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Original Article

Bone metastasis: evaluation of 1100 patients with breast cancer

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Abstract: The aim of this study is to determine the relationship between the demographics and the clinical characteristics of breast cancer (BC) patients with bone metastasis (BM). The study included 1100 BC patients, of whom 174 had BMs and 926 had no BMs. Immunohistochemical methods were employed to understand estrogen receptor (ER)/progesterone receptor (PgR) receptor levels, Ki-67 protein levels and human epidermal growth factor receptor 2 (HER2) expression levels. Data were collected based on the hospital records of these patients, and ultrasonography or magnetic resonance imaging (MRI) results were employed for tumor localization. Positron emission tomography (PET)-computed tomography (CT) data were employed for the BM evaluation. The mean age (P = 0.067) and tumor diameter (P = 0.022) of BC cases who showed BM were significantly different from those who did not show BM. In addition, a significant relationship between the tumor diameter (P = 0.001) and axillary lymph node (ALN) number (P = 0.000) and BM was observed. The percentages of ER and PgR (r = 0.639; P = 0.000) were positively correlated, while the percentage of ER and Ki-67 protein levels (r = -0.505; P = 0.000) were negatively correlated. However, these correlations were not significant between the groups. The tumor diameter and positive ALNs may have an important role in BM of BC. There was no significant effect of ER/PgR receptor levels, Ki-67 protein levels, or HER2 expression levels in BMs of BC.

Keywords: Breast cancer, bone metastasis, ER, PgR, HER2, Ki-67

Introduction

Ninety to ninety-five percent of breast cancer (BC) cases are diagnosed at an early stage. However, only 20-30% of patients diagnosed with BC show metastasis [1]. BC tends to metastasize to different organs, especially in progressive stages, resulting in high morbidity and mortality [2]. Bone is the most common site of metastasis in BC, which may cause osteolysis accompanied with nerve compression, fracture, anemia, hypercalcemia, and severe pain [3, 4].

According to an evaluation of 4932 patients with metastatic BC between 2010 and 2013, 17% of patients were ≤ 50, 51% of patients were between 50 and 69 years old and 31% of patients were > 69 years old [5, 6]. In addition, in a study of 2097 patients, the mean age of diagnosis was 55.9 ± 38.1 years old [7]. In a study conducted with 2249 participants, it has been suggested that 60% of patients with bone metastasis (BM) have a tumor diameter that ranges from 0 to 1 cm, and 27% of patients have a tumor diameter that ranges from 2 to 4 [8].

Another variable evaluated in the study is the number of axillary lymph nodes (ALNs). Both monoclonal origins and polyclonal origins of metastasis are frequently investigated in studies that involve metastatic BC. In addition, few studies refer to ALN metastasis in distant metastasis seeding [9]. Metastatic involvement of ALNs is an important diagnostic factor in BC cases [10].

In this study, in terms of the etiopathology of patients with BM; estrogen receptor (ER)/progesterone receptor (PgR), human epidermal growth factor receptor 2 (HER2), and Ki-67 protein levels are included. Due to their proliferative effects, ER/PgR hormones and HER2 are considered to have a key role in the etiology of BC [11]. The ER and PgR receptors largely me-

Table 1. Values of age, tumor diameter, estrogen and progestrone receptor percentages, and Ki-67 antibody reactivity

Characteristic	N (%)	Min./Max.	*Mean ± s.d.*
Age	1100 (100)	28/95	55.04 ± 12.78
Tumor Diameter		0.5/12	2.48 ± 1.56
ER (%)		0/100	66.48 ± 35.98
PgR (%)		0/100	47.04 ± 38.46
Ki-67		1/100	26.69 ± 21.38

N: Number; Min.: Minimum; Max.: Maximum; s.d.: standard derivation; ER: Estrogen Receptor; PgR: Progesterone Receptor.

