

# Comparison of clinical features and the impact of reproductive factors on by age at diagnosis young and elderly breast cancer patients in the middle Anatolian region of Turkey

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**Abstract. – OBJECTIVE:** Reproductive risk factors have been shown to influence breast cancer etiology for women of different origin worldwide; most studies in young/older patients have been limited to analyzing survival or tumor characteristics within their age group. This study aimed to compare the clinicopathological characteristics, treatment regimens, survival outcomes, and the impact of reproductive risk factors on young and elderly breast cancer patients.

**PATIENTS AND METHODS:** The data were collected retrospectively between October 2015 and March 2021, where 77 young patients ( $\leq 40$  years) and 107 elderly patients ( $>65$  years) were included out of a total of 567 patients undergoing treatment at Kayseri City Training and Research Hospital General Surgery Clinic, Turkey. Logistic regression analysis was performed to assess the impact of risk factors according to age.

**RESULTS:** Luminal-like tumors were in the majority in both age groups; there was no difference in diagnostic stages and survival between groups. The nulliparity ratio, total breastfeeding duration, number of biological children, first full-term pregnancy age, body mass index (BMI), and breast density distribution were significantly statistically different between groups. According to the multiple binary logistic regression analysis results for age, the most significant factors with risk effects were variables age of menarche OR= 3.36 (95% CI: 1.44-7.86) and child number OR= 2.58 (95% CI: 1.75-3.79), respectively.

**CONCLUSIONS:** The importance of looking at the impact of different risk factors on breast cancer risk lies in the potential to develop valid risk prediction models that can allow targeted screening and preventive interventions for high-risk women. By identifying more influential risk factors in different geographical profiles, risk-

based screening, and targeted prevention efforts can be encouraged, and these factors can be included in risk prediction models.

*Key Words:*

Breast cancer, Elderly, Young adult, Risk factors, Survival.

## Introduction

Breast cancer is the most prevalent malignancy in women and is the second leading cause of cancer-related deaths worldwide<sup>1</sup>. According to data from the National Cancer Institute (Surveillance, Epidemiology, and End Results [SEER] Program), the most commonly diagnosed age group for breast cancer is in the age range 55-64 years (median 62 years) with a rate of 25.6%<sup>2</sup>. Breast cancer-related deaths occur most frequently in the age group 65-74 years (mean 68 years), with a rate of 22.9%. The average incidence of breast cancer is 7% under 40 years old. This rate decreases to 1.9% under 34 years old and 5.6% above 84 years old<sup>3</sup>.

Risk factors for breast cancer include demographic factors (e.g., gender, age, race), reproductive risk factors (e.g., age, family history, early menarche, late menopause, nulliparity, late age in first full-time pregnancy), and familial-genetic factors, which are classified as other factors (e.g., mammographic density, obesity, proliferative breast diseases, lifestyle habits)<sup>4-6</sup>. Although many studies have suggested that age is an independent prognostic factor for breast cancer, it remains controversial. It has been shown that cancers

with more aggressive biological behavior, estrogen receptor (ER) negative, poor prognosis, and diagnosed at later stages are more common in the younger age group<sup>7</sup>. Conversely, lower grade, ER and progesterone receptor (PR) positive, human epidermal growth factor receptor 2 (HER-2) negative, and less aggressive tumors have been observed in the elderly<sup>8</sup>. Indolent tumor types, such as lobular, mucinous, and papillary breast carcinoma are more common in the elderly<sup>9</sup>. On the other hand, Singh et al<sup>10</sup> showed that breast cancer was more aggressive in a subgroup of patients >70 years old and is associated with distant metastasis. In another study<sup>11</sup>, an association with increased axillary lymph node involvement was observed in elderly patients with a small tumor, and it related to a reduced immune system in elderly patients.

Breast cancer has molecular subtypes based on the expression of hormone receptors and HER-2 and has been shown to have different clinicopathological characteristics and prognoses<sup>12</sup>. The risk factors associated with ER- and PR-positive breast tumors have been suggested to include mechanisms related to endogenous hormone exposure. In contrast, the etiology of ER- and PR-negative breast cancers is not hormonal<sup>13,14</sup>. The results of different meta-analyses<sup>15-17</sup> have shown that reproductive risk factors influence the etiology of breast cancer in tumor subtypes for women of different races around the world.

