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Distribution and Clinicopathological Characteristics of Breast Cancer Molecular Subtypes in Turkish Women

Şeref Dokcu, Mehmet Ali Çaparlar, Salim İlksen Başçeken, and Aydan Eroglu

ABSTRACT

Purpose: **Today, racial/ethnic differences in the incidence and prognosis of breast cancer (BC) are a well-known fact. This study aimed to examine the distribution of BC molecular subtypes in Turkish women and their relationship with other prognostic clinicopathological variables.**

Methods: **In our surgical oncology clinic, the database of 480 BC cases was retrospectively scanned between January 2008 and December 2020, and the demographic and histopathological results of the patients were recorded. Patients were classified into five main molecular subtypes. Survival curves were estimated using the Kaplan – Meier method. The relationship between categorical variables was analyzed using the chisquare test.**

Results: **The mean age of the patients at the time of diagnosis was 54.5 years, 46.3% were premenopausal, the mean tumor size was 28.7 mm, most of them were T1 (54%), ER, PR, HER-2 positivity rates were 79.6%, 73.1%, 38.3%, respectively and Ki-67 index average was 31.6. The most common molecular subtype was Luminal B Her2B-(33.5%). During a mean follow-up period of 56.9 months, 5 and 10-year overall survival (OS) rates were 89.5%, 79.6%, respectively, and disease-free survival (DFS) rates were 86.9%, 70.5%, respectively. The recurrence rate was 12.3%, distribution by molecular subtypes was significant (p=0.02). Luminal A and Luminal B/Her2- were in relation with Lobular Carcinoma (p=0.005), low histological grade (p=0.00), small tumor size (p=0.00), absence of lymphovascular invasion (LVI) (p=0.00), breast conserving surgery (p=0.022), presence of menopause (p =0.005) and local disease (p =0.013).**

Conclusions: **This study showed that there are differences in molecular subtyping for symptomatic BC in Turkish women.**

Keywords: Breast cancer, clinicopathological features, histological grade, molecular subtypes, Turkish women.

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I. Introduction

Breast cancer (BC), one of the most common malignancies in the world, is one of the leading causes of death in women [1], [2]. Prevalence and mortality rates have increased in developing countries [2]. This increase is explained by changes in lifestyle and eating habits [3]. Research performed today show that BC is a heterogeneous disease consisting of many biological entities, including different pathological features and their different clinical consequences. Several factors such as histological grade, histopathological subtype and size, nodal metastasis, estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER-2) affect prognosis and response to treatment [4].

Significant advances have been made in treatment parallel to the increasing understanding of cancer biology. Separating breast cancer into relevant molecular subtypes is a decisive prognostic and predictive factor in therapeutic decision-making. Classical immunohistochemistry (IHC) markers such as ER, PR, HER2, and Ki-67 are currently used for patient prognosis and management, together with traditional clinicopathological variables, including tumor grade and nodal involvement. Unfortunately, and despite

all efforts so far, a nearly perfect classification of breast cancer has not been determined [5].

According to St. Gallen Consensus 2011, the molecular subtypes of breast cancer were categorized into four subtypes: Luminal A, Luminal B, HER2+, and triple-negative breast cancers (TNBC). In the 2013 consensus report, Luminal B subtypes were categorized as HER2+ and HER2, and a total of 5 subtypes were accepted [6], [7]. Large-scale genomic analyzes of BC suggest that other molecular subsets may exist within categories defined by hormone receptor status. It is hoped that new molecular classification schemes can improve patient selection for treatment [8].

The molecular properties of BC affect susceptibility to chemotherapy. While luminal tumors most likely respond to endocrine treatments such as tamoxifen, they are added to chemotherapy in addition to this treatment by their KI-67

levels. HER2+ subtype responds positively to treatment with trastuzumab and anthracycline taxane. On the other hand, triple-negative tumors have high genomic instability with an aggressive clinical course, so treatment options are limited and non-specific [8]-[10].

