Progesterone Receptor (PR).

nodes, and tumor characteristics between the two groups. However, statistically significant differences were found in the N stage, stage, and TNM stage when comparing the survival rates of patients who survived and those who died ($p=0.003$, $p=0.004$, $p=0.004$) (Table 3).

In the analysis based on PR levels, there was no statistically significant difference in the cumulative survival rates between the PR <20% and PR ≥20% patient groups ($p=0.157$) (Fig. 1). Similarly, no significant difference was observed in the cumulative survival rates between the Ki-67 <20% and Ki-67 ≥20% patient groups ($p=0.381$) (Fig. 2).

Disease-Free Survival Rates

The mean values for surgery, tumor size, and the number of metastatic lymph nodes were significantly higher in patients with recurrence compared to those without recurrence ($p=0.002$, $p=0.022$). No significant differences were found between the two groups in terms of age at diagnosis, number of excised lymph nodes, and tumor characteristics. However, statistically significant differences were observed in the T stage, stage, and TNM stage when comparing the recurrence rates of patients with and without recurrence ($p=0.015$, $p=0.012$, $p=0.005$) (Table 4).

Table 3. Age at diagnosis and pathological tumor information of surviving and deceased patients

	Current Status				p
	Alive Median-Min-Max		Exitus Median-Min-Max		
Age at Diagnosis (years)	55/(28-85)		56/(34-77)		0,750
Tumor Size (cm)	2,2/(0,6-13)		3/(1-6)		0,054
Dissected LN	16,5/(0-53)		22/(2-52)		0,068
Metastatic LN	4/(1-42)		13,5/(2-51)		0,002
	n	%	n	%	
T Stage					
T1	55	36,4	3	21,4	0,125
T2	83	55,0	8	57,1	
T3	9	6,0	1	7,1	
T4	4	2,6	2	14,3	
N Stage					
N1	38	25,3	0	0,0	0,003
N2	19	12,7	5	35,7	
N3	18	12,0	5	35,7	
N0	74	49,3	4	28,6	
Nx	1	0,7	0	0,0	
Pathological Prognostic Stage					
1A	67	45,9	1	8,3	0,004
1B	41	28,1	3	25,0	
2A	9	6,2	1	8,3	
2B	4	2,7	0	0,0	
3A	15	10,3	3	25,0	
3B	7	4,8	1	8,3	
3C	3	2,1	3	25,0	
TNM Stage					
1	37	24,8	1	7,1	0,004
2A	43	28,9	1	7,1	
2B	28	18,8	1	7,1	
3A	19	12,8	4	28,6	
3B	3	2,0	1	7,1	
3C	19	12,8	6	42,9	

Lymph Node (LN), Tumor-Nodes-Metastasis (TNM).

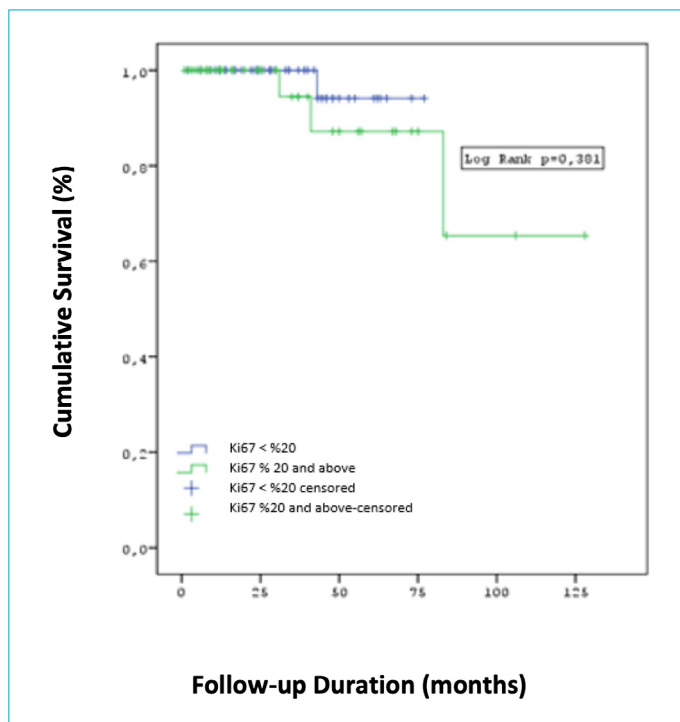


Figure 1. Cumulative Survival Rates of Patient Groups with ER+ & PR <20% and ER+ & PR ≥20%.

Additionally, the mean Ki-67 level and the percentage of patients with Ki-67 ≥20% were significantly higher in the recurrence group than in the non-recurrence group ($p=0.002$, $p=0.022$). This finding highlights the importance of Ki-67 as a predictive biomarker for recurrence, contributing to our understanding of tumor aggressiveness and prognosis.