Most of the studies with young and elderly patients were limited to analyzing survival or tumor characteristics within their age group. This study aimed to compare the clinicopathological characteristics, reproductive risk factors, treatment regimens, and survival outcomes of 107 elderly age patients ( $\geq 65$  years) and 77 young breast cancer patients ( $\leq 40$  years) treated at Kayseri City Training and Research Hospital, Turkey.

## Patients and Methods

### Data and Sources

A total of 567 patients who received treatment at the General Surgery Clinic of Kayseri City Training and Research Hospital between October 2015 and March 2021 were retrospectively analyzed. Patients with no pathological diagnosis, follow-up data unknown, and surgical treatment performed in another center were excluded from the study. A total of 184 patients were included in the study (77 patients  $\leq 40$  years and 107 patients >65 years).

Data, such as demographic characteristics, tumor characteristics, BMI, type of surgery, and local recurrence or metastasis development of the patient were obtained through medical records in the hospital information system. Missing data on reproductive risk factors was completed by phone calling with patients, and informed consent of patients was provided. This study was approved by the Kayseri City Training and Research Hospital Clinical Research Ethics Committee (Protocol No: 71/2020).

### Breast Imaging Reporting and Data

The fifth edition of Breast Imaging Reporting and Data System (BI-RADS) categorizes breast density into four groups: a) almost entirely fatty breast tissue; b) scattered areas of fibroglandular density; c) heterogeneously dense; d) extremely dense<sup>18</sup>.

### Histological Analysis and Staging

Histological tumor grade was evaluated according to the Nottingham modification of Bloom-Richardson criteria. Data on ER and PR statuses and HER-2 expression were obtained from medical record reviews. ER and PR status were assessed by immunohistochemistry (IHC). The nuclear staining in more than 5% of tumor cells was considered positive. Expression of HER-2 was also determined immunohistochemically.

HER-2 positivity (a score of 3+) was defined as strong complete membrane staining in more than 10% of tumor cells; scores of 0 and 1 were considered negative, and dual-color silver *in situ* hybridization was carried out for all 2+ tumors. Anatomical stage and breast cancer subgroups categories were defined according to the American Joint of Cancer Classification System<sup>19</sup>.

### Statistical Analysis

Statistical evaluations were performed on computers using the SPSS 24 statistics software (SPSS, IBM, Armonk, NY, USA). Descriptive statistics were given as median with the interquartile range (IQR), minimum maximum (min-max), while categorical variables were summarized as numbers and percentages.

The Kolmogorov-Smirnov test controlled the normality test of the numerical variables. Kaplan-Meier plots were used to examine overall survival (OS) and disease-free survival (DFS) probabilities. Univariate and multiple logistic regression analyses were performed to identify the risk factors of age groups in the study pop-

**Table I.** BMI and reproductive risk factors analyze according to age.

Variables	Young women n (%)	Elderly women n (%)	<i>p</i>
<b>Breast Density (BI-RADS)</b>			
A	5 (6.5)	34 (31.8)	<b>0.000</b>
B	24 (31.2)	44 (41.1)	
C	30 (39.0)	21 (19.6)	
D	18 (23.4)	8 (7.5)	
<b>BMI</b>			
<25	29 (20.8)	23 (24.2)	<b>0.042</b>
≥ 25	46 (61.3)	72 (75.8)	
<b>Family History</b>			
Yes	16 (20.8)	15 (14.0)	0.236
No	49 (63.6)	66 (61.7)	
Unknown	12 (6.5)	26 (14.1)	
<b>Age at menarche (year)<sup>¶</sup></b>	13 (1) [10-16]	12 (2) [10-17]	0.105
<b>Parity</b>			
Nullipar	15 (22.4)	1 (1.2)	<b>0.000</b>
Multipar	52 (77.6)	80 (98.8)	
<b>Age of first full-term pregnancy (year)<sup>§†</sup></b>	22 (6) [15-40]	18 (3) [15-35]	<b>0.000</b>
<b>Child number<sup>§†</sup></b>	2 (1) [1-5]	4 (2) [1-9]	<b>0.000</b>
<b>Total lactation time (months)<sup>§†</sup></b>	36 (30) [0-108]	60 (59.3) [3-210]	<b>0.000</b>

§: Calculated for n: 132, ¶: Calculated for n: 145, †: Given as median (IQR) [min-max]. BI-RADS: Breast Imaging Reporting and Data System BMI: Body mass index.

ulation. Significant variables at  $p < 0.25$  were considered into multiple models, and the forward elimination method was used with likelihood ratio statistic to detect the independent risk factors. Odds ratios were calculated with 95% confidence intervals. Statistical analyses were conducted using on computers using the SPSS 24 statistics software (SPSS Corp., Armonk, NY, USA). A  $p$ -value less than 0.05 was considered statistically significant.

