



# Clinical and Histopathological Findings in Elderly Breast Cancer Patients: Single Center Results

Yaşlı Meme Kanseri Hastalarda Klinik ve Histopatolojik Bulgular: Tek Merkez Sonuçları

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## Abstract

**Aim:** In the literature, there are clinical and histopathological differences in elderly breast cancer patients compared to younger patients. In our study, we compared elderly breast cancer patients treated in our hospital with younger patients in terms of clinical and histopathological features.

**Material and Methods:** In our study, the results of breast cancer patients treated between 01.01.2018 and 31.07.2021, Sancaktepe Martyr Prof. Dr. İlhan Varank Training and Research Hospital was evaluated retrospectively after the approval of the Ethics Committee dated 27/10/2021 and numbered 2021-1999. The clinical features, histopathological findings and surgical treatment methods of the patients were evaluated from their personal files. The patients were evaluated by dividing them into young and old patient groups, and 65 years was determined as the threshold value for the separation of young and old patients.

**Results:** 142 female breast cancer patients were included in our study, 103 (72.53%) were younger than 65 years old and 39 (27.47%) were older than 65 years old. The presence of co-morbid disease was significantly higher in the elderly patient group than in the younger patient group ( $p=0.0001$ ). It was observed that the diagnosis of breast cancer was mostly made with clinical findings in both young and old patient groups, routine breast screening remained in the background, and large tumor size and lymph node positivity were encountered in both groups. ER and PR receptor positive, luminal type A, grade II and III tumors and invasive ductal carcinomas with Ki 67 >15% were detected in elderly patients. Compared to the younger patients in our study, papillary carcinoma was significantly more common in elderly patients.

Among the surgical treatments applied to elderly patients, axillary sentinel lymph node sampling and breast-conserving surgical treatment techniques were observed most frequently.

## Öz

**Amaç:** Literatürde yaşlı meme kanserli hastalarda genç hastalara göre klinik ve histopatolojik farklılıklar bulunmaktadır. Çalışmamızda hastanemizde tedavi edilen yaşlı meme kanserli hastaları klinik ve histopatolojik özellikler açısından genç hastalarla karşılaştırdık.

**Gereç ve Yöntem:** Çalışmamızda 01.01.2018 ve 31.07.2021 tarihleri arasında tedavi edilen meme kanseri hastaların sonuçları, Sancaktepe Şehit Prof. Dr. İlhan Varank Eğitim ve Araştırma Hastanesi 27/10/2021 tarihli ve 2021-199 numaralı Etik Kurul onayı alındıktan sonra geriye dönük olarak değerlendirildi. Hastaların klinik özellikleri, histopatolojik bulguları ve cerrahi tedavi yöntemleri kişisel dosyalarından değerlendirildi. Hastalar genç ve yaşlı hasta gruplarına ayrılarak değerlendirildi, genç ve yaşlı hastalar ayrımında eşik değer olarak 65 yaş belirlendi.

**Bulgular:** Çalışmamıza 65 yaş altı 103 (%72.53) ve 65 yaş üstü 39 (%27.47) meme kanserli kadın hasta dahil edildi. Yaşlı hasta grubunda ek hastalık varlığı genç hasta grubuna göre anlamlı olarak daha yüksekti ( $p=0.0001$ ). Hem genç hem de yaşlı hasta gruplarında meme kanseri tanısının çoğunlukla klinik bulgularla konulduğu, rutin meme taramasının arka planda kaldığı, her iki grupta da büyük tümör boyutu ve lenf nodu pozitifliği ile karşılaşıldığı görüldü. Yaşlı hastalarda ER ve PR reseptör pozitif, luminal tip A, grade II ve III tümörler ve Ki 67 >15 olan invaziv duktal karsinomlar tespit edildi. Çalışmamızdaki genç hastalarla karşılaştırıldığında, yaşlı hastalarda papiller karsinom anlamlı olarak daha sıklıkla görüldü. Yaşlı hastalara uygulanan cerrahi tedaviler arasında en sık aksiller sentinel lenf nodu örnekleme ve meme koruyucu cerrahi tedavi teknikleri gözlemlendi.





**Discussion and Conclusion:** We believe that the importance of breast cancer screening programs for young and old women should be increased and treatment protocols for older breast cancer patients should be determined by taking into account geriatric risks.

**Key words:** Breast Cancer, Breast Cancer In The Elderly, Breast Cancer Screening Program

**Tartışma ve Sonuç:** Genç ve yaşlı kadınlara yönelik meme kanseri tarama programlarının öneminin artırılması ve yaşlı meme kanseri hastalarına yönelik tedavi protokollerinin geriatrik riskler dikkate alınarak belirlenmesi gerektiğine inanıyoruz.

