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Aggressive breast cancer in young women: Single-center experience

Genç kadınlarda agresif meme kanseri: Tek merkez deneyimi

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Abstract

Aim: Breast cancer is the most common malignancy among women, with poorer survival outcomes in younger patients. Adolescents and young adults (AYAs), typically defined as women under 40–45 years, often present with aggressive tumor subtypes and advanced-stage disease. This study analyzes the epidemiological and demographic characteristics of breast cancer patients under 45 at our center to provide insights into this high-risk group.

Materials and Methods: This retrospective study analyzed 90 breast cancer patients aged 45 years or younger, diagnosed at our clinic between January 2015 and December 2023.

Results: A total of 90 female breast cancer patients, with a median age of 39 years (25–45), were analyzed in our study. At diagnosis, 27.8% were in early stages (stage 1–2), 57.8% had locally advanced disease (stage 3), and 14.4% were *de novo* metastatic. Axillary lymph node positivity was observed in 72.2%, and invasive ductal carcinoma was the most common histological subtype (61.1%).Tumor grades 2 and 3 were identified in 24.4% and 56.7% of patients, respectively. Hormonal receptor positivity was detected in 86.7% of patients, HER2 positivity in 41.1%, and BRCA mutation in 20%. Metastases were most commonly found in the bone (20%) and lung (12.2%).

Conclusion: Our study underscores the aggressive nature of breast cancer in young patients, marked by advanced stages and high-risk features at diagnosis. These findings highlight the need for enhanced early detection and personalized treatment approaches to improve outcomes for young breast cancer patients.

Keywords: Young breast cancer; invasive ductal carcinoma; HER2 positivity; BRCA mutation.

Öz

Amaç: Meme kanseri, kadınlar arasında en sık görülen malignitedir ve genç hastalarda sağkalım oranları daha düşüktür. Genellikle 40–45 yaş altındaki kadınlar bu grupta tanımlanır ve sıklıkla agresif tümör alt tipleriyle birlikte ileri evre hastalıkla tanı alırlar. Bu çalışma, merkezimizde takip edilen 45 yaş altındaki meme kanseri hastalarının epidemiyolojik ve demografik özelliklerini inceleyerek yüksek riskli bu grup hakkında daha fazla bilgi sağlamayı amaçlamaktadır.

Gereç ve Yöntem: Çalışmamızda Ocak 2015 ile Aralık 2023 tarihleri arasında kliniğimizde tanı alan 45 yaş ve altındaki 90 meme kanseri hastasını analiz ettik.

Bulgular: Çalışmamızda, ortalama yaşı 39 (25–45) olan toplam 90 kadın meme kanseri hastasını analiz ettik. Tanı anında hastaların %27,8'i erken evrede (evre 1–2), %57,8'i lokal ileri evrede (evre 3) ve %14,4'ü *de novo* metastatik evredeydi. Hastaların %72,2'sinde aksiller lenf nodu pozitifliği gözlemlendi ve en sık görülen histolojik alt tip invaziv duktal karsinom (%61,1) idi. Tümör grade'leri 2 ve 3 olan hastaların oranları sırasıyla %24,4 ve %56,7 olarak belirlendi. Hormonal reseptör pozitifliği hastaların %86,7'sinde, HER2 pozitifliği %41,1'inde ve BRCA mutasyonu %20'sinde saptandı. Metastazlar en sık kemik (%20) ve akciğerde (%12,2) görüldü.

Sonuç: Çalışmamız, genç hastalarda meme kanserinin agresif doğasını, tanı anında ileri evre ve yüksek riskli özelliklerle belirgin bir şekilde ortaya koymaktadır. Bu bulgular, genç meme kanseri hastalarının tedavi sonuçlarını iyileştirmek için geliştirilmiş erken teşhis yöntemlerine ve kişiselleştirilmiş tedavi yaklaşımlarına olan ihtiyacı vurgulamaktadır.

Anahtar Kelimeler: Genç meme kanseri; İnvaziv duktal karsinom; HER2 pozitifliği; BRCA mutasyonu.

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Introduction

Breast cancer is the most common cancer among women and continues to be a significant health concern.[1] Survival rates in the metastatic stage are significantly lower compared to early-stage Breast cancer due to various contributing factors.