## Results

### Age

Of 184 patients, 77 were 40 years of age or younger, and 107 were above 65 years old. The median age was 36 years (5) [23-40] in the young patient group and 72 years (8) [65-91] in the elderly age group. In the young patient group, 12 patients (15.6%) were under 30 years old, and in the elderly age group, 16 patients (15.0%) were 80 years of age or older.

### BMI

The median BMI was 26.4 (9.8) [17.6-39.4] in the young age group and 27.7 (6.21) [20.6-48.5] in the elderly age group. The number of patients with a BMI of 25 and above in the elderly age group was statistically significantly higher ( $p = 0.042$ ).

### Family History

There was a family history of breast or ovarian cancer in 16 patients (20.8%) in the young age group and 15 patients (14.0%) in the elderly age group, and no statistically significant difference between groups ( $p = 0.236$ ).

### Parity, Age at First Full-Term Pregnancy and Breastfeeding

While 15 patients (22.4%) were nulliparous at the young age group, only one patient was nulliparous in the elderly age group (1.2%), and there was a statistically significant difference ( $p = 0.000$ ). The total duration of breastfeeding, the number of biological children, and the first full-term pregnancy age were statistically significantly different between groups (Table II).

### Breast Density

There was a statistically significant difference in breast density between both groups ( $p = 0.000$ ). The difference was due to BI-RADS 1 full-fat breast tissue being more in the elderly age group, and the BI-RADS 3-4 dense breast tissue was more at the young age group (Table II).

### Tumor Size and Characteristics

T2 tumors were the majority in both age groups, with ductal carcinoma *in situ* (DCIS) detected in 4 patients in the young age group

**Table II.** Tumor characteristics according to age groups.

Variables	Young women n (%)	Elderly women n (%)	p
<b>T Stage</b>			
Tis-T1	24 (31.2)	29 (27.1)	0.556
T2	40 (51.9)	66 (61.7)	
T3	5 (6.5)	5 (4.7)	
T4	8 (10.4)	7 (6.5)	
<b>Stage</b>			
0-1	16 (20.8)	26 (24.3)	0.172
2	41 (53.2)	67 (62.6)	
3	15 (8.2)	10 (9.3)	
4	5 (6.5)	4 (3.7)	
<b>Side</b>			
Right	38 (49.4)	40 (37.4)	0.265
Left	37 (48.1)	63 (58.9)	
Bilateral	2 (2.6)	4 (3.7)	
<b>Subgroup</b>			
Luminal A	25 (32.5)	45 (42.1)	0.200
Luminal B	24 (31.2)	20 (18.7)	
HER- 2	21 (27.3)	28 (26.2)	
TNG	7 (9.1)	14 (13.1)	
<b>Histopathological subtype</b>			
Invasive ductal cancer	63 (81.8)	88 (82.2)	0.484
Invasive lobular cancer	2 (2.6)	6 (5.6)	
Ductal carcinoma in situ	4 (5.2)	2 (1.99)	
Other	8 (10.4)	11 (10.3)	
<b>Surgery</b>			
Mastectomy	38 (49.4)	71 (66.4)	<b>0.021</b>
BCS	39 (50.6)	36 (33.6)	
<b>Axillary surgery</b>			
SLNB	57 (74.0)	63 (58.9)	<b>0.033</b>
ALND	41 (53.2)	59 (55.1)	
<b>Sistemic Treatment</b>			
Neoadjuvant Treatment	42 (54.5)	26 (24.3)	<b>0.000</b>
Adjuvant Traetment	30 (39)	52 (48.6)	
No-Treatment	5 (6.5)	29 (27.1)	
<b>Ki67<sup>§</sup></b>	<b>30 (35) [3-90]</b>	<b>25 (25) [3-80]</b>	<b>0.013</b>
<b>Grade</b>			
1	10 (13.7)	22 (21.0)	0.433
2	43 (58.9)	59 (56.2)	
3	20 (11.2)	24 (22.9)	

§: Calculated for n= 175, †: Given as median (IQR) [min-max], TNG: Triple-negative, BCS: Breast-conserving surgery, SLNB: Sentinel lymph node dissection, ALND: Axillary lymph node dissection.

and 2 patients in the elderly age group. Luminal-like tumors were the majority in both age groups, and luminal A tumors were present in 25 patients (32.5%) in the young group and 45 (42.1) patients in the elderly group. Luminal B tumors were present in 24 patients (31.2%) in the young group and 20 patients (18.7%) in the elderly group. Although it was not statistically significant, Triple-negative (TNG) subtype was detected to be higher rate in the elderly age group with 14 patients (13.1%). The clinical characteristics of the tumors between both groups are summarized in Table II. The most common subtype was invasive ductal carcinoma

(IDC) in both groups. All histological subtypes are given in Table III.