The World Health Organization established a cancer research center called the International Agency for Research on Cancer (IARC) in 1965 and the International Association of Cancer Registries (IACR) in 1966 [1]. IARC publishes global health statistics and incidences as GLOBOCAN, covering all countries in the world every 3-5 years. In Turkey, the Cancer Control Department was established only in 1983 to keep and control records. It was reported that the incidence of BC in Turkey has doubled in the last 20 years, and the incidence in the western parts is more than twice that in the eastern parts [11], [12].

In the present day, racial/ethnic differences in BC incidence and prognosis are a known fact [13]. Recent data revealed significant molecular differences in cancers in various ethnic groups. As molecular properties are increasingly used to predict cancer prognosis and response to treatment, better knowledge of ethnic molecular features is essential [14]. Differences in breast cancer incidence rates among most racial/ethnic groups are largely explained by the distribution of risk factors, except for African Americans [15]-[17]. However, racial differences in BC survival vary according to tumor subtype [18].

In light of the current literature, we aimed to discuss the clinicopathological characteristics and distribution of molecular subtypes of Turkish women admitted to our oncology center for BC and who underwent surgery.

II. Methods

Our study was initiated with the approval of the Medical Faculty Ethics Committee (Decree number: İ2-121-21).

The study included 480 patients operated on for breast cancer in the Surgical Oncology Clinic between 2009-2020. The database was scanned retrospectively, demographic and clinicopathological variables of the patients were recorded. The following parameters were extracted from the histopathological reports, and receptor status (ER, PR, and HER2), Ki-67 percentage, histopathological subtype, size, Scarff-Bloom-Richardson (SBR) grade, and information such as LVI status, axillary nodal state were recorded. The patients were categorized according to their age as under 40 years old, 40-49 years old, and over 50 years old. For patients with recurrence, distant recurrences were defined as those occurring beyond the boundaries of the ipsilateral breast, chest wall, or regional lymph nodes. Distant recurrence sites were categorized as bone, brain, liver, lung, distant nodal, and multiple organ recurrence.

After the patients were staged according to the TNM system based on the American Joint Committee on Cancer (AJCC) 18th Edition, they were categorized as local (Stage1,2) and locally advanced (Stage3) [19].

ER and PR statuses were determined using immunohistochemical staining (IHC). Positive ER or PR was accepted when ≥1% of invasive malignant cells exhibiting nuclear staining or immunoreactivity. Tumors were considered HER2-positive only if they showed HER2 amplification (ratio >2) using 3+ staining with IHC staining or fluorescent in situ hybridization (FISH). ER, PR and HER2 tests were scored as per the American College of Pathologists Guidelines [20].

Histological grade was evaluated according to the Nottingham modification of the Bloom-Richardson

system. Accordingly, grading was performed based on the Elston-Ellis modification by histochemical features such as tubular differentiation percentage, presence of nuclear atypia/pleomorphism, and the number of mitoses [20].

The patients were categorized as follows according to the recommendations of the St. Gallen International Expert Consensus Report (2013) by molecular breast cancer subtypes: Luminal A (ER+ and/or PR+ and HER2-, Ki-67 < 14%); luminal B /HER2- (ER+ and/or PR+, HER2- and Ki-67 ≥14%); luminal B/HER2+ (ER+ and/or PR+, HER2+, any Ki-67); HER2-enriched (ER- and PR- and HER2+) and TNBC (ER- and PR- and HER2-) [7].

The status of lymph node metastasis was determined by histopathological evaluation of the axillary lymph nodes obtained. The total number of lymph nodes was determined by summing the number of noninvasive lymph nodes and the number of lymph nodes positive for metastasis.

Descriptive statistical analyzes of quantitative variables were made in SPSS software (version 24.0), and all data were expressed as mean±standard deviation (SD), number, percentage, maximum and minimum values. Categorical variables were presented as frequency and percentage. Survival curves were estimated using the Kaplan-Meier method, and the significance of the differences between these curves was determined using the log-rank test.