**Anahtar kelimeler:** meme kanseri, yaşlılarda meme kanseri, meme kanseri tarama programı

## Introduction

With the increasing average life expectancy worldwide, the incidence of cancer in elderly patients is increasing (1). BC is the most common cancer among women in our country (2). It has been reported that the risk of BC in women increases due to age and the rates of mortality due to BC increase significantly, especially in the population over 65-70 years of age (3).

Many studies have also shown that BC is detected in older patients at a later stage than in younger patients. Because of comorbid diseases, poor performance of daily activities, and treatment side effects in elderly BC patients, treatment cannot be applied as effectively as in young patients. As a result, it is reported that the survival rates of elderly BC patients have decreased (3-5).

In our study, elderly BC patients who were admitted to our hospital were compared with young BC patients in terms of clinical and histopathological characteristics of their tumors.

## Materials and Methods

In our study, the clinical characteristics and histopathological findings of the tumors and the surgical treatment methods applied to the patients were evaluated retrospectively by accessing the hospital records of BC patients who admitted to our clinic and underwent surgery between January 2018 and July 2021 with Sancaktepe Martyr Prof. Dr. İlhan Varank Training and Research Hospital Ethic Committee approval, number 2021-199, at 27/10/2021.

Patients were evaluated by separating them into groups of young and old patients. In the definition of elderly BCs, different age limits are set in the literature (5). Some studies point to the age of 65 set by the World Health Organ-

ization (WHO) as the age limit for old age, while some studies point to the age limit set by Breast International Group (5-7). In our study, the age of 65 was determined as the cutoff value when separating young and old patients.

The patient's file data evaluated whether they had symptomatic results such as palpable mass in the breast, nipple / skin retraction, nipple discharge, changes in the breast skin at first admission, or whether they had BC detected without symptoms through routine breast screening imaging methods.

The retrospective pathological assessment and categorization was performed after the receptor status. Estrogen receptor, progesterone receptor, Her-2 oncogene receptor positivity, Ki-67 index, luminal assessment, histological grade, tumor size, histopathological subtype and presence of lymph node metastases of breast tumors were evaluated. In the evaluation of ER and PR positivity, the guidelines of the American Society of Clinical Oncology (ASCO) / College of American Pathologists (CAP) were followed.

Immunohistochemical luminal subtyping of tumors was grouped as Luminal A (ER + and/or PR +, HER 2 -), Luminal B (ER + and /or PR +, HER 2 +), HER 2 positive (ER - & PR -, HER 2 +) and triple negative (ER -, PR -, HER 2 -).

**Statistical Analyses:** Statistical analysis was performed using SPSS software (Version 25.0, SPSS Inc., Chicago, IL, USA). If normal distribution was observed, they were described as the mean  $\pm$  standard deviation ( $p > 0.05$  in Kolmogorov-Smirnov test or Shapiro-Wilk ( $n < 30$ )), and if the continuous variables were not normal, they were described as the median. The continuous variables were compared by the use of Mann-Whitney U test depending on non-parametric values; respectively. The categorical variables between the groups were analyzed by using the



Chi square test or Fisher's Exact Test.

The level for statistical significance was predetermined at  $p < 0.05$ .

## Results

A total of 142 female BC patients were included in our study within the specified date range. Of these patients, 103 (72.53%) were in the group of young patients under 65 and 39 (27.47%) in the group of older patients over 65. When the patients were evaluated according to their age distribution, it was found that the presence of additional diseases in the elderly patient group was significantly higher than in the younger patient group ( $p = 0.0001$ ) (Table 1).

When the distribution of patients' tumors according to their histopathological characteristics and age groups was evaluated, the mean tumor size in the young patient group was  $24.5 \pm 11.5$  mm, while in the elderly patient group it was  $20.1 \pm 14.6$  mm ( $p = 0.176$ ). It was remarkable that BCs with a large tumor diameter (60 mm- 80 mm) were detected in both groups. In both young and elderly patient groups, the diagnosis of BC was mostly clinical (68.0% vs. 69.2%). The rates of BC patients detected by routine screening methods were low in percentages in both groups (32.0 vs 30.8%) (Table 1).