### Tumor Localization

In the young patient group, 38 patients (49.4%) originated from the left breast, and 2 cases of malignancy had bilateral. In the elderly patient group, 63 patients (58.9%) had left breast cancer, and 4 patients (3.7%) had bilateral. There were 11 (14.3%) multicentric tumors, 28 (36.4%) upper external quadrants, 16 (20.8%) upper internal quadrants, 6 (7.8%) lower internal quadrants, 6 (7.8%) lower external quadrants, and 10 (13.0%) centrally located tumors at the young age group. There were 11 cases (10.3%) of

**Table III.** Histopathological subtypes.

	Young women n (%)	Elderly women n (%)
<b>Invasive ductal carcinoma</b>	63 (81.8)	88 (82.2)
<b>Ductal carcinoma <i>in situ</i></b>	4 (5.2)	2 (1.9)
<b>Invasive lobular carcinoma</b>	2 (2.6%)	6 (5.6)
<b>Medullary carcinoma</b>	1 (1.3%)	1 (0.9)
<b>Invasive ductal + lobular carcinoma</b>	3 (3.9 %)	3 (2.8)
<b>Mucinous carcinoma</b>	0	1 (0.9)
<b>Invasive papillary carcinoma</b>	1 (1.3%)	2 (1.9)
<b>Invasive micropapillary carcinoma</b>	0	1 (0.9)
<b>Invasive cribriform carcinoma</b>	0	1 (0.5)
<b>Neuroendocrine carcinoma</b>	1 (1.3)	0
<b>Metaplastic carcinoma</b>	2 (2.6)	2 (1.9)

multicentric tumors, 43 (40.2%) of upper external quadrants, 19 (17.8%) of upper internal quadrants, 5 (4.7%) of lower internal quadrants, 15 (14.0%) of lower external quadrants, and 14 (13.1%) of centrally located tumors in the elderly age group. No statistically significant difference was observed between the two groups in tumor location ( $p = 0.664$ ).

### Staging

The stage of the patients is given in Table II. Metastatic disease was detected in 5 patients at the young age group and 4 patients in the elderly age group in scans before neoadjuvant chemotherapy (NAC). They were operated on after responding to the treatment.

### Systemic Treatment Modality

At the young age group, the treatment of 54.5% of patients started with NAC, and it was statistically significantly higher than in the elderly age group ( $p = 0.000$ ). The elderly patients who did not receive systemic chemotherapy were statistically significantly higher than the young age group (27.1% and 6.5%, respectively,  $p = 0.000$ ). Systemic treatment distribution is shown in Table II. In the young age group, as systemic treatment, 17 (25%) patients received cyclophosphamide-anthracycline-based chemotherapy, whereas 49 (72.1%) received taxane in addition to cyclophosphamide-anthracycline-based chemotherapy. 2 (2.9%) patients received only taxane-based chemotherapy.

**Table IV.** Univariate and multiple logistic regression analysis indicating the risk factors of age group in breast cancer patients.

Variables	Univariate Logistic Regression		Multiple Logistic Regression	
	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>
<b>Total lactation time (months)</b>	1.03 (1.01-1.04)	<0.001		
<b>Breast Density (BI-RADS)</b>				
D	1.00	-		
C	15.30 (4.36-53.67)	<0.001		
B	4.13 (1.56-10.88)	0.004		
A	1.58 (0.58-4.29)	0.374		
<b>Age at menarche</b>				
≥12 years	1.00	-	1.00	-
<12 years	2.43 (1.24-4.77)	0.010	3.36(1.44-7.86)	0.005
<b>Number of children</b>	2.60 (1.78-3.81)	<0.001	2.58(1.75-3.79)	<0.001
<b>Age of first full-term pregnancy (years)</b>	0.81 (0.73-0.90)	<0.001		
<b>BMI</b>				
<25	1.00	-		
≥25	1.97 (1.02-3.82)	0.044		
<b>Family history</b>				
Yes	1.00	-		
No	1.44 (0.65-3.18)	0.372		
Unknown	2.31 (0.87-6.17)	0.094		

OR: Odds ratio, CI: Confidence Interval. BI-RADS: Breast Imaging Reporting and Data System BMI: Body mass index.