Table 2. Intergroup distributions of ages, existence of bone metastasis, type of breast cancer, localization of breast cancer, tumor diameter by category, number of axillary lymph nodes, existence of estrogen and progestrone receptors, and HER2 protein

Characteristic	N (%)
Groups of Age	
< 30	3 (0.3)
30-39	112 (10.2)
40-49	312 (28.4)
50-59	271 (24.6)
> 60	402 (36.5)
Bone Metastasis	
(+)	174 (15.8)
(-)	926 (84.2)
CA Type	
Invasive Ductal Carcinoma (IDC)	926 (84.2)
Invasive Lobular (IL) & Ductal Carcinoma (DC)	90 (8.2)
Invasive Lobular Carcinoma (ILC)	63 (5.7)
Phyllodes	1 (0.1)
Tubular Carcinoma	16 (1.5)
Metaplastic Carcinoma	4 (0.4)
CA Localization	
Left Upper Outer	297 (27.0)
Left Upper Inner	93 (8.4)
Left Lower Outer	81 (7.2)
Left Lower Inner	76 (6.9)
Right Upper Outer	269 (24.4)
Right Upper Inner	68 (6.2)
Right Lower Outer	86 (7.8)
Right Lower Inner	55 (5.0)
Left Central	3 (0.3)
Left Retroareolar	34 (3.1)
Right Retroareolar	38 (3.5)
Tumor Diameter	
< 1 cm	101 (9.2)
1-1.99 cm	357 (32.4)
2-2.99 cm	322 (29.3)

diate the proliferative effects of these hormones. Expression of these receptors in breast tissue may develop a tissue-specific response to these hormones [12]. Estrogen is a mitogen for the ERα in BC cells [13]. Therefore, an increase in the ERα ratio appears to affect metastasis. In addition, although some studies have shown a high prevalence of ER-primary positive tumors in BC cases with BM, and metastasis in ER-primary negative tumor patients have been shown [14, 15]. HER2 is a transmembrane tyrosine kinase receptor of the ErbB family and does not have an identified natural ligand. In the initial diagnosis of carcinoma in situ, HER2 is overexpressed in approximately 8% of cases; this rate is associated with poor survival [16]. In 40% of cases, clonal differentiation, which caused discrepancy in HER2 expression between primary tumor and metastasis, was observed [17]. Ki-67 protein, a cell proliferation biomarker, appears only in the active phase of the cell cycle. Highly proliferative cells are a response to an increase in the Ki-67 level and are prone to mutation onset and cell expansion [18]. Studies that measure ER, PgR, and Ki-67 protein levels from carcinoma in situ-free breast tissues show that these proteins and receptors are linked to the subsequent risk of BC [19].

In the studies performed with positron emission tomography (PET)-computed tomography (CT), BM was seen in the following regions: vertebra, costa (rib), pelvis, sternum, and femur [20]. However, these regions show some variability among studies. According to several studies, the average number of sections with metastasis was 6.5 in patients with bone metastases. It is beneficial to repeat these studies, which have very few participants as both patients and BC cases [21]. Therefore, the percentages of metastases in these regions were also considered when planning the research.

The aim of this study is to evaluate cases of BC showing BM from the demographic point of the view. Another asset of this study is to investigate the relationship

> 3 cm	320 (29.1)
Num. of Axillary Lymph Nodes	
0	576 (52.4)
1-3	306 (27.8)
≥ 4	218 (19.8)
Estrogen Receptor (ER)	
Positive	906 (82.4)
Negative	194 (17.6)
Progesterone Receptor (PgR)	
Positive	811 (73.7)
Negative	289 (26.3)
HER2	
Positive	170 (15.5)
Negative	826 (75.1)
Indefinite Positive	104 (9.5)
HER2 Score	
(-)	662 (60.2)
(+)	165 (15.0)
(++)	119 (10.8)
(+++)	154 (14.0)

N: Number; CA: Cancer; HER2: Human Epidermal Growth Factor Receptor 2.

Table 3. Distribution of patients according to age, tumor diameter, estrogen and progestrone percentages, and Ki-67 antibody reactivity

Characteristic	Bone Metastasis (mean ± s.d.)		*p value*
	+ (174)	- (926)	
Age	56.68 ± 13.78	54.73 ± 12.58	*.067*[a]
Tumor Diameter	3.07 ± 1.71	2.37 ± 1.51	*.022*
ER (%)	65.75 ± 34.427	66.81 ± 36.30	*.384*
PgR (%)	43.36 ± 37.68	47.73 ± 38.61	*.491*
Ki-67	29.02 ± 23.39	26.25 ± 20.98	*.214*

a: Results of breast cancer cases with bone metastasis according to independent sample t test; ER: Estrogen Receptor; PgR: Progesterone Receptor; s.d.: standard derivation.

