# GENÇ KADINLARDA MEME KANSERİ TÜMÖRLERİNİN AGRESİFLİĞİNİN ANALİZİ

## Analysis of the Aggressiveness of Breast Cancer Tumors in Younger Women

Refik BADEMCİ[1](0000-0001-9378-4438), Ersan EROĞLU[2](0000-0002-6654-185X), Arzu AKAN[3], (0000-0001-8435-9771)

[1]İstanbul Medipol Üniversitesi Genel Cerrahi AD., İstanbul

[2]İstanbul Bilim Üniversitesi, Genel Cerrahi AD.,İstanbul, Turkey

[3]SBU Okmeydanı Eğitim ve Araştırma Hastanesi, Genel Cerrahi Kliniği., İstanbul,

Refik BADEMCİ, Op. Dr.
Ersan EROĞLU, Op. Dr.
Arzu AKAN, Doç. Dr.

## ÖZET

**Giriş:** Genç yaşta tespit edilen meme kanseri insidansı artmakta olup bu hastalarda mortalite yüksek seyretmektedir. Çalışmamızın amacı kırk yas altı kadınlarda görülen meme kanseri hastalarının klinik, histopatolojik ve operatif ozelliklerini belirlemek.

**Materyel ve metod:** 2013 ile 2017 tarihleri arasında 40 yaş altında olup meme kanseri tanısı konulmuş hastaların klinikopatolojik ve operatif özellikleri değerlendirildi.

**Bulgular:** 103 hastamız olduğunu tespit ettik. Ortalama yaş 35.4 (3.8) olarak tespit edildi. Hastalarımızın %13.4' üne evre 1, %57.2'sine evre 2, %22.3'ü evre 3, %6.7'si tanı anında uzak metastazı olduğu için evre 4 olarak tespit edildi. %22.3 T1, %48.5 T2, %23.3 T3, %2.9 T4 olarak tespit edildi. Tümörlerin ortalama çapını 2.1 cm (±1.3) olarak belirledik. %37.8 luminal A, %35.9 luminal B, %20.3 tripple negatif ve HER 2 pozitifliğini %21.3 olarak tespit edildi. %55.3 hastaya modifiye radikal mastektomi, %39.8 hastaya segmenter mastektomi yapıldı. 76 (%73.7) hasta da aksillar lenf nodalarında metastaz saptandı.

**Sonuç:** Genç yaşta tespit edilen meme kanseri hastalarını özellikli hasta grubu olarak değerlendirip tedavi protokollerini buna göre belirlemekte fayda olduğunu düşünüyoruz.

**Anahtar kelimeler:** *Genç yaş meme kanseri; Tümör histolojisi; Tedavi*

## ABSTRACT

**Background:** The incidence of breast cancer detected at a young age is increasing in the modern age and mortality is also observed to be high in these types of patients. The aim of this study is to determine the clinical, histopathological and operative characteristics of breast cancer patients under 40 years of age.

**Materials and Methods:** In this study, clinicopathologic and operative characteristics of patients under the age of 40, who were diagnosed with breast cancer between the years of 2013 and 2017, were evaluated.

**Results:** We identified 103 patients for the study. The mean age was determined to be 35.4 (3.8). 13.4% of our patients were observed to be at Stage 1, 57.2% were at stage 2, 22.3% were at stage 3, and 6.7% were found to have Stage 4 Cancer due to distant metastasis at the time of the diagnosis. 22.3% were identified as T1, 48.5% as T2, 23.3% as T3, and 2.9% were identified as T4. The mean diameter of the tumors was 2.1 cm (± 1.3). It was determined that 37.8% were luminal A, 35.9% were luminal B, 20.3% were triple negative and HER 2 positivity was found to be 21.3%. Modified radical mastectomy was performed in 55.3% of the patients and segmental mastectomy was performed in 39.8% of the patients. 76 (73.7%) patients were found to have metastasis in their axillary lymph nodes.