No significant differences were observed in the hormonal characteristics between the recurrence and non-recurrence groups (Table 5).

Discussion

Research aimed at improving treatment and survival rates in breast cancer focuses on the identification of prognostic and predictive biomarkers. In early-stage breast cancer, the main prognostic biomarkers include tumor size, grade, number of metastatic lymph nodes, estrogen receptor (ER) status, progesterone receptor (PR) status, and HER2 status. These parameters are used to identify patients who are more likely to benefit from hormonal therapy and adjuvant chemotherapy.^[3]

Various studies have investigated the classification of breast cancer into subtypes (luminal A, luminal B, HER2-enriched, basal-like, and normal-like subtypes) and the relationship of these classifications with prognostic outcomes. These different prognostic relationships can be supported by immunohistochemical markers such as hormone receptors (ER, PR) and HER2.^[4]

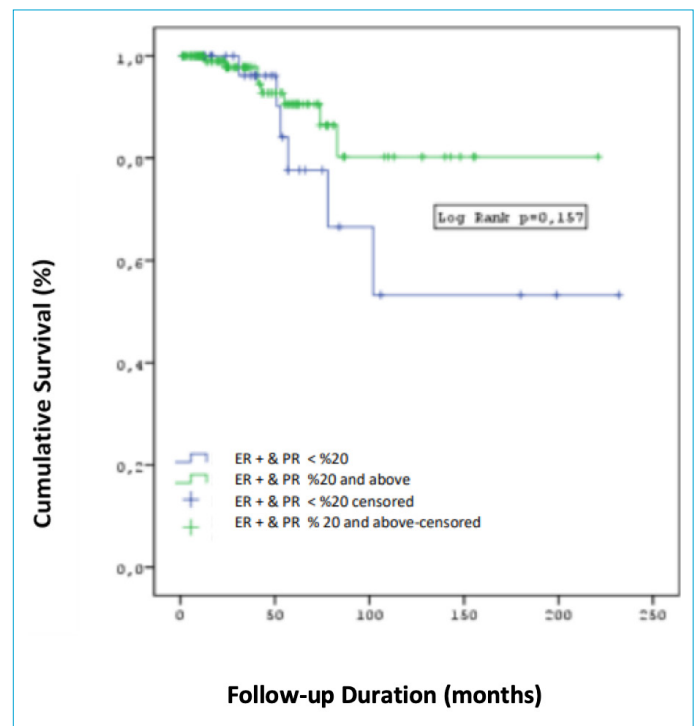


Figure 2. Cumulative Survival Rates of Patient Groups with Ki67 <20% and Ki67 ≥20%.

In our study, statistically significant differences were found in the TNM staging of hormone receptor-positive (HR+), HER2-negative patients, in terms of the proportion of patients alive and deceased during follow-up ($p=0.004$). Additionally, statistically significant differences were observed in survival based on pathological staging ($p=0.004$). An increase in mortality rates was observed with the progression of stage. In a study conducted by Mariana Chavez-MacGregor and colleagues in November 2017, significant differences were observed in 5-year survival rates based on staging in 43,938 breast cancer patients, with the most favorable results found in HR+ patients.^[5]

Tumor size and the number of lymph node metastases are among the most important prognostic factors in breast cancer. In a study conducted in Korea in 2016, the effects of lymph node metastasis and tumor size on survival were investigated in 39,826 breast cancer patients. The study found that even when the tumor size was small, survival was lower in patients with lymph node metastasis. It was also observed that T1 tumors with lymph node metastasis exhibited more aggressive behavior compared to T2 tumors without lymph node metastasis.^[6] In our study, statistically significant differences were found in the rates of lymph node metastasis between patients with recurrence and those without recurrence ($p=0.0022$). Furthermore, a significant increase in breast cancer recurrence rates was observed as tumor size increased ($p=0.002$).

Table 4. Recurrence Status of Patients Based on Tumor Characteristics, Age at Diagnosis, Cancer Location, and Type of Surgery