Table 4. Distribution of patients according to grouped age, type of breast cancer, localization of breast cancer, tumor diameter by category, number of axillary lymph nodes, estrogen and progestrone receptors, and HER2 protein levels

Characteristic	Bone Metastasis (n)		*p value*[b]
	+ (174)	- (926)	
Groups of Age			*.530*
< 30	0	3	
30-39	16	96	
40-49	52	260	
50-59	32	239	
> 60	74	328	

among the ER, PgR, HER2, and Ki-67 values and BM rates in BC cases.

Materials and methods

Study design and participants

The study included 1100 patients who approved the voluntary consent form approved by the Yeditepe University Clinical Research Ethics Committee No. 1090, dated 09/2019. The study was completed between 09/2019 and 11/2019. Informed consent obtained from the participants was exempted by the institutional review board of Yeditepe University, which approved the study due to its retrospective design. All procedures in studies involving human participants were performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration, as revised in 2008, and its amendments or comparable ethical standards.

Data collection and measurement

Retrospective clinical data of 1100 patients who underwent surgery for BC between 2012 and 2019 were utilized in the study. For the data on ER/PgR levels, Ki-67 protein levels, and HER2 expression levels, certain pathology laboratory findings approved by the Ministry of Health were employed. PET-CT results from the same laboratory were used to evaluate bone metastases. USG and MRI results from the same laboratory for tumor localization were also included in the study.

Statistical analysis

Patient demographics and clinical features were described using frequency tables, means, and graphics. Differences between patient subgroups were investigated using the chi-square and Fisher exact tests for categorical data and the Independent Samples t test and analysis of variance (ANOVA) for continuous data. Differences with a *p* value of 0.05 or less were considered significant. In addition, regression analysis was performed

CA Type			*.626*
IDC	143	783	
IL-DC	20	70	
ILC	11	52	
Phyllodes	0	1	
Tubular Carcinoma	0	16	
Metaplastic Carcinoma	0	4	
CA Localization			*.979*
Left Upper Outer	52	245	
Left Upper Inner	17	76	
Left Lower Outer	13	68	
Left Lower Inner	9	67	
Right Upper Outer	43	226	
Right Upper Inner	6	62	
Right Lower Outer	16	70	
Right Lower Inner	10	45	
Left Central	1	2	
Left Retroareolar	4	31	
Right Retroareolar	4	34	
Tumor diameter			*.001*
< 1 cm	3	98	
1-1.99 cm	45	312	
2-2.99 cm	47	275	
> 3 cm	79	241	
Num. of axillary lymph nodes			*.000*
0	3	573	
1-3	54	252	
≥ 4	117	101	
Estrogen Receptor (ER)			*.472*
Positive	148	758	
Negative	26	168	
Progesterone Receptor (PgR)			*.836*
Positive	130	681	
Negative	44	245	
HER2			*.886*
Positive	24	146	
Negative	134	692	
Indefinite	16	88	
HER2 Score			*.727*
(-)	101	561	
(+)	32	134	
(++)	20	98	
(+++)	21	133	

N: number; CA: Cancer; IDC: Invasive Ductal Carcinoma; IL-DC: Invasive Lobular-Ductal Carcinoma; ILC: Invasive Lobular Carcinoma; HER2: Human Epidermal Growth Factor Receptor 2.

to evaluate the presence of bone metastases and numerical variables.

Results

Patients' clinical and demographic characteristics

As shown in **Table 1**, the mean patient age was 55.04 ± 12.78 (range: 28-95) years. The mean tumor diameter of the patients was 2.48 ± 1.56 (range: 0.5-12 cm). Estrogen and progesterone receptor percentages were also included in the clinical evaluation. Accordingly, the lowest and highest ER and PgR percentages were found to be 0 and 100, respectively. The mean ER (%) with standard errors was 66.48 ± 35.98, and the mean PgR (%) was 47.04 ± 38.46. The mean Ki-67 antibody indication, which is considered an important marker in BC diagnosis, was 26.69 ± 21.38.

In addition to the variables listed in **Table 1**, age group, BM, CA type and localization, tumor diameter category, presence of ALNs, ER, and PgR, and CerbB2 protein levels were also included (**Table 2**). Accordingly, 0.3 percent of the patients who participated in the study were younger than 30 at the lowest rate. The highest rate of 36.5 percent was seen in patients aged 60 and over. Only 15.8 percent of the patients included in the study had BMs. No BMs were detected in 84.2 percent of the patients (**Table 2**).