**Conclusion:**We think it is useful to evaluate and treat breast cancer patients diagnosed at young age as a special patient group and thus we recommend determining the treatment protocols accordingly.

**Keywords:** *Young women breast cancer; Tumor histology; Treatment*

**İletişim:**
Op. Dr. Refik BADEMCİ
stanbul Medipol Üniversitesi Genel Cerrahi AD., İstanbul
**Tel:** +905326641200
**e-mail:**
refikbademci@gmail.com

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## INTRODUCTION

Breast cancer is generally observed to be a disease of the advanced age. However, it has been determined that breast cancer is observed in 5 to7% of women who are under the age of 40 and furthermore it has also been observed that the prevalence of breast cancer in women under the age of 40 has also increased in the recent years. (1-3). In the US, 14,000 breast cancer patients under the age of 40 years are diagnosed annually and 3,000 young women die each year due to breast cancer. Hence, breast cancer is the leading cause of cancer death in the world at a young age (4). Low rates of five-year survival are observed in young breast cancer patients in both western and in developing countries [5, 6]. There are also reports indicating that young patients have more aggressive biological tumor properties as compared to elder patients. There are also reports indicating that the risk of distant metastasis is higher in young breast cancer patients (7). Young age in breast cancer has also been shown to be an independent risk factor in many studies (8-10).

The aim of our study was to determine the clinical, histopathological and operative characteristics of breast cancer patients under 40 years of age.

## MATERIALS AND METHODS

Clinicopathologic and operative characteristics of patients, who were diagnosed with breast cancer between the years of 2013 and 2017, who were also under the age of 40 were evaluated in the Okmeydanı Training and Research Hospital and at Şişli Florence Nightingale General Surgery Clinic.

During the study, it was recorded whether surgical procedures were performed on the patients as well as the surgical procedure type (modified radical mastectomy, segmental mastectomy, mastectomy) performed, along with Sentinel lymph node biopsy (snlb) and / or axillary dissection.

Histologic features of the specimens, estrogen and progesterone receptors, their cerb2 (+) status, tumor grade, axillary involvement and the stages of the patients were also recorded. The TNM staging system for breast carcinoma of the 7th edition of the American Joint Cancer Committee was used as a staging system. The four molecular subtypes of breast cancer have been identified:

1-Luminal A; estrogen receptor (ER) + and / or Progesterone receptor (PR) +, HER2, grade 1 and grade 2 tumor,

2- Luminal B; ER + and / or PR + and HER2 + tumors or ER + and / or PR + and HER2 grade 3 tumors,

3- HER2 +; ER -, PR - and HER2 + tumors,

4- Triple negative; ER-, PR-, HER2- tumors.

Statistical analysis was performed using SPSS 25.0. (SPSSFW; SPSS Inc., Chicago, IL, USA).

## RESULTS

We identified 103 patients for our study. The mean age was observed to be 35.4 (3.8). We found that 55% of the patients had cancer in their right breast. When we looked at the stage of the patients, it was observed that 13.4% were at Stage 1, while 57.2% were at Stage 2 and 22.3% were found to be in Stage 3, and 6.7% was diagnosed as Stage 4, since these patients had distant metastases. As for the distant metastases results, we found that most of them were metastases of the liver, lungs and then the metastases of the brain and bone. As a pathological diagnosis, we found that 90% of the patients had ductal adenocarcinoma and 3.8% of them had lobular carcinoma. The tumors were found to be 22.3% T1, 48.5% T2, 23.3% T3, 2.9% as T4. The mean diameter of the tumors was 2.1 cm (± 1.3). We found 1.9% grade 1, 65% grade 2, 30% grade 3. Ki 67 positivity rate was 69.9%, ER positivity was 54.3% and PR positivity was 46%. In our findings, it was observed that 37.8% were luminal A, 35.9% luminal B, 20.3% triple negative and HER 2 positivity was found to be 21.3%. Modified radical mastectomy was performed in 55.3% of the cases and segmental mastectomy was performed in 39.8% of the patients. 5 (4.8%) patients could not be operated on, because they were at metastatic stage. 46 (44.6%) patients underwent snlb, while 27 (61.3%) of these patients were not detected with the metastasis of the sentinel lymph node. Also, in 19 (38.7%) patients who underwent snlb were detected with metastatic lymph node and thus axillary lymph node dissection was performed. Overall, 76 (73.7%) patients had metastases in axillary lymph nodes. It was