	Recurrence				p
	Absent Median(Min-Max)		Present Median (Min-Max)		
Age at Diagnosis (years)	55,5/ (29-85)		53/ (28-68)		0,234
Tumor Size (cm)	2,2/ (0,6-10)		3/ (1,5-13)		0,002
Dissected Lymph Node	17/ (0-53)		22/ (1-52)		0,183
Metastatic Lymph Node	1/(1-42)		3/ (0-51)		0,022
	n	%	n	%	
T Stage					
T1	56	38,9	2	9,5	0,015
T2	76	52,8	15	71,4	
T3	8	5,6	2	9,5	
T4	4	2,8	2	9,5	
N Stage					
N1	36	25,2	2	9,5	0,061
N2	20	14,0	4	19,0	
N3	16	11,2	7	33,3	
N0	70	49,0	8	38,1	
Nx	1	0,7	0	0,0	
Pathological Prognostic Stage					
1A	65	46,1	3	17,6	0,012
1B	40	28,4	4	23,5	
2A	9	6,4	1	5,9	
2B	4	2,8	0	0,0	
3A	12	8,5	6	35,3	
3B	7	5,0	1	5,9	
3C	4	2,8	2	11,8	
TNM Stage					
1	38	26,8	0	0,0	0,005
2A	38	26,8	6	28,6	
2B	26	18,3	3	14,3	
3A	20	14,1	3	14,3	
3B	3	2,1	1	4,8	
3C	17	12,0	8	38,1	

In breast cancer, Ki-67 is a tumor proliferation marker that is expressed in all stages of the cell cycle (except G0) and is associated with mitosis. The Ki-67 index is defined as the percentage of tumor cells showing positive nuclear staining in histological fields. Some studies have reported that a high Ki-67 index increases the risk of recurrence and treatment response in breast cancer.^[7]

The commonly used clinical cutoff value for Ki-67 is 14%. In the study by Dixon JM et al., it was found that survival was longer in patients diagnosed with invasive lobular carcinoma who had Ki-67 values below 20%, compared to those with higher values.^[8] In this study, Ki-67 levels were assessed using two different cut-off values: 14% and 20%.

This approach was chosen based on various sources in the literature suggesting different thresholds for determining the prognostic significance of Ki-67 in breast cancer. By considering both cut-off points, we aimed to capture a wider range of potential clinical implications related to tumor proliferation, which may vary depending on the chosen threshold.

The differences in Ki-67 percentages between patients with and without recurrence indicate that the recurrence rate was higher in patients with a cutoff value above 20%. However, when evaluating with the 14% cutoff value, no significant difference was observed in terms of recurrence or disease-free survival. The Ki-67 cut-off value of 20% is

Table 5. Recurrence Status of Patients Based on Tumor Markers

	Recurrence				p
	Absent Median (Min-Max)		Present Median (Min-Max)		
CEA	1,76 / (0,5-39,5)		1,57/ (0,68-89,9)		0,573
CA 15-3	16,6/(4,8-255)		20,2/ (6,7-233,5)		0,684
Ki 67	14,5 (0-70)		40/ (14-80)		0,002
	n	%	n	%	
Luminal					
Luminal A	43	50,0	1	12,5	0,063
Luminal B	43	50,0	7	87,5	
Ki 67					
<%20	50	58,1	1	12,5	0,022
20% and higher	36	41,9	7	87,5	

particularly relevant, as it can be used to stratify patients with higher risk of recurrence, emphasizing the need for more aggressive treatment or closer monitoring in those with higher Ki-67 expression.

Approximately 80% of breast cancers are ER and/or PR positive. Endocrine therapies are the cornerstone of treatment for HR-positive patients and reduce recurrence rates in early-stage cancers. Despite advances in hormone therapy, many women may experience recurrence after completing adjuvant treatment. Single-agent therapy with tamoxifen or aromatase inhibitors has shown limited clinical benefit in these patients. This is associated with resistance to endocrine therapy.^[9] Both genomic and non-genomic factors contribute to this resistance. The mechanisms underlying this resistance have not yet been fully clarified.^[10] In our study, no significant difference in survival was found when comparing the hormone therapy and chemotherapy protocols applied to HR+ patients.

In one study, the association of PR negativity with lymphovascular invasion and the negative effect of this condition on disease-free survival was determined. Based on these findings, PR negativity may be associated with poor prognosis in patients with breast cancer.^[11] In another study, low levels of hormone receptor immunoreactivity and lack of progesterone receptors were shown as causes of endocrine insensitivity.^[12] In our study, it was observed that PR percentage did not create a statistically significant difference in the survival rates of patients.

Our study has several limitations. First, due to its retrospective design, the observations are based solely on historical data. This may complicate the accurate determination of cause-and-effect relationships and could lead to the omis-

sion of important variables. Additionally, the limited patient population in our study resulted in a small sample size, which restricts the generalizability of the findings. Since the study was conducted at a single center, the results may be specific to the patient population at that center, and different results may be observed in other geographical regions or institutions.