The relationship between categorical variables was analyzed using the chi-square (χ 2 test) test. Accordingly, molecular subtypes were compared with the following variables; age category at the time of diagnosis, menopausal status, tumor size, nodal status, histopathological subtype, histological grade, LVI status, and local stage of the tumor. Statistical analysis was done at a 95% confidence interval. The results were considered statistically significant if the p-value was <0.05.

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III. Results

All 480 patients included in the study were women. The affected breast was on the right side in 54% (n=261) of the patients and left in 46% (n=219). The mean follow-up period of the patients was 56.9±36.1 (1-154) months. The distribution of demographic and clinicopathological features of all patients by molecular subtypes is shown in Table I and Table II.

A. Age and Menopausal Status

The mean age of the patients was 54.5±13.3 (24-93) years. By their menopausal status, 46.3% (n=222) of the patients were pre-menopausal, 53.8% (n=258) were post-menopausal. The distribution of molecular subtypes by age was not significant (p=0.413). However, Luminal A and Luminal B/Her2- subtypes were observed more frequently in post-menopausal women (p=0.005).

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TABLE I: DISTRIBUTION OF CLINICOPATHOLOGICAL CHARACTERISTICS BY MOLECULAR SUBTYPES IN 480 WOMEN WITH BREAST CANCER

Characteristics	Lum A	Lum B/ Her2-	Lum B/Her2+	Her2 +	TNBC	Total, n(%)	P
TNM							
T1	68(73.9)	80(49.7)	79(55.2)	19(47.5)	14(31.8)	260(54.2)	P<0.05
T2	20(21.7)	54(33.5)	44(30.8)	17(42.5)	25(56.8)	160(33.3)	P<0.05
T3	4(4.3)	27(16.8)	20(14.0)	4(10.0)	5(11.4)	60(12.5)	P<0.05
T4	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	P<0.05
N0	69(75.0)	99(61.5)	72(50.3)	22(55.0)	26(59.1)	288(60.0)	P>0.05
N1	19(20.7)	35(21.7)	44(30.8)	12(30.0)	13(29.5)	123(25.6)	P>0.05
N2	3(3.3)	18(11.0)	15(10.5)	3(7.5)	3(6.8)	42(8.8)	P>0.05
N3	1(1.1)	9(5.6)	12(8.4)	3(7.5)	2(4.5)	27(5.6)	P>0.05
Histopathology							
IDC	63(68.5)	117(72.7)	114(79.7)	36(90.0)	36(81.8)	386(76.3)	P<0.05
ILC	14(15.2)	20(12.4)	5(3.5)	2(5.0)	0(0)	41(8.5)	P<0.05
Others	15(16.3)	24(14.9)	24(16.8)	2(5.0)	8(18.2)	73(15.2)	P<0.05
Grade							
1	37(40.2)	29(18.0)	15(10.5)	2(5)	4(9.1)	87(18.1)	P<0.05
2	43(46.7)	64(39.8)	58(40.6)	11(27.5)	1(2.3)	177(36.9)	P<0.05
3	12(13.0)	68(42.2)	70(49.0)	27(67.5)	39(88.6)	216(45.0)	P<0.05
LVI							
No	74(80.4)	97(60.2)	58(40.6)	21(52.5)	20(45.5)	270(56.3)	P<0.05
Yes	18(19.6)	64(39.8)	85(59.4)	19(47.5)	24(54.5)	210(43.8)	P<0.05
Local stage							
Early	86(93.5)	123(76.4)	114(79.7)	32(80.0)	38(86.4)	393(81.9)	P<0.05
LA	6(16.7)	38(29.2)	29(20.3)	8(20.0)	6(13.6)	87(18.1)	P<0.05

TNBC, triple negative breast cancer; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; LVI, lymphovascular invasion; LA, locally advanced.