observed that 31 (30%) patients received neoadjuvant therapy. 14 (13.5%) patients were observed to have a family history of breast cancer. It was also observed that 45 (43.6%) patients had given birth, and 3 (2.9%) of the patients were found to be pregnant at the time of the diagnosis (Table 1).

**Table 1.** Clinicopathologic and operative characteristics of patients under 40 years

| | | Total: 103 |
|---|---|---|
| Age* | | 35.4 (3.8) |
| Right Breast n (%) | | 57 (55) |
| Stage n (%) | | |
| | 1 | 14 (13.4) |
| | 2 | 59 (57.2) |
| | 3 | 23 (22.3) |
| | 4 | 7 (6.7) |
| Pathological diagnosis n (%) | | |
| | ductal adenocarcinoma | 93 (90) |
| | Lobular carcinoma | 4 (3.8) |
| | Ductal adenocarcinoma+Lobular carcinoma | 3 (2.9) |
| | Other | 3 (2.9) |
| T | | |
| | 1 | 23 (22.3) |
| | 2 | 50 (48.5) |
| | 3 | 24 (23.3) |
| | 4 | 3 (2.9) |
| Tumor diameter, (cm)* | | 2.1 (1.3) |
| Tumor grade n (%) | | |
| | Grade 1 | 2 (1.9) |
| | Grade 2 | 67 (65) |
| | Grade 3 | 31 (30) |
| Ki67 positive n (%) | | 72 (69.9) |
| ER n (%) | positive | 54 (54.3) |
| PR n (%) | positive | 48 (46) |
| Molecular subtype n (%) | | |
| | Luminal A | 39 (37.8) |
| | Luminal B | 37 (35.9) |
| | Triple negative | 21 (20.3) |
| | Her 2 n (%) | 22 (21.3) |
| Surgical procedure n (%) | | |
| | Breast conservative surgery | 41 (39.8) |
| | Modified radical mastectomy | 55 (53.3) |
| | Mastectomy | 2 (1.9) |
| | Unoperated | 5 (4.8) |
| SNLB n (%) | | 46 (44.6) |
| | (+) | 19 (38.7) |
| | (-) | 27 (61.3) |
| Axillary metastatic lymph node n (%) | | 76 (73.7) |
| neoadjuvant chemotherapy n (%) | | 31 (30) |
| Family history of breast cancer n (%) | | 14 (13.5) |
| | mean±SD * estrogen receptor: ER, Progesterone receptor: PR | |
| | SNLB: Sentinel lymph node biopsy | |

## DISCUSSION

Women with breast cancer are the largest group among women who have cancer. Breast cancer on women below 40 years of age constitutes 6% of breast cancers (7).

Despite the inconsistencies in the negative prognostic factors, it was reported that the mortality rate was higher in young women and that the mortality rate was higher even in the early stages as compared to the women aged over 40 years. (8).

In our study, we aimed to determine the clinical, histopathological and operative characteristics of breast cancer patients in women who are under forty years old.