When the frequency of BC types was evaluated, the most common type was invasive ductal carcinoma (IDC) with 84.2 percent of cases. In second place was invasive lobular (IL) and ductal carcinoma (DC) with a corresponding value of 8.2 percent. When the localization of CA was evaluated, the most common sites were left upper outer (27.0%) and right upper outer (24.4%) (**Table 2**).

Tumor diameters of 1-1.99 cm (32.4%), 2-2.99 cm (29.3%), and tumors larger than 3 cm (29.1%) were detected. ALNs were not seen to a great extent (52.4%). In addition, ERs (82.4%) and PgRs (73.7%) were detected in the majority of cases. When the presence of HER2 proteins was evaluated, 15.5% were positive for CerbB2, 75.1% were negative for CerbB2, and

Table 5. Distribution of bone metastasis positivity according to existence of estrogen and progesterone receptors and HER2 protein levels

Characteristic	Bone Metastasis		*p value*
	(+)	(-)	
IDC			
Estrogen Receptor (ER)			*0.482*
Positive	119	630	
Negative	24	153	
Progesterone Receptor (PgR)			*0.824*
Positive	106	569	
Negative	37	214	
HER2			*0.818*
Positive	23	135	
Negative	107	569	
Indefinite	13	79	
IL-DC			
Estrogen Receptor (ER)			
Positive	17	63	*0.909*
Negative	3	7	
Progesterone Receptor (PgR)			
Positive	16	53	*0.815*
Negative	4	17	
HER2			
Positive	0	8	
Negative	18	59	*0.491*
Indefinite	2	3	
ILC			
Estrogen Receptor (ER)			
Positive	11	48	*0.521*
Negative	0	4	
Progesterone Receptor (PgR)			
Positive	8	45	*0.605*
Negative	3	7	
HER2			
Positive	0	2	
Negative	10	49	*0.727*
Indefinite	1	1	

IDC: Invasive Ductal Carcinoma; IL-DC: Invasive Lobular-Ductal Carcinoma; ILC: Invasive Lobular Carcinoma; HER2: Human Epidermal Growth Factor Receptor 2.

9.5% were negative for HER2. The HER2 scores were found to be mostly negative (60.2%). Refer to **Table 2** for detailed evaluation.

Distribution of demographic and clinical data according to BM

As shown in **Table 3**, 174 of 1100 patients who participated in the study had bone metastases. The relationship among age, tumor diameter, Ki-67 protein levels and percentages of ER and PgR by BM in BC patients was evaluated by the *Independent Samples t Test*. According to these results, no significant relationship among the Ki-67 protein level, ER, and PgR percentages and BM ($P > 0.05$) was observed. In addition, the relationship between age and BM was significant at the trend level ($P = 0.067$). When the relationship between the tumor diameter and bone metastases of the participants was evaluated, the mean tumor diameter of the BM positive patients was 3.07 ± 1.71 and that of the BM negative patients was 2.37 ± 1.51 ($P = 0.022$) (**Table 3**).

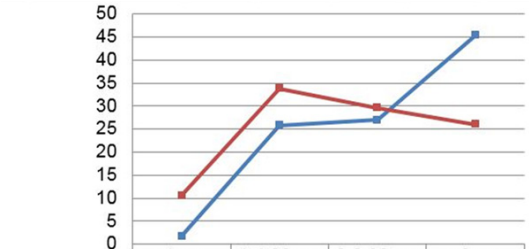
When the relationship between the presence of BM and the clinical characteristics of BC was evaluated, no significant relationship among the group of ages, types of BC, localization of BC, presence of ER and PgR and CerbB2 protein levels was observed with the *chi-square/Fisher Test* ($P > 0.05$) (**Table 4**). According to breast cancer types (IDC, IL-DC, ILC), the results of ER, PgR, and HER2 protein levels did not have a significant effect on bone metastasis formation (**Table 5**).

However, when the relationship between the tumor diameter and the presence of BM was evaluated by category, approximately 45.4% of the cases with BM had a tumor diameter greater than 3 cm ($P = 0.001$) (**Table 4**; **Figure 1**).