TABLE III: DISTRIBUTION OF DEMOGRAPHIC AND CLINICAL CHARACTERISTICS BY MOLECULAR SUBTYPES IN 480 WOMEN WITH BREAST CANCER

Characteristics	Lum A	Lum B/ Her2-	Lum B/Her2+	Her2 +	TNBC	Total n(%)	P
Total n(%)	92(19.2)	161(33.5)	143(29.8)	40(8.3)	44(9.2)	480(100)	
Age							
≤40 years	7(7.6)	20(12.4)	15(10.5)	7(17.5)	8(18.2)	57(11.9)	P>0.05
40-49	27(29.3)	50(31.1)	42(29.4)	16(40.1)	11(25.1)	146(30.4)	P>0.05
≥50 years	58(63.1)	91(56.5)	86(60.1)	17(42.5)	25(56.8)	277(57.7)	P>0.05
Menopaus							
No	35(38.3)	71(44.1)	64(44.8%)	29(72.5)	23(52.3)	222(46.3)	P<0.05
Yes	57(62.1)	90(55.9)	79(55.2%)	11(27.5)	21(47.5)	258(53.8)	P<0.05
Surgery							
BCS	54(58.7)	90(55.9)	65(45.5%)	19(47.5)	20(45.5)	248(51.7)	P<0.05
Mastectomy	38(41.3)	71(44.1)	78(54.5%)	21(52.5)	24(54.5)	232(48.3)	P<0.05
Recurrence							
No	83(90.2)	143(88.8)	124(86.7%)	31(77.5)	40(90.9)	421(87.7)	P>0.05
Yes	9(9.8)	18(11.2)	19(13.3%)	9(22.5)	4(9.1)	59(12.3)	P>0.05

BCS, Breast-conserving surgery.

B. Tumor Size

The mean tumor size was 28.7±24.3(1-150) mm at the time of diagnosis. More than half of the patients had a tumor size of T1 (n=260, 54%), 1/3 (n=160, 33.3%) T2, and the remaining T3 (n=60, 12.5%). Luminal A and Luminal B/Her2- subtypes were mostly associated with small-sized T1 tumors, while the other subtypes were more associated with T2 tumors (p=0.00). However, T3 tumors were more likely to be associated with the Luminal B/Her2- subtype.

C. Ki-67 Proliferation Index

The mean Ki-67 proliferation index of all patients was 31.6±22.8 (1-95). Its distribution by molecular subtypes is shown in Table III.

TABLE II: DISTRIBUTION OF MOLECULAR SUBTYPES ACCORDING TO THE MEAN KI-67 PROLIFERATION INDEX

Molecular subtypes	Mean Ki-67 index	Standard deviation (SD)
Luminal A	8.32	3.3
Luminal B/HER2-	31.76	17.0
Luminal B/HER2+	30.22	17.6
HER2-enriched	47.63	19.1
Triple-negative	69.20	21.4

D. Molecular Sub-types

ER, PR, HER-2 positivity rates of the patients were 79.6%, 73.1%, 38.3%, respectively. Their distribution by molecular classes is shown in Table I.

In the molecular classification made accordingly, the most commonly observed molecular subtype was Luminal B/Her2- (n=161, 33.5%). This was followed by Luminal B/Her2+ (n=143, 29.8%), Luminal A (n=92, 19.2%), Triple negative (n=44, 9.2%) and Her-2+ (n=40, 8.3%) subtypes.

E. TNM Classification and Local Stage Status

The distribution of the patients by the TNM classification is shown in Table IV. Accordingly, the patients were also categorized as local stage (Stage 1,2) and locally advanced stage (Stage 3,4). Approximately 4/5 (82%) of the patients were local stage tumors, while the rest were in the locally advanced stage. Local stage disease was more likely to be associated with Luminal A subtype, while the locally advanced disease was more likely to be associated with Luminal B/Her2-subtype (p=0.013).

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TABLE IV: DISTRIBUTION OF PATIENTS BY TNM CLASSIFICATION

TNM stage	Number (n)	Percentage (%)	Cumulative (%)
1A	206	42.9	42.9
1B	44	9.2	52.1
2A	68	14.2	66.3
2B	75	15.6	81.9
3A	60	12.5	94.4
3B	0	0	94.4
3C	27	5.6	100.0
4	0	0	100.0

F. Histopathological Subtypes and Degree of Differentiation

Most of the cases (n=386, 76.3%) were ductal by their histopathological subtypes, a minority of them (n=41, 5.5%) were lobular, the remaining cases were from other histological subtypes such as medullary, tubular, mucinous, metaplastic, and papillary carcinoma. Most of the cancer cases detected were poorly differentiated (n=183, 38.1%) followed by moderately differentiated (n=149, 31%) and severely differentiated (n=148, 30.9%). While lobular carcinomas were more associated with luminal A and Luminal B/Her2- subtypes (p=0.005), ductal carcinomas were more associated with subtypes containing HER2 receptors and other carcinomas with TNBC subtypes.