When the histopathological characteristics of breast tumors of patients were examined, ER positivity was found in 91 (88.3%) patients in the young patient group and 37 (94.9%) patients in the elderly patient group. PR was positive for 81 (78.6%) patients in the young patient group and 34 (87.2%) patients in the elderly patient group. Although the percentage distribution of positive ER and PR patients in both young and elderly patients was higher, the distribution of ER and PR receptors was not statistically different between age groups ( $p = 0.350$ ;  $p = 0.339$ ). Although the number of HER 2 oncogene positive patients was low in both young ( $n = 28$ , 27.2%) and elderly ( $n = 5$ ; 12.8%), there was no statistically significant difference in their distribution between age groups ( $p = 0.079$ ). When the tumor size of patients was calculated according to clinical TNM staging, T2 tumors were found in 61 (59.2%) patients in the young patient group and 24 (61.5%) patients in the elderly patient group. There was no significant difference between the groups in the distribution of tumor size ( $p = 0.967$ ). Al-

though grade 2 tumors ( $n = 56$ , 54.4% vs.  $n = 18$ , 46.2%) were most common in both the young and elderly patient groups, there was no difference in the distribution between the groups ( $p = 0.650$ ). The Ki 67 value was found above the risk limit of 15 in 65 (63.1%) young patients and 24 (61.5%) older patients. There was no statistically significant difference in the distribution of Ki 67 values between the groups ( $p = 1.000$ ). Lymph node metastases were detected in 54 (52.4%) patients in the young patient group and 29 (74.4%) patients in the elderly patient group. The positivity of lymph nodes was significantly higher in the elderly patient group ( $p = 0.022$ ) (Table 2).

When young and old patients were evaluated according to their immunohistochemical luminal subtyping, Luminal type A tumors were most common in both young ( $n=67$ , 65.0%) and elderly ( $n=33$ , 84.6%) patient groups. There was no statistically significant difference in the distribution of luminal subtypes between the groups ( $p=0.149$ ) (Table.2).

When histological subtypes of tumors were assessed, invasive ductal carcinoma was most common in both age groups, in 82 (79.6%) patients in the young patient group and 24 (61.5%) patients in the elderly patient group ( $p = 0.046$ ). Among the other tumor subtypes, invasive lobular carcinoma and mixed ductal and lobular carcinoma had similar distributions between young and elderly patients. Papillary carcinoma ( $n=7$ ) was significantly more common in the elderly patient group than in the younger patient group ( $n=1$ ) ( $p=0.0001$ ) (Table 2).

Breast-conserving surgery was preferred in 76 (73.8%) patients in the young patient group and in 23 (59.0%) patients in the elderly patient group when the surgical treatment method was evaluated. There was no significant difference in the distribution of surgical treatment methods between the groups ( $p = 0.103$ ). (Table 2).

## Discussion

Female gender and age are the two most important risk factors for the development of BC (8-10). BC is the cancer with the greatest incidence and mortality risk in women (2, 9). The reasons for the increase in the risk of BC in the elderly are the increase in estrogen sensitivity with aging of the breast structure,



changes in epithelial cells that are secondary to aging, immune changes and differences in the microenvironment of the tumor (8).

As a result of the successes in early diagnosis and treatment of BC, it has been reported that there has been a decrease in BC-related mortality rates in the last 15 years in developed countries, but this success has not been achieved in elderly BC patients (7, 11, 12). In the past, it was thought that BC spread more slowly and less aggressively in elderly patients, it was claimed that these patients lost their lives due to comorbidities, and there were disruptions in BC diagnosis and treatment protocols (12, 13). However, later studies with large patient numbers showed that these assumptions were not correct (5, 14). In their review of 63 original studies on older BC, M Lodi et al found that BC patients over 80 years of age had larger tumors than patients over 70-80 years of age, and that lymph node and distant metastases were observed in these patients at 5 years and 10 years with higher mortality rates for BC (8). Especially in developed countries, as a result of the extension of life expectancy, it is anticipated that the population over 80 years old will increase three times compared to 2000 until 2050 (5). Although limits such as 65-74 years of age have been determined for BC screening programs even in developed countries, epidemiological studies emphasize that this limit should be increased up to 85 years of age (15, 16). In general, it has been shown that elderly patients often present with symptomatic masses (5, 17). In the WISDOM study, which recommended that routine breast screening be organized according to personal risk factors, it was suggested that better results would be obtained with individual screenings based not only on age, but also on breast density, family history, ethnicity, co-morbidities, and

genomic profiling (18).

There is no specific upper age limit for breast screening in Republic of Turkey Ministry of Health cancer screening program (ICCP 2016). However, the low rate of patients diagnosed with BC by routine breast screening in our patient group, both under the age of 65 and over the age of 65, shows that the importance of routine breast screening is not sufficiently understood in Turkish society. The comorbidity rate in our elderly BC group is higher in older patients like the literature.