As shown in **Figure 2**, in approximately 67.2 percent of BC cases with BM, the number of ALNs was 4 or greater ($P = 0.000$). Multivariate regression analysis of age, tumor diameter, and ALNs are shown in **Table 6**.

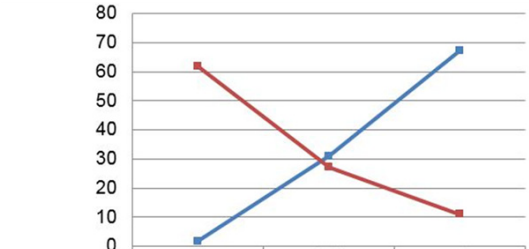
Correlation between demographic and clinical data

The relationship among age, tumor diameter, percentage of ER and PgR, and Ki-67 protein levels was evaluated by Pearson correlation. Accordingly, there was a significant positive correlation between the ER percentage and the PgR percentage ($r = 0.639$; $P \leq 0.001$). That is, the increase in the ER percentage appeared to affect the increase in the PgR percentage. In addition, a negatively significant moderately sig-



	<1 cm	1-1.99 cm	2-2.99 cm	>3 cm
BM(+)(%)	1.8	25.8	27	45.4
BM(-)(%)	10.6	33.8	29.6	26

Figure 1. Tumor diameter by category. Number of tumor diameters by category reported over the course of study in 1100 patients with breast cancer. Mean percentages of BM existence (95% confidence interval).



	0	1-3	>4
BM(+)(%)	1.8	31	67.2
BM(-)(%)	61.8	27.2	11

Figure 2. Number of axillary lymph nodes. Number of axillary lymph nodes by category reported over the course of study in 1100 patients with breast cancer. Mean percentages of BM existence (95% confidence interval).

nificant correlation between the ER percentage and the Ki-67 protein level ($r = -0.505$; $P \leq 0.001$) was observed. A similar correlation was observed between the Ki-67 protein level and the PgR percentage ($r = -0.380$; $P \leq 0.001$). An increase in the percentage of the ER and the PgR was considered to cause a decrease in the Ki-67 protein level (**Table 7**).

As seen in **Figures 3** and **4**, a significant correlation between the PgR percentage and ER percentage and a significant correlation between the Ki-67 protein level and the ER percentage did not differ between patients with BMs and patients without BMs.

BM localization in participants

BM was seen in the data of the 174 of the 1100 BC patients who participated in the study. When the PET-CT data of 174 patients were considered, the bones with metastasis were as follows: 75.2% were detected in the vertebra, 53.4% were detected in the pelvis, and 28.7% were detected in the rib bones. In **Table 8**, different BM involvement areas/localizations of 174 BC patients could also be observed.

Discussion

In this study, the clinical and demographic distributions of 1100 patients who underwent surgery for BC and the relationship among these clinical values and BM were evaluated. The mean age of the patients with BM was 56.68 ± 13.78 ($P = 0.067$), which was significant. The age at diagnosis was between 28 and 95 years. A recent study of 174 BC cases (43 BM) by Ecclestone et al. revealed that the median age was 62 years old and the diagnosis ranged from 36 to 93 years old [22]. According to another study on the incidence of BM in early BC patients with 2097 participants, the median age was 55.9 years and the age range was 22 to 94 years [7]. When 1100 participants were divided into age groups, it was seen that 36.5% (N = 402) of the patients were > 60 years old and 24.6% (N = 271) of the patients were between 50 and 59 years old. However, no significant relationship between the age groups of patients with BM and without BM ($P = 0.530$) was observed.

Another finding that was significant with BM in the study was the tumor diameter. In the study, the tumor diameter of the patients with BM was 3.07 ± 1.71, and that of the patients without BM was 2.37 ± 1.51 ($P = 0.022$). Sun et al. found that patients with BM (N = 20/60) had a tumor size of 2.74 ± 1.36 [24]. In recent studies, no detailed information about tumor diameter was observed in different studies [24, 25]. In addition, the minimum tumor diameter in the cases of BC that showed BM was 3 cm. In previous studies, the tumor diameter generally varied between 2 and 4 [24, 26]. These results are similar to those of our study. Furthermore, in the data employed in this study, tumor diameters of 3 cm and greater were not separated in itself [25]. Therefore, the data do not meet the carcinoma in situ leveling criteria applied in different studies (such as T1, T2, T3 and T4).