G. Histological Grade and LVI Status

According to the histological grades of the patients, 45% (n=216) were Grade 3, 37% (n=177) were Grade 2 and 18% (n=87) were Grade 1, respectively. Again, 56% (n=216) of these patients did not have LVI. Luminal B/HER2-tumors, primarily Luminal A, showed less LVI (p=0.00), while they were more likely to be associated with low histological grade (Grade 1,2) tumors (p=0.00).

H. Axillary Nodal Status

There was no axillary involvement in 60% (n=288) of the patients. The rest of the patients had involvement at the level of N1 in 26%, N2 in 9%, and N3 in 5%. The mean number of pathological lymph nodes excised was 2.7± 4 (1-31), and the mean number of total lymph nodes excised was 17± 7.1(1-35). Molecular subtypes were not correlated with the axillary nodal state (p=0.591).

I. Type of Surgery

While one of the breast-conserving surgery (BCS) procedures were performed in 52% of the patients (n=248), the remaining patients underwent a mastectomy. BCS was mostly associated with luminal B/HER2-subtypes (p=0.022), mainly luminal A.

J. Recurrence and Metastasis Sites

Recurrence was observed in 12.5% (n=59) of the patients. The most common metastasis sites were as follows; isolated bone (n=20, 34%), mixed type multiorgan metastases (n=20, 34%), axilla (n=11, 18.6%), 3 lungs, 2 livers, 2 distant nodal and 1 local recurrence. Multiorgan involvement was usually in the form of internal organ metastasis such as liver and lung accompanying bone metastases, and a few of them contained different combinations. While the relationship between molecular subtypes and recurrence was insignificant (p=0.273), the relationship between them and metastasis sites was significant (p=0.02). The majority of bone metastases were associated with Luminal B/Her2-sup types, primarily Luminal A. Luminal B Her+ and Her+ subtypes were more common in mixed type and isolated visceral involvement.

K. Survival

Recurrence was observed in 12.5% (n=59) of the patients. In survival analysis with the Kaplan-Meyer method, the overall survival (OS) rates of 1, 2, 5, and 10 years were 98.5%, 95.7%, 89.5%, and 79.6%, respectively, and disease-free survival (DFS) rates were 96.4%, 93.1%, 86.9%, and 70.5%, respectively. OS and DFS curves are presented in Fig. 1 and 2. Also, the distribution of DFS percentages by molecular subtypes is shown in Table V. The best DFS rates were observed in Luminal A and Luminal B/HER2- subtypes.

In conclusion, Luminal A and Luminal B/Her2- subtypes without Her2 B receptor were associated with lobular type carcinoma, low histological grade (Grade1), low tumor size (<2 cm), absence of LVI, BSC, presence of menopause, and good prognostic conditions such as local stage disease.

TABLE V: 1, 2, 5, AND 10-YEAR DFS RATES BY MOLECULAR SUBTYPES

Molecular subtypes	Disease-Free Survival (%)			
	1-year	2-year	5-year	10-year
Luminal A	96.5	93.7	89.3	74.4
LuminalB/HER-	97.4	92.5	90.1	80.2
LuminalB/HER+	97.0	95.3	87.8	75.5
HER2+	87.3	77.1	73.0	73.0
TNBC	95.7	92.6	61.8	30.9