One of the variables determining the prognosis in BC patients is the histopathological feature of the tumor. The luminal typing of the tumor determined according to estrogen, progesterone receptor expressions and HER 2 oncogene receptor positivity and Ki67 value guide the selection of neoadjuvant - adjuvant therapy (19). It is noticed that the results are variable in studies evaluating the histopathological features of elderly BCs (7).

In a study conducted by Chukwuemeka U et al. which evaluated the data of 372 African-American patients, it was reported that luminal type A BC was the most common in patients over 65 and in the overall BC population, while the rate of triple negative BC was significantly higher in the group of patients under 35 (19). In this study, it was reported that large tumor size, high tumor grade, and axillary lymph node positivity, which are among the poor prognostic factors, were higher in the younger patient group (19).

Suk Jung Kim et al. retrospectively evaluated the data of 87 Korean BC patients over 70 years of age. It has been reported that the rates of luminal type B and triple negative tumors are higher. As a conclusion Korean elderly BC patient have been reported to have more aggressive tumors than younger patients and other elderly BC pa-

**Table 1.** Additional disease, tumor size and diagnostic method differences according to age

Age		<65		≥65		Total		P value
Additional diseases	Yes	40	38.8	34	87.2	74	52.1	0.0001
	No	63	% 61.2	5	% 12.8	68	% 47.9	
Tumor size (mean) mm		24,5±11,5	23(7-80)	20,1±14,6	15(5-60)	23,6±18,7	15(1-90)	0.176
Cancer Diagnosis	Radiology	33	% 32.0	12	% 30.8	45	% 31.7	1.000
	Clinics	70	% 68.0	27	% 69.2	97	% 68.3	



tients around the world (20).

Galeana et al., in their study evaluating the data of 5488 BC patients from Mexico, showed that 851 (15.5%) of the patients were 65 years of age or older, and the patients in this group had hormone receptor positive tumors with a lower grade compared to younger patients. However, it was reported that the elderly patients included in the study had tumors that were diagnosed at a more advanced stage and required more treatment

compared to the elderly patients in developed countries (11).

A cohort study by Plichta et al. conducted on American patients with BC in extreme age groups followed 1,201,252 patients for an average of 58.7 months. It was observed that 13% of the patients were 45 years old and younger, and 17.5% were 75 years old and over. Patients aged 45 years and younger included in the study were compared with patients aged 75 years

**Table 2.** Differences in tumor and surgical treatment characteristics according to age

Parameter	Age	<65		≥65		Total		p value
		n	%	n	%	n	%	
Histologic subtype	Invasive Ductal Ca	82	79.6	24	61.5	106	74.6	<b>0.046</b>
	Invasive Lobular Carcinoma	7	6.8	4	10.3	11	7.7	0.736
	Mixt Ductal + Lobular Ca	6	5.8	3	7.7	9	6.3	1.000
	Papillary Carcinoma	1	1.0	7	17.9	8	5.6	<b>0.0001</b>
	Other	7	6.8	1	2.6	8	5.6	0.645
ER	-	12	11,7	2	5,1	14	9,9	0,350
	+	91	88,3	37	94,9	128	90,1	
PR	-	22	21,4	5	12,8	27	19,0	0,339
	+	81	78,6	34	87,2	115	81,0	
HER 2+	-	75	72,8	34	87,2	109	76,8	0,079
	+	28	27,2	5	12,8	33	23,2	
Tumor size	T1 (<2 cm)	39	37,9	14	35,9	53	37,3	0,967
	T2 (2-5 cm)	61	59,2	24	61,5	85	59,9	
	T3 (>5 cm)	0	0	0	0	0	0	
	T4 (invasion +)	3	2,9	1	2,6	4	2,8	
Grade	I	22	21,4	9	23,1	31	21,8	0,650
	II	56	54,4	18	46,2	74	52,1	
	III	25	24,3	12	30,8	37	26,1	
Ki 67	<15	38	36,9	15	38,5	53	37,3	1,000
	≥ 15	65	63,1	24	61,5	89	62,7	
Lymph node metastasis	Yes	54	52,4	29	74,4	83	58,5	<b>0,022</b>
	No	49	47,6	10	25,6	59	41,5	
Luminal subtyping	Luminal A	67	63	33	84,6	100	70,4	0,149
	Luminal B	24	23,3	4	10,3	28	19,7	
	Her-2/neu	4	3,9	1	2,5	5	3,5	
	Basal Cell like	8	7,8	1	2,5	9	6,4	
Surgical Treatment	Lumpectomy	76	73.8	23	59.0	99	69.7	0,103
	Mastectomy	27	26.2	16	41.0	43	30.3	