In the elderly age group, as systemic treatment, 19 (27.1%) patients received cyclophosphamide+anthracycline based chemotherapy whereas 44 (62.9) received cyclophosphamide-anthracycline+taxane and 6 (5.8%) patients received only taxane. Cyclophosphamide+ taxane-based chemotherapy was given to only one patient (0.7%). Endocrine therapy was administered in 66 patients (86.7%) at the young age group and 85 patients (79.4%) in the elderly age group, and no statistically significant difference was observed.

### **Surgical Treatment**

The percentage of patients who underwent mastectomy was 49.4% (38 patients) in the young age group and 66.4% (71 patients) in the elderly age group, and it was statistically significantly higher in the elderly age group ( $p=0.021$ ). Initially, clinically negative axilla or negative after NAC treatment, sentinel lymph node biopsy (SLNB) was performed in 57 patients (74%) in the young age group and 63 patients (58.9%) in the elderly age group. Statistically, significantly higher rates of SLNB were performed in the younger patient group ( $p = 0.033$ ). There was no statistically significant difference in the rates of axillary lymph node dissection (ALND). Tumor features and treatment modalities are summarized in Table II.

### **Risk Factor Effect**

In Table IV, the factors affecting the age at the time of diagnosis were evaluated using single and multiple binary logistic regression analyses. When the effect of reproductive risk factors according to age was evaluated, the risk effect of the age of menarche was statistically significant according to the result of a single binary logistic regression analysis in young and elderly patients ( $p < 0.05$ ). Those with menarche age earlier 12 years old were at 2.43 times more risk than those after than 12 years. According to the multiple binary logistic regression analysis results, the most significant factors that influence risk are the age of menarche OR= 3.36 (95% CI: 1.44-7.86), and the number of children OR= 2.58 (95% CI: 1.75-3.79) variables were found.

### **Prognostic Analysis**

The median follow-up period was 34 (18.5) [6-63] months in the young age group and 32 (15) [4-66] months in the elderly age group ( $p = 0.574$ ). The estimated breast cancer-specific OS was 58.7 months, and DFS was 54.9 months for the younger age group. In the elderly patient group, the OS was

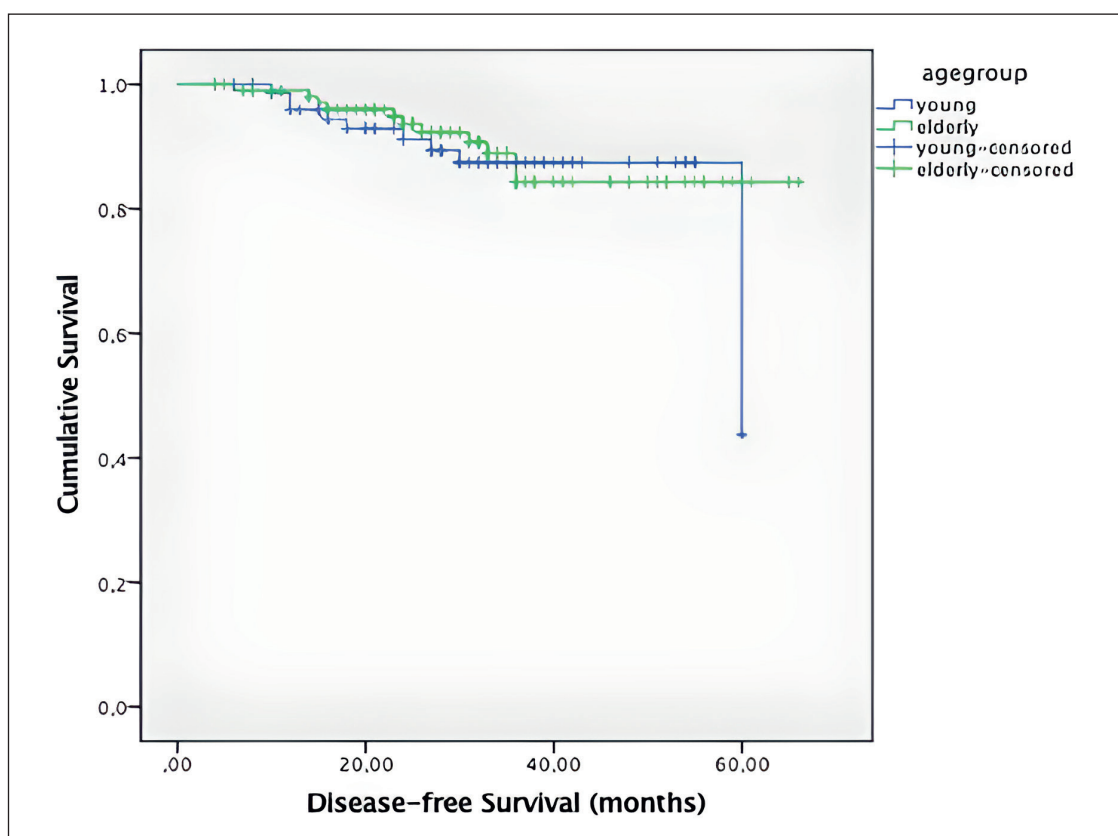
61.4 months, and the DFS was 59.8 months, and no statistically significant difference was observed in either condition ( $p = 0.881$  and  $p = 0.735$ , respectively) between groups. Kaplan- Meier plots of DFS and OS age groups are shown in Figures 1 and 2.