Age is an independent risk factor, and Breast cancer in adolescents and young adults (AYAs) has been linked to lower survival rates.[2,3] While the definition of AYAs breast cancer has not yet been standardized, the literature generally categorizes women under the age of 40–45 in this group. Although the incidence of breast cancer increases with age, approximately 7–10% of cases occur in AYAs.[4] According to a large database study conducted in our country, 48% of breast cancer cases are diagnosed in women under the age of 50, with 17% of these in women under 40.[5]

AYAs are more likely to develop aggressive cancer subtypes compared to individuals over 50 years old. This group faces higher mortality rates and significantly poorer survival outcomes.[6,7] Several factors contribute to this disparity, including advanced-stage diagnosis, more aggressive tumor phenotypes, lower hormone receptor positivity rates, higher HER2 positivity rates, larger tumor sizes, increased lymph node involvement, higher histological grades, and poorer responses to treatment.[2,3,5,8-10]

In this study, we aimed to contribute to the literature by analyzing the epidemiological and demographic characteristics of patients diagnosed with breast cancer under the age of 45 at our center.

Materials and Methods

In this study, patients diagnosed with breast cancer at our clinic between January 2015 and December 2023 were retrospectively analyzed. Patients aged 45 years and younger were included in the study, while those whose complete information was not available in their medical records or the hospital's computer system at the time of diagnosis were excluded. Incomplete information was defined as missing key clinical data, including tumor histology, receptor status (ER, PR, HER2), TNM staging, or treatment details. In total, 90 patients were included in the analysis. The demographic and clinicopathological characteristics of the patients were documented, including age, tumor size, histological subtype, hormone receptor status, HER2 status, histological grade, TNM stage, lymph node involvement, and treatment modalities such as surgery type, chemotherapy, and radiotherapy. Additionally, follow-up data, including disease-free survival and overall survival, were recorded.

Statistical analysis

Statistical analyses were conducted using IBM SPSS Statistics version 22.0 (IBM SPSS, USA). Descriptive statistics were used to analyze the clinical and demographic characteristics of the patients. Categorical and numerical data were presented as counts and percentages (n%), while continuous variables were summarized using median values.

Ethics committee approval

The study was conducted according to the principles of the Declaration of Helsinki, and approval was obtained from the ethics committee of Ankara Etlik City Hospital on April 24, 2024, with approval number 2024-322. Since the study was retrospective in nature, informed consent could not be obtained from the patients.

Results

In our study, a total of 90 patients were evaluated. All patients were female, with a median age at diagnosis of 39 years (25–45). Of these, 79 patients (87.8%) had no smoking history and 79 patients (87.8%) had at least one child before diagnosis. A family history of breast cancer was reported in 17 patients (18.9%). At the time of diagnosis, 25 patients (27.8%) were in the early stages (stage 1–2), 52 patients (57.8%) had locally advanced disease (stage 3), and 13 patients (14.4%) were diagnosed with *de novo* metastatic disease. Axillary lymph node positivity was detected in 65 patients (72.2%).A total of 79 patients (87.8%) had surgery, including 48 (53.3%) who had modified radical mastectomy (MRM) and 31 (34.4%) who had breast-conserving surgery (BCS). Additionally, 62 patients

(68.9%) had axillary lymph node dissection (ALND). Pathological examination revealed that invasive ductal carcinoma was the most common subtype, identified in 55 patients (61.1%), followed by invasive lobular carcinoma, observed in 32 patients (35.6%). Among the patients, 78 (86.7%) were hormone receptor (HR) positive, 37 (41.1%) were HER2 positive, and only 2 (2.2%) were triple-negative. In our study, 22 patients (24.4%) had grade 2 tumors, while 51 patients (56.7%) had grade 3 tumors. BRCA mutation positivity was identified in 18 patients (20%). Neoadjuvant therapy was administered to 27 patients (30%), all of whom were treated with anthracyclines. Among HER2-positive patients, all received trastuzumab during the neoadjuvant and adjuvant periods, while 8 patients (8.9%) also received pertuzumab. Additionally, 62 patients (68.9%) had adjuvant radiotherapy (RT). The number of *de novo* metastatic patients was 13 (14.4%). Including 16 patients (17.8%) who developed metastases during follow-up, the total number of metastatic patients reached 29 (32.2%). Among these metastatic patients, 1 was triple-negative, 12 were HER2-positive, and 28 were hormone receptor-positive. The most common site of metastasis was the bone, observed in 18 cases, followed by the lung, seen in 11 cases. (Table 1)

Table 1. Clinical, laboratory, and demographic characteristics of patients.