and older, and younger patients were shown to have more advanced and high-risk tumor characteristics. Although the tumor grade of the patients in the elderly patient group was lower, hormone receptor positivity was high, and lymph node positivity was low, distant metastasis rates were found to be higher (3). In their review, Flora V et al. reported that high-grade and hormone receptor positive invasive ductal carcinomas were detected in the elderly in most of the studies (7). In a study conducted by Vahit Özmen on 13,240 BC patients in Turkey, the average tumor size was 2.5 cm, luminal type A tumor (62%) and invasive ductal carcinoma (79%) were the most common tumors in all age groups. The mean age of the patient group was 51.6 years and 18% of all patients were over 65 years old. ER and PR positivity were lower in the younger patient group, HER 2 positivity, histological grade, average tumor size and axillary lymph node positivity were higher. The ratio of detection of patients in clinical stage I (26%) at the time of first admission was higher in the patient group over 70 years of age than in patients under 40 years of age (21%). In the patient group over 70 years of age, the rate of Her 2 positivity and triple negative patients was found to be lower compared to the patient groups under the age of 40 and between the ages of 50-59. The high incidence of BC in the younger age group in Turkey is caused by the fact that women under the age of 40 make up 68% of the entire female population. Compared with the data of developed countries, it has been shown that Turkish patients present with tumors at a younger age, at a more advanced stage, and with poor prognostic factors (2).

In our study, corresponding to literature data, it was shown that the mean tumor size of younger patient groups was larger, their ER and PR receptor positivity was higher, and this younger group most had luminal type A tumors. Grade II and III tumors and Ki 67 > 15% tumors were found to be high in percentage in both young and old patient groups, indicating that the tumors were aggressive. Lymph node positivity was significantly more frequently found in the elderly patient group than in younger patients. Invasive ductal carcinoma was the most common tumor subtype in all patient groups, corresponding to the literature. Compared with the younger patients in our study, papillary carcinoma was significantly more common in elderly patients.

In the literature, the surgical treatment method could

not be optimized for elderly BC patients, due to comorbidities, the effects of surgery on quality of life, short life expectancy, low mental and physical capacity, patient preference, and tumor characteristics (7). Although breast surgery is generally a low-risk surgery, it has been reported that the risk of complications increases in elderly patients due to comorbidities. While determining the type of breast surgery of the patients, it was emphasized that the tumor type and additional diseases of the patient should be carefully evaluated, and it should be clearly determined whether the patient is suitable for chemotherapy, radiotherapy and hormone therapy. In many studies, it has been recommended to limit surgical treatment to breast tissue in elderly patients and to avoid lymph node dissection by conducting sentinel axillary lymph node sampling (7, 21, 22). In our study, breast-conserving surgical treatment techniques with axillary-sentinel lymph node sampling were more frequently used in both patient groups.

Among the limitations of our study, we would like to state that we have a relatively small number of patients based on a single hospital data. We think that elderly BCs will increase in the coming years due to the increasing life expectancy and geriatric population in our country. It would be more appropriate to evaluate elderly BC patients in our country and to make appropriate preparations for the future with studies to be carried out in multicentric and to include more patients. By increasing the number of patients, it will be possible to divide the elderly patients into special subgroups and to achieve statistically significant results. The fact limited our study that our hospital was a newly established hospital, and it was impossible to reach 5-year survival rates in our data. Long-term metastasis and mortality rates should be provided with patient series with long-term follow-up in the future.

## Conclusion

According to the data we have collected, we have not reached sufficient levels of routine breast screening in both young and old patients, and we encounter large and lymph node-positive tumors. We believe we need to do more to raise awareness of BC prevention and early diagnosis.

Considering the growing geriatric population and the high incidence of BC, we believe there is a need for BC



screening programs and treatment protocols organized in a multidisciplinary manner with a detailed geriatric evaluation.

**Ethics Committee approval date and decision number:** Sancaktepe Martyr Prof. Dr. İlhan Varank Training and Research Hospital Ethic Committee approval dated 27/10/2021 and numbered 2021-199 was obtained.

**Etik Kurul kararı tarih ve sayısı:** Sancaktepe Prof. Dr. İlhan Varank Eğitim ve Araştırma Hastanesi Etik Komitesi 27/10/2021 tarih ve 2021-199 numaralı Etik Kurul onayı alındı.

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