It has been reported that young patients are usually diagnosed in advanced stages (11). The reason for the diagnosis of advanced stage in young patients is the lack of routine screening under the age of 40, as well as the low quality of mammography in dense breasts, the lack of knowledge of women concerning breast cancer and finally their low expectation of cancer. It has been reported that diagnosis, which is late for more than 3 months, adversely affects prognosis (12). In addition, breast cancer is now considered a heterogeneous disease based on different molecular subgroups, and this sub-classification may exhibit a prognostic value (13). In the literature, breast cancer in very young women has different histopathological features compared to advanced age breast cancer. Higher rates of high grade, advanced stage and lymph node positive tumors, vascular or lymphatic invasion and low HR positivity, high P53 gene mutation, high tumor proliferation rate and higher HER2 positivity can be detected. As a result, it has been shown to cause a more aggressive breast cancer molecular subtype frequency (7, 14, 15). In a study comparing young patients with advanced age patients, low ER positivity rate and high recurrence rate were determined in young age breast cancer patients (16). In our series, ER positivity was 54.3%, PR positivity was 46%, Ki 67 positivity rate was 69.9%, 55% were grade 2, 30% were grade 3, 37.8% were found to be luminal A, 35.9% luminal B, and 20.3% were found to be triple negative. Furthermore, it was seen that 57.2% of the patients were at stage 2, while 22.3% of them were at stage 3 and these findings were seen to be compatible with the literature.

HER2 positive disease is more common in young women (14). It has been shown that overexpressing subtypes of HER2 are the most aggressive subtypes of breast cancer and there is a positive correlation between the number of metastatic lymph nodes and HER2 amplification in many studies (18, 19). It has been reported that a greater rate of HER2 expression was detected in young patients with breast cancer [20, 21]. This can show that the more negative results of the younger age patients can be partially explained (22, 23). It was observed that HER positivity was determined as 21.3% and 76 (73.7%) patients had metastasis in their axillary lymph nodes.

There are also specific problems in the treatment of breast cancer at a younger age. These problems appear to be potentially aggressive tumor biology, larger tumor size, as well as psychosocial factors specific to young women. These problems should be considered when treating these patients. Breast-conserving surgery is an acceptable cosmetic appearance, so that there is less anxiety, lesser depression, and also more improved body image as compared to mastectomy (23, 24). Many young women are more likely to have a lower survival rate and higher overall failure rates as compared to older premenopausal counterparts, with local recurrence, mastectomy and breast conservation (23, 26). As the patients in our series had larger tumors, 55.3% of the patients underwent a modified radical mastectomy and 39.8% of the patients underwent segmental mastectomy.

Family history of breast cancers at a young age may be as high as 16%, suggesting a high rate of familial breast cancer, such as breast cancer susceptibility gene 1 [BRCA1] and breast cancer susceptibility gene 2[BRCA2] (27, 28). P53 gene mutation and Cowden syndrome are rarely caused by familial breast cancer (29). Therefore, it is important to perform gene screening especially in young patients with a family

history. We found that the rate of familial breast cancer was 13.5%, but we couldn't reach the results of the patients whom we requested BRCA 1-2 test and this was seen as a deficiency in our study.

The choice of chemotherapy regimen is determined by prognostic factors. Preoperative or neoadjuvant chemotherapy can locally reduce advanced disease and make them operable and also increases the chances of BCS rather than mastectomy (30). In our series, 31 (30%) patients received neoadjuvant treatment, but 5 (4.8%) patients could not be operated on, because of non-regression in their follow-up after chemotherapy. The fact that our study was retrospective, as well as the fact that the long-term prognosis of the patients was not specified and the lack of comparison with the elderly patients were seen as the deficiencies in our study. It may be useful to study with larger groups of breast cancer patients at a young age who show the effects of molecular subgroups on prognosis.

## CONCLUSION

It is stated that the prognosis of breast cancer in young patients is poor and the reason for this is that there is no advanced stage diagnosis and also that the histological structure of these tumors is more aggressive. The results of our study have supported these conclusions and it is observed that young breast cancer patients differ from advanced breast cancer patients in many ways such as expectation of pregnancy and psychosocial factors. For these reasons, we think that these patients should be treated as a specific patient group in surgical and in oncological treatments.

There is no conflict of interest pertaining to this study among the authors.

The authors have no financial interests in companieas or other entities that have an interest in the information included in the contribution.

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