Selection bias is another limitation of our study. The selection of patients based on certain criteria may result in the exclusion of certain patient groups or a bias towards specific treatment protocols. This may impact the accuracy of the results. Furthermore, some patients in our study may have missing data; for instance, not all biomarkers (such as Ki-67, ER, PR, etc.) were available for every patient, which could complicate a comprehensive analysis of the data. The heterogeneity of treatment protocols is another limitation; the variation in hormonotherapy and chemotherapy protocols across different patient groups led to a more complex assessment of their effects on treatment response and survival. Additionally, the study was conducted with a short follow-up period, and more definitive results regarding long-term survival and recurrence rates were not obtained. Without long-term follow-up, it is challenging to draw definitive conclusions about the long-term effects of treatment responses. Furthermore, the lack of external validation and the absence of certain key patient-specific factors such as genetic predispositions or socioeconomic status may influence the outcomes. The impact of these factors, along with potential recall bias, may also contribute to inaccuracies in the results.

Finally, the limited follow-up duration prevented us from obtaining more robust conclusions about long-term sur-

vival rates, recurrence, and treatment effects over time.

These limitations restrict the generalizability of our study findings to a broader population, and these factors should be considered when evaluating the accuracy and validity of the results.

In conclusion, our study found that tumor size, lymph node count, and Ki-67 percentage are significant factors affecting survival in hormone receptor-positive, HER2-negative breast cancer patients. Considering these factors plays a critical role in the development of early diagnosis and appropriate treatment strategies.

Disclosures

Ethics Committee Approval: Ethical approval for the study was obtained from the Ethics Committee of Abant İzzet Baysal University Faculty of Medicine on December 27, 2018 (decision no: 2018/280).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – G.B., Ü.Ü.; Design – G.B., Ü.Ü.; Supervision – Ü.Ü.; Materials – G.B., Ü.Ü.; Data collection and/or processing – G.B.; Analysis and/or interpretation – G.B., Ü.Ü.; Literature search – G.B., Ü.Ü.; Writing – G.B., Ü.Ü.; Critical review – G.B., Ü.Ü.

References

1. World Health Organization. Global Health Observatory. Geneva: World Health Organization; 2018. Available at: <http://www.who.int/gho/database/en/>. Accessed Jun 21, 2018.
2. Ünçel M, Aköz G, Yıldırım Z, Pişkin G, Değirmenci M, Solakoğlu Kahraman D, et al. Evaluation of clinicopathological features of breast cancer according to the molecular subtypes. *Tepecik Egit Hast Derg* 2015;25(3):151–6.
3. Goussia A, Simou N, Zagouri F, Manousou K, Lazaridis G, Gogas H, et al. Associations of angiogenesis-related proteins with specific prognostic factors, breast cancer subtypes and survival outcome in early-stage breast cancer patients. *A Hel-lenic Cooperative Oncology Group (HeCOG) trial. PLoS One* 2018;13(7):e0200302.
4. Chávez-MacGregor M, Mittendorf EA, Clarke CA, Lichtensztajn DY, Hunt KK, Giordano SH. Incorporating tumor characteristics to the American Joint Committee on Cancer breast cancer staging system. *Oncologist* 2017;22(11):1292–1300.
5. Davies C, Godwin J, Gray R, Clarke M, Cutter D, Darby S, et al; Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. *Lancet* 2011;378(9793):771–84.
6. Ryu JM, Lee HJ, Yoon TI, Lee ES, Lee SJ, Jung JH, et al; Korean Breast Cancer Society Consortium. Breast cancer-specific mortality in small-sized tumor with node-positive breast cancer: A nation-wide study in Korean Breast Cancer Society. *Breast Cancer Res Treat* 2016;159(3):489–98.
7. Chung YR, Jang MH, Park SY, Gong G, Jung WH; Korean Breast Pathology Ki-67 Study Group. Interobserver variability of Ki-67 measurement in breast cancer. *J Pathol Transl Med* 2016;50(2):129–37.
8. Dixon JM, Anderson TJ, Page DL, Lee D, Duffy SW. Infiltrating lobular carcinoma of the breast. *Histopathology* 1982;6(2):149–61.
9. Turner NC, Ro J, André F, Loi S, Verma S, Iwata H, et al; PALOMA3 Study Group. Palbociclib in hormone-receptor-positive advanced breast cancer. *N Engl J Med* 2015;373(3):209–19.
10. Fan W, Chang J, Fu P. Endocrine therapy resistance in breast cancer: Current status, possible mechanisms and overcoming strategies. *Future Med Chem* 2015;7(12):1511–9.
11. Chung SR, Choi WJ, Cha JH, Kim HH, Shin HJ, Chae EY, et al. Prognostic factors predicting recurrence in invasive breast cancer: An analysis of radiological and clinicopathological factors. *Asian J Surg* 2019;42(5):613–20.
12. Wunderle M, Pretscher J, Brucker SY, Volz B, Hartmann A, Fiessler C, et al. Association between breast cancer risk factors and molecular type in postmenopausal patients with hormone receptor-positive early breast cancer. *Breast Cancer Res Treat* 2019;174(2):453–61.