## **Discussion**

Breast cancer is one of the most common cancers worldwide, and the incidence of breast cancer is increasing every year<sup>20</sup>. When looking at the incidence of breast cancer by geographical distribution, the age of the diagnosis was between 45-50 years old in the Asian countries, while in Western countries, the age range of 55-60 years is the highest age of diagnosis<sup>21</sup>. Owing to the increase in the elderly population, the number of elderly patients with breast cancer is also gradually increasing. In Turkey, the incidence of breast cancer has been shown to peak in the age group of 45-49 years (17%)<sup>22</sup>. Incidence rate gradually decreases to 7.6% at 65-69 years old and increases again to 10% over 70 years old<sup>21</sup>. In our study, when including breast cancer patients of all ages, 13.2% of the patients were under 40 years old, 11.8% were 70 years old and over, and 7% were between 65-69 years old.

There was a difference in surgical treatment between the groups in this study, and mastectomy rates were higher in the elderly age group. Breast-conserving surgery (BCS) is known to provide local control similar to mastectomy, and in 2013, the St. Gallen Consensus meeting stated that extensive surgery does not provide better local control<sup>23</sup>. High rates of mastectomy in the elderly age group may be related to sociocultural factors and patients' willingness to less for BCS. In addition, surgeons' less encouragement for mastectomy in patients in this age group may have been effective. The literature shows that mastectomy rates for breast cancer are higher in patients younger than 40 years<sup>24</sup>. In our series, the higher rate of NAC treatment of the young age group may have contributed to the higher BCS rate. The overall mastectomy rate is 59.2% (102 patients), which is similar to the rate of 60.7% in the multicenter study of 20,000 patients published by Özmen et al<sup>25</sup> in Turkey.

Compared with elderly patients, young patients generally have different molecular subtypes with more aggressive biological features, poor prognoses, and later stages. This suggests that the dis-