	n (%)
Median Age	39 (25-45)
Smoking History	
Yes	11 (12.2)
No	79 (87.8)
Child	
Yes	79 (87.8)
No	11 (12.2)
Family History	
Yes	17 (18.9)
No	73 (81.1)
Stage at Diagnosis	
Stage 1-2	25 (27.8)
Stage 3	52 (57.8)
Stage 4	13 (14.4)
Axillary Lymph Node Involvement at Diagnosis	
Yes	65 (72.2)
No	25 (27.8)
Type of Surgery	
MRM (Modified Radical Mastectomy)	48 (53.3)
BCS (Breast-Conserving Surgery)	31 (34.4)
Pathological Subtype	
Invasive Ductal Carcinoma	55 (61.1)
Invasive Lobular Carcinoma	32 (35.6)
Other (Medullary, Mucinous, etc.)	3 (3.3)
Lymphovascular Invasion	
Yes	25 (27.8)
No	53 (58.9)
Unknown	12 (13.3)
Perineural Invasion	
Yes	16 (17.8)
No	62 (68.9)
Unknown	12 (13.3)
HR and HER2 Status	
HR +, HER2 +	32 (35.5)
HR +, HER2 -	51 (56.7
HR -, HER2 +	5 (5.6)
HR -, HER2 -	2 (2.2)

Tumor grade	
Grade 1	7 (7.8)
Grade 2	22 (24.4)
Grade 3	51 (56.7)
Sites of Metastasis	
Bone	18 (20)
Lung	11 (12.2)
Other (Brain, Liver, Peritoneum, Abdominal)	7 (7.8)
Ki67(%)	
≤20	**35 (38.9)**
>20	**55 (61.1)**

Discussion

Young age is considered a poor prognostic factor in breast cancer, as demonstrated by various studies reporting worse survival outcomes and more aggressive tumor characteristics in AYAs.[2,3,5,7] Although the definition of AYAs breast cancer has not been fully standardized, women under the age of 40–45 are typically included in this group in studies.[2,5,10,11] This group represents approximately 7–10% of all breast cancer cases.[4,5]In our study, we classified patients aged 45 years and younger within this category.

Studies have shown that breast cancer in AYAs tends to have a more aggressive biological behavior, often resulting in diagnosis at more advanced stages and poorer survival rates.[2,5,8,10] Even among patients with early-stage disease, survival rates are lower compared to women diagnosed at older ages. [5,12] This disparity has been linked to several factors, including advanced-stage diagnosis, more aggressive tumor phenotypes, lower hormone receptor positivity, higher HER2 positivity rates, larger tumor sizes, increased lymph node involvement, and higher histological grades.

Similar to the findings of Çulha et al., our study also revealed that young breast cancer patients frequently present with advanced-stage disease (57.8% stage 3, 14.4% metastatic at diagnosis) and exhibit high-risk tumor features such as elevated HER2 positivity (41.1%) and axillary lymph node involvement (72.2%).[13] These findings align with the work of Anders et al., who highlighted that younger patients are more likely to develop biologically aggressive subtypes, including triple-negative and HER2-positive tumors, which significantly impact prognosis.[14]

Ki-67, a marker of tumor proliferation, is a well-recognized prognostic factor in breast cancer. In our study, 61.1% of patients had Ki-67 levels >20%, indicating a higher proliferation rate and supporting the notion of aggressive tumor biology in younger patients. This observation is consistent with the findings of Cancello et al., who demonstrated that elevated Ki-67 levels are associated with poorer survival outcomes, particularly in HER2-positive and triple-negative subtypes.[15]

When compared to large-scale studies such as Ozmen et al., our cohort had a higher proportion of advanced-stage diagnoses (57.8% vs. 19% stage 3) and a slightly different distribution of histological subtypes. While Ozmen et al. reported invasive ductal carcinoma in 79% of patients, we observed this subtype in 61.1%, reflecting potential regional or institutional differences.[5] Similarly, our BRCA mutation positivity rate of 20% was higher than the rates typically reported in international literature, such as Anders et al. (10–15%), which may suggest the need for broader genetic screening in young breast cancer patients in Turkey.[14]

Another critical aspect is the discrepancy in hormone receptor (HR) positivity. Our study reported an HR positivity rate of 86.7%, higher than the rates reported by Çulha et al. and Oflazoğlu et al., which were approximately 61–72%.[13,16] This difference may reflect variations in patient demographics or institutional practices. Higher HR positivity rates in our cohort may partially explain the favorable response to endocrine therapies, although HER2 positivity and high Ki-67

levels remain significant contributors to disease aggressiveness and recurrence risk.