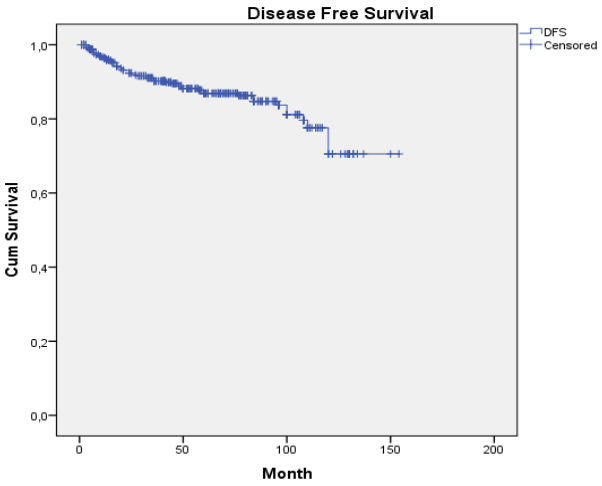

Fig. 1. Disease-Free Survival (DFS) curves of the patients.

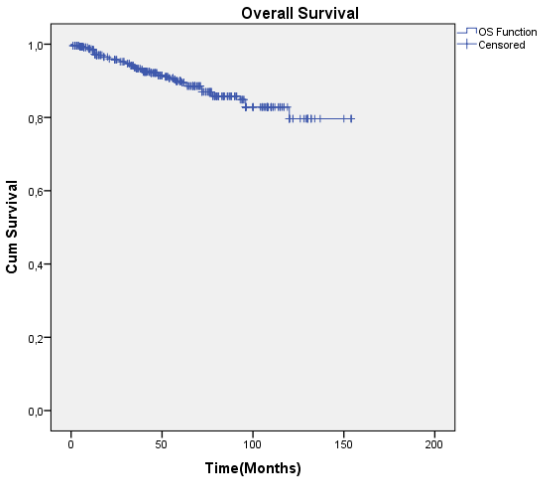

Fig. 2. Overall survival (OS) curves of the patients.

IV. Discussion

In this study, we evaluated the distribution of molecular subtypes of BC and the differences in clinicopathological features among these subtypes in Turkish women admitted to the surgical oncology clinic of our tertiary hospital.

Reference [12] shared the data of 20 thousand patients from 36 centers in our country in their study. Their data revealed that median age was 51, 17% of cases were under 40 years of age, 37% were premenopausal, BSC rate was 39%, histopathology was 77% invasive ductal type, local stage cancer was 48%, mean tumor diameter was 2.5±1.7 cm, ER, PR and HER-2 receptors were positive in 70%, 59%, and 23% of patients, with a mean of 51, the total recurrence rate during the 6-month follow-up period was 8.9%. When these results are compared with the approximately 13 thousand patients they shared five years ago, it is seen that the pre-menopausal BC rate decreased, and BSC rates increased [21]. Although our results coincided with these studies, there were differences. Our BSC rate was higher due to the high rate of the local-stage tumor. Considering the age distribution, it was observed that our patients were more than 50 years old in the menopausal period. BC is most commonly diagnosed in the 55-64 age range in developed countries, and the average age at diagnosis in the USA is 62 years [22]. The mean age in this study is 54.5, and we can explain this as a reflection of the young population age. Besides, in contrast to these studies and population-based studies in the literature, the most common subtype in our study was Luminal B instead of Luminal A. This result may be due to the average Ki-67 index and our high HER-2 receptor positivity rates [23]. However, one of the most important reasons for this difference is molecular classification differences. As [12], many studies reported their results by the classification that included four subtypes without including the Ki-67 index. For example, in the results they reported, the rate of those with a Ki-67 value of >14% was 62.7%, whereas the ratio of Luminal A subtype was 57.7%. Different results have been reported in other studies for similar reasons [12], [16], [24]-[29]. Breast cancers detected by other cause screening programs have been associated with older age, smaller size, more hormone receptor positivity, less lymph node involvement, earlier stage, and decreased mortality compared to symptomatic breast cancer. Therefore, the most common subtype is Luminal A [30]. Some authors have reached many different degrees of prevalence in their series involving symptomatic breast cancer [23]. This again emphasizes that there are regional differences in prevalence. Another reason is technological inequality, and although the same antibodies are used in the staining performed as IHC, different laboratories can report different results reaching a statistically significant size due to method differences. Even in the same patient sample, up to 25% different results can be obtained [31].