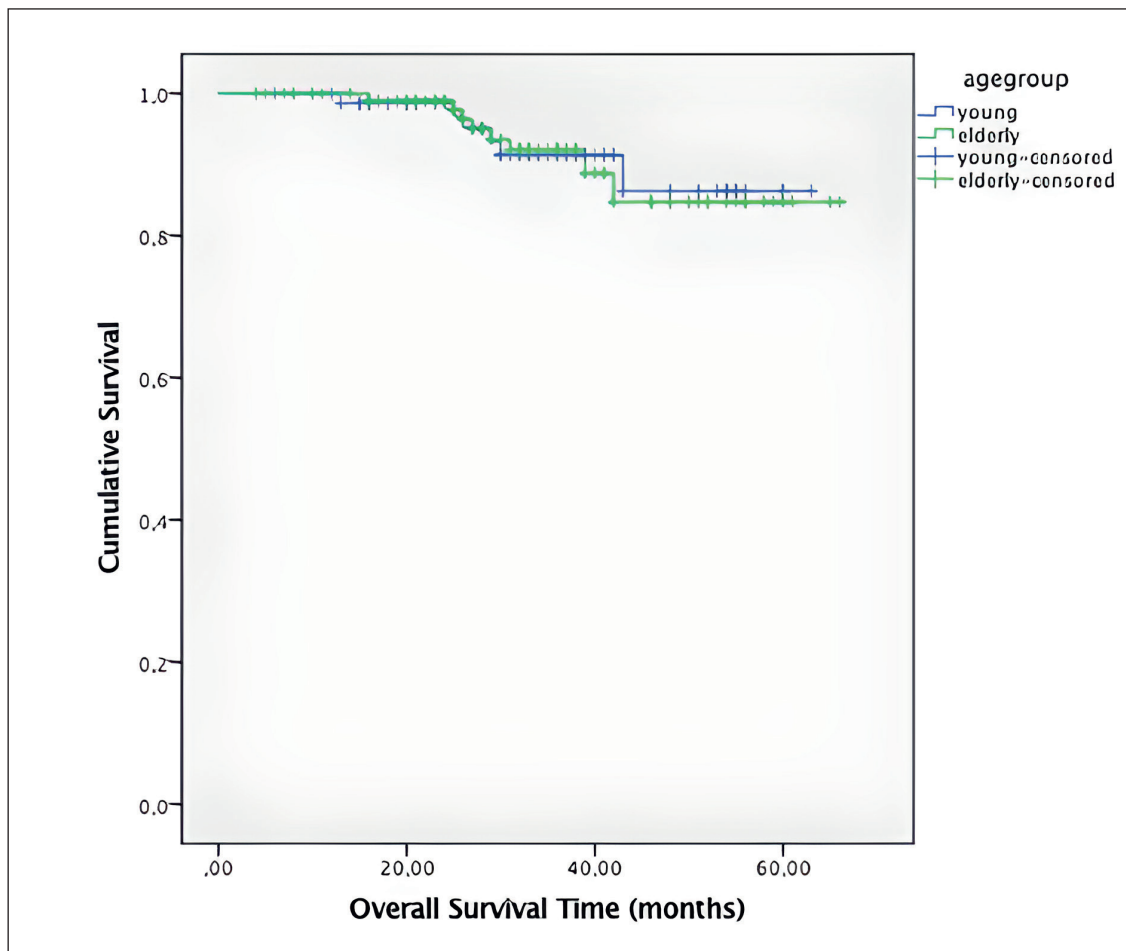


**Figure 1.** Disease-free survival analysis by age groups.

ease's pathogenesis in young patients is different from that in older patients<sup>26</sup>. On the other hand, for the elderly patient group, multiple comorbid conditions, reduced tolerability of systemic therapy, and sometimes potential overtreatment make standard treatment management difficult<sup>27,28</sup>. Elderly cancer patients without comorbidities have been shown to have significantly better survival than patients with moderate/severe comorbidities<sup>29</sup>. So, elderly patients require therapeutic strategies adapted to their individual risk profile. In this study, the disease's stage, grade, and survival were not different between both groups, and only the young age group had tumors with higher Ki67 levels. There was no significant difference in the development of metastasis or local relapse between the two age groups ( $p = 0.782$ ).

A few studies<sup>30,31</sup> have shown that the rates of luminal B and TNG subtypes in young patients are significantly higher than in elderly patients. In our study, in accordance with the literature, Luminal B tumors were found to be higher in the young age group, but TNG tumors were higher in the elderly age group. While total ER-positive tumors accounted for 81%, this rate was 83.1%

in the young age group and 79.4% in the elderly group. PR-positive tumors accounted for 66.3% of the total number of patients, while in the elderly age group, this percentage was 60.7%, and in the younger age group was 74%. Only 2 patients had ER-negative/PR-positive tumors, and both were of the young age group. In a study based on a large number of breast cancer cases from the SEER database, ER-PR+ patients were more likely to be younger than 40 years. It has been mentioned that this finding may be related to younger, menstruating women's higher estrogen levels, which downgrade ER expression<sup>32</sup>. Lambertini et al<sup>33</sup> showed that the risk of developing luminal breast cancer is associated with a 25% reduction in women who have given birth, while the results are inconsistent for the TNG patient group. Li et al<sup>34</sup> showed that giving birth at an age less than 45 years was associated with a reduced risk of developing TNG cancer. In contrast, some other studies showed that parity and lactation are not related. In this study, reproductive factors were statistically significantly different between the two groups and parity was associated with cancer development regardless of molecular subtype.