Similarly, the number of ALNs was found to be significantly different between the groups ($P = 0.000$). According to the study, the minimum number of ALNs in BC cases that showed BM

Table 6. Significant factors affecting bone metastasis, multiple logistic regression analysis

	β coefficient	Standard Error	Wald	P	Exp (β)	95% CI for Exp (B)	
						Lower	Upper
Num. of axillary lymph nodes	-2.033	0.214	90.012	0.000	0.131	0.086	0.199
Tumor diameter	-0.061	0.082	0.555	0.456	0.940	0.800	1.105
Age	-0.003	0.011	0.075	0.784	0.997	0.976	1.018
Constant	6.232	0.790	62.181	0.000	508.797		

Dependent Variable: bone metastasis; Nagelkerke R2=0.436. Exp (β): Exponentiation of the B coefficient; CI: Confidence Interval.

Table 7. Correlation of 1100 breast cancer cases according to age, tumor diameter, percentages of estrogen and progestrone receptors, and Ki-67 protein level

	Age	Tumor diameter	ER (%)	PgR (%)	Ki-67 protein
Age	1	.030	.170**	.112**	-.179**
Tumor diameter	.030	1	-.095*	-.036	-.022
ER (%)	.170**	-.095*	1	.639**	-.505**
PgR (%)	.112**	-.036	.639**	1	-.380**
Ki-67 protein	-.179**	-.022	-.505**	-.380**	1

*: Correlation is significant at the 0.05 level (2-tailed). **: Correlation is significant at the 0.01 level (2-tailed). ER: Estrogen Receptor; PgR: Progesterone Receptor.

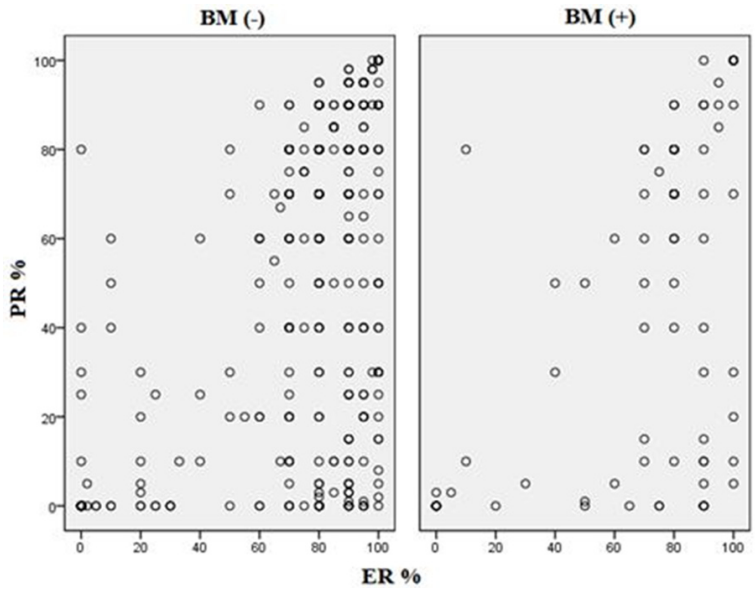


Figure 3. Distribution of the correlation between percentages of ER and PgR according to bone metastatic and non-bone metastatic patients (99% confidence interval).

was 4. Accordingly, the risk of developing metastasis varied according to the ALNs. According to previous research results, although the cancer in an ALN is not a breast tumor, it should be treated. In addition, according to a study conducted on 29 BC patients with and without tumors, no relationship between the number of axillary nodules and survival rates was identified [27]. According to a clinical study conducted by Chen et al. of 2133 patients with 327 BMs, patients with BM developed frequent ALN metastases [28]. In addition, the study showed that ALN metastasis is an important risk factor for BM in BC patients. In addition, studies have found that BC patients with a minimum of four ALNs have a high incidence of BM [29].