Reference [26] found significant differences in breast cancer molecular subtypes in Indonesian women regarding age, histological grade, nodal status, and staging. However, the difference was insignificant in terms of tumor size. Her2+ subtype BC was more commonly associated with large size, positive lymph node, and poor histological grade, while Luminal A subtype was associated with low histological grade, negative lymph node in women over 50 years of age. Similarly, in the literature, luminal A has been associated with low histological grade and small-size tumors, and HER-2 with the opposite conditions, as in our study [16].

Like the studies reported from Turkey, the most common histopathological subtype in this study was the invasive ductal type (76%). Lobular carcinomas were mostly associated with Luminal subtypes and ductal carcinomas with non-luminal subtypes [12]. A study in Saudi women also showed that the most common ductal carcinomas were observed, and lobular carcinomas were more associated with Luminal A and TNBC subtypes. This study also reported that these two subtypes are the most common molecular subtypes in Saudi women [17].

In their study based on the Spanish cancer registries, [29] linked BSC to luminal A subtype (60%) and positive lymph node metastasis with HER2 subtype. In our study, BSC was more commonly associated with luminal A subtype (59%), but HER-2 and luminal/HER-2 subtypes were equally associated with positive lymph node metastasis. Our high BSC rate was generally due to the high rate of local disease morbidity.

Reference [32] reported recurrence rates of 11%, with Luminal A, the subtype with the best prognosis, in population-based studies based on data from the Italian cancer registry center. As in many studies, their findings confirmed that the molecular subtype is an independent prognostic factor for BC [26], [32]. While the recurrence rate was 12.5% in our study, the subtypes with the best prognosis were Luminal A and Luminal B/Her2-. The majority of bone metastases were associated with Luminal B/Her2- subtype, primarily luminal A subtype. Luminal B Her+ and Her+ subtypes were more common in mixed type and isolated visceral involvement accompanied by visceral involvement. Except for patients with widespread metastases, there are two main disease patterns in recurrent breast cancer. Patients with ER +/PR + (luminal) tumors tend to develop more bone metastases but no brain metastases. The situation is the opposite in patients with ER−/PR−(non-luminal) tumors [33]. Clinically, the most common metastasis sites are organs such as bone, lung, central nervous system, liver [34], [35]. In our study, the most common metastasis site was bone (59%), followed by organ involvement such as lung, liver, distant nodal regions, and brain. Multiorgan involvement was present in one-third of metastases. These involvements were generally in the form of combinations of organ involvement accompanying bone involvement.

In the study of [12], they reported the 5 and 10-year OS rates as 85.8% and 75.7%, respectively. In the USA, 5-year OS has increased in recent years and is reported as 90.9%. Our OS rates in this study were 89.5% for 5-year and 79.6% for 10-year.

In a study conducted on Chinese women, the 5-year DFS rates of four subtypes (Luminal A, B, HER2, and TNBC) were reported as 83.52%, 68.88%, 71.66%, and 75.83%, respectively, (28). In our study, these rates were better, except for TNBC, 89.3%, 87.8%, 73%, and 62%, respectively (Table V).

There are also significant uncertainties about using new molecular markers in routine clinical decision making and their selection or categorization of patients for future clinical research. However, new classification methods based on

IHC, genetic and molecular findings are also being developed [36].

In conclusion, this study showed differences in molecular subtypes for symptomatic BC in Turkish women. It also reveals that IHC-based classification is required for BC and that there are different prognosis and recurrence patterns for each subtype. Therefore, the use of techniques that enable molecular classification in clinical practice must provide more accurate information about the patient specific prognosis and risk of recurrence. Also, an aggressive treatment strategy or increased surveillance can be designed for patients at high risk of relapse.

CONFLICT OF INTEREST

Authors declare that they do not have any conflict of interest.

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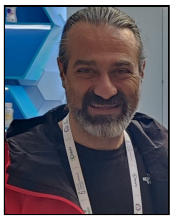

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