**Figure 2.** Overall survival analysis by age groups.

Takeuchi et al<sup>35</sup> analyzed nine cohort studies, evaluated six reproductive factors, and showed that giving birth to more children reduced the incidence of breast cancer in the postmenopausal period. A prospective study<sup>36</sup> evaluating breast cancer risk factors before and after the age of 40 years showed that young women develop tumors with less favorable prognostic factors; however, the relationship of reproductive factors, such as the first age of birth, parity, and menarche with breast cancer is similar regardless of the age. This study revealed that early menarche and the number of births were associated with the risk of breast cancer in a multiple regression analysis. High mammographic density is known to increase the risk of breast cancer; women with breast tissue density  $\geq 75\%$  have a 4-5 times higher risk than those with dense breasts below 5%<sup>37,38</sup>. Likewise, an increased BMI is a well-defined risk factor for the development of breast cancer in postmenopausal women because of

the aromatization of androgens into estrogens<sup>39</sup>. Studies<sup>40-43</sup> have shown that breast density is associated with breast cancer risk factors, such as age, reproductive factors, and BMI, and the effect of breast density may increase or decrease according to the presence of these factors. Studies<sup>40</sup> have shown that women with a greater number of children and younger age of their first child's birth have more favorable breast density patterns, which may explain the decrease in the risk of later breast cancer. In this study, the young age group had significantly dense breast tissue, and the elderly group had a higher number of obese patients. Nevertheless, the analysis of multiple regressions showed that the number of children, not dense breast tissue and obesity, is associated with breast cancer by age. However, the relationship between other risk factors and breast density of patients was not evaluated.

In the United States, DCIS accounts for 20% of all newly diagnosed breast cancers<sup>14</sup>. Özmen et



al<sup>23</sup> showed that DCIS rates in Turkey account for 5% of all patients diagnosed with breast cancer. In our study, DCIS rates were found to be reasonably low. This situation may be due to the age group with the highest incidence of breast cancer was not included in the study. In addition, patients under 40 years old and over 70 years old are not included in the screening programs, and the elderly patient group may be less willing to participate in regular check-ups.

According to the GLOBOCAN data, there is a more significant variation in breast cancer death rates worldwide than incidence rates in young women, indicating a significant disparity in breast cancer deaths in women younger than 40 years of age across countries and regions<sup>40</sup>. In countries with a higher level of human development, the incidence rate and prevalence of early detection increase, but the mortality rate decreases<sup>21</sup>. Among regions, there are only minor differences in known breast cancer risk factors for young women, and those factors are known to be less effective for this age group<sup>44</sup>. Even within the same country, mortality and incidence rates can change. According to the same data, the incidence rates vary more in older women than the mortality rates. Delayed diagnosis due to missing screening mammograms and presenting with a mass, especially in young patients, has been accepted as a poor prognosis factor. However, the same risk is also valid for elderly patients excluded from screening programs. In our study, the advanced stage diagnosis rates of the patients did not differ between the two age groups, but it was limiting that the study did not include inoperable patients.

When systemic treatment was evaluated between groups, only 5 patients in the young age group did not receive chemotherapy, and 3 of them were DCIS, and the other two patients were stage 1 and 2 luminal A patients. In contrast, the rate of chemotherapy was lower in the elderly age group. However, no difference was observed in survival rates between both groups. In total, 68 (89.5%) patients in the younger age group and 86 (80.4%) patients in the elderly age group received radiotherapy, and no statistically significant difference was observed ( $p = 0.097$ ).

This study has some limitations. Our findings are the results of a single tertiary care center, limiting the generalizability of the findings. As this study was a retrospective study, information was obtained from patient file records or imaging reports, and the small number of patients

limits the power to detect differences between groups.

## Conclusions

Women with premenopausal or postmenopausal breast cancer are known to have at least one breast cancer risk factor. Many established breast cancer risk factors are used in clinical risk prediction models, but the proportion of breast cancers explained by these factors is unknown, and the models are general risk models developed in specific countries. More research is required to examine the risk factors, differences in survival and mortality, and the factors affecting these younger and older breast cancer patients, which may be considered riskier for diagnosis and treatment planning.

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## Acknowledgments

The authors gratefully acknowledge Best Edit& Proof ([www.besteditproof.com](http://www.besteditproof.com)) for English Language Editing.

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## Authors' Contributions

SKE: Concept and design of the work and protocol, statistical analysis, and paper draft.

EÇÇ, EA, NÖ: Data acquisition, the paper's conception, draft, and critical review.

AA, ÖT, TE: Critical review, approval of the final version of the manuscript.

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## Conflicts of Interest

The authors declare no conflict of interest.

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## Funding Sources

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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