According to the work of Coleman and Rubens, patients with ER-positive primary tumors were found to have a higher risk of developing BMs [14]. However, some studies showed that BM could be seen in ER-negative patients with ER-positive primary tumor [15]. However, no relationship was found between the percentage or presence of ER and BM in our study. Similar results were noted for the PgR and HER2 percentages and scores and Ki-67 data. Although the numbers of PgR and Ki-67 expression levels and the likelihood of developing metastases were low, in a retrospective study of 490 BC in situ patients, Molnár et al. found that high PgR expression levels were associated with better survival [30]. Similarly, according to a biomarker study conducted by Bohn et

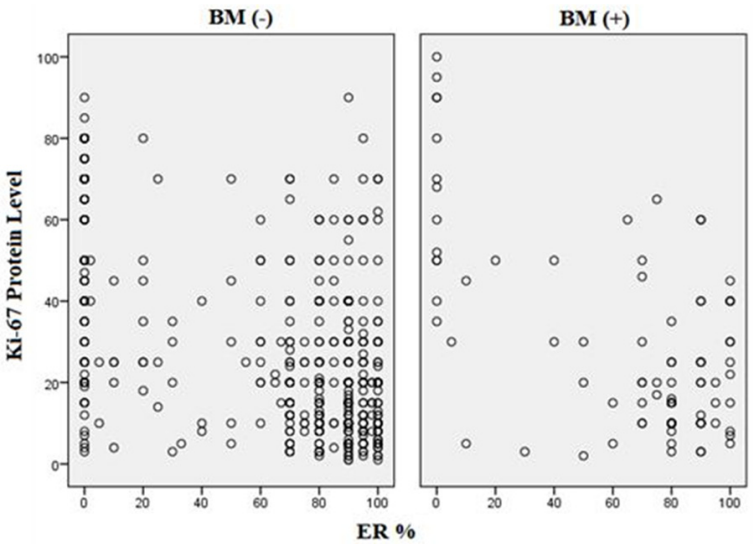


Figure 4. Distribution of the correlation between percentage of ER and Ki-67 protein levels according to bone metastatic and non-bone metastatic patients (99% confidence interval).

Table 8. Distribution of involvement areas according to 174 bone metastasis positive patients

Metastasis Location	N (%)
Vertebra	131 (75.2)
Pelvis	93 (53.4)
Ribs	50 (28.7)
Scapula	40 (22.7)
Proximal Femur	39 (22.4)
Femur Diaphysis	30 (17.2)
Humerus	28 (16.0)
Sternum	20 (11.4)
Clavicle	11 (6.3)

N: number.

al. of cases with (N = 16) BM and without (N = 64) BM, there was no significant relationship between the ER rate and PgR rate between the groups [31].

Although some retrospective studies indicate that overexpression in HER2 is related to central nervous system metastasis, few studies show an association with BM [32]. In addition, according to a multivariate analysis performed on 3.726 patients with an average of 15-year data by Kennecke et al., HER2-enriched tumors were highly associated with brain, liver, and lung metastasis. However, this relationship was not found with the BM rate [1, 33]. According to existing studies, BC patients with BMs are likely to be HER2-positive [31, 32]. However, we did not find such a relationship in our study.

The mean number of metastatic sites in BC patients with BMs was 2.6. When the involvement sites were examined, it was found that metastasis was mostly detected in the vertebra (75.2%), pelvis (53.4%), ribs (28.7%), and scapula (22.7%). Different results were obtained by Krishnamurthy et al. In that study, 19 of 62 BC patients with soft tissue tumors were examined [21]. In the BC in situ patients, 22.0% of BM was located in the ribs, 13.0% of BM was located in the scapula and 14.8% of BM was located in the vertebra. In our study, BM was observed extensively in the vertebra, pelvis, and costa. The reason for this difference may be the difference in the amount of data. Unlike our study, the average number of lesions in this study was found to be 6.5 [21, 31]. A recent study of 160 patients, 103 of whom had BC, obtained similar results in terms of incidence but not proportion. According to this finding, BM is mostly seen in the vertebra (16.8%), costa (15.0%), and pelvis (8.4%) in BC patients. In addition, there was no information about the mean number of metastatic sites in the study [20].

One of the limitations of the study is that organ metastases, other than bone metastases, were not included in the study. Additionally, chronic diseases of the patients could be included in the study. The effects of BM on the survey could also be investigated.

The risk of developing BM was found to be related to age, tumor diameter, and number of ALNs. Patients with a tumor diameter higher than 3 cm and more than 4 ALN may have a higher risk of BM. In addition, in previous studies, no significant results were found regarding the ERs/PgRs and Ki-67 protein expression, which are closely related to cancer development. In general, the study was planned to determine the clinical features, but a more detailed analysis of these clinical data would be useful for future studies.

Disclosure of conflict of interest

None.

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