Furthermore, survival outcomes in younger patients are heavily influenced by advanced-stage diagnosis and tumor biology. Partridge et al. and Gnerlich et al. noted that younger patients, even those with early-stage disease, often have worse outcomes due to aggressive subtypes and higher recurrence rates.[12,17] In our study, the majority of metastatic patients were HR-positive (96.6%), with bone being the most common site of metastasis, consistent with the findings of Partridge et al.[17]

Despite these findings, our study has certain limitations. The retrospective design and single-center data may limit the generalizability of our results, and the relatively small sample size could reduce the statistical power of certain analyses. Additionally, the lack of multicenter data restricts broader conclusions that could be drawn from a more diverse patient population. However, the high proportion of advanced-stage diagnoses and aggressive tumor characteristics in our cohort underscores the pressing need for improved early detection programs and more personalized treatment strategies for younger breast cancer patients. These findings highlight the importance of considering specific molecular and clinical factors that contribute to the poorer prognosis in this group, and further studies are necessary to validate our results across different populations.

Conclusion

Our study highlights the aggressive nature of breast cancer in young patients, consistent with previous data, and emphasizes the advanced stages and high-risk features observed at diagnosis. These findings underscore the importance of improving early detection efforts, addressing factors specific to the study population or healthcare setting, and implementing personalized treatment strategies to enhance outcomes for young breast cancer patients. Furthermore, the study calls for future research to explore the molecular characteristics of aggressive tumors in this group and to consider larger, multi-center studies to validate these findings and improve generalizability.

Ethics Committee Approval

The study was conducted according to the principles of the Declaration of Helsinki and approval was obtained from the ethics committee of Ankara Etlik City Hospital on April 24, 2024, with approval number 2024-322.

Informed Consent

All participants provided informed consent upon enrollment.

Author Contributions

O.D. took part in the planning, data collection, ethics committee application and writing of the manuscript. Y.D contributed to the statistical analysis. E.C. contributed to the planning and data collection of the manuscript. T.E contributed to data collection.

Conflict of interest

The authors declare that there is no conflict of interest for this article.

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References

1. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians*. 2024;74(3):229-263.
2. Anders CK, Fan C, Parker JS, et al. Breast carcinomas arising at a young age: unique biology or a surrogate for aggressive intrinsic subtypes? *Journal of clinical oncology*. 2011;29(1):e18-e20.
3. Bleyer A, Barr R, Hayes-Lattin B, et al. The distinctive biology of cancer in adolescents and young adults. *Nature Reviews Cancer*. 2008;8(4):288-298.
4. DeSantis CE, Ma J, Gaudet MM, et al. Breast cancer statistics, 2019. *CA: a cancer journal for clinicians*. 2019;69(6):438-451.
5. Özmen V. Breast cancer in Turkey: clinical and histopathological characteristics (analysis of 13.240 patients). *The journal of breast health*. 2014;10(2):98.
6. Chung W-P, Lee K-T, Chen Y-P, et al. The prognosis of early-stage breast cancer in extremely young female patients. *Medicine*. 2021;100(1):e24076.

7. El Saghir NS, Seoud M, Khalil MK, et al. Effects of young age at presentation on survival in breast cancer. *BMC cancer*. 2006;6:1-8.
8. Tichy JR, Lim E, Anders CK. Breast cancer in adolescents and young adults: a review with a focus on biology. *Journal of the National Comprehensive Cancer Network*. 2013;11(9):1060-1069.
9. Anders C, Hsu S, Acharya C, et al. Molecular signatures characterize early stage breast cancer arising in young women and have prognostic and therapeutic implications independent of ER status. *Journal of Clinical Oncology*. 2007;25(18_suppl):522-522.
10. Cathcart-Rake EJ, Ruddy KJ, Bleyer A, Johnson RH. Breast cancer in adolescent and young adult women under the age of 40 years. *JCO oncology practice*. 2021;17(6):305-313.
11. Anastasiadi Z, Lianos GD, Ignatiadou E, Harissis HV, Mitsis M. Breast cancer in young women: an overview. *Updates in surgery*. 2017;69:313-317.
12. Gnerlich JL, Deshpande AD, Jeffe DB, Sweet A, White N, Margenthaler JA. Elevated breast cancer mortality in women younger than age 40 years compared with older women is attributed to poorer survival in early-stage disease. *Journal of the American College of surgeons*. 2009;208(3):341-347.
13. Culha Y, Davarci SE, Ünlü B, Özaşkin D, Demir H, Baykara M. Comparison of clinicopathological and prognostic features of breast cancer patients younger than 40 years and older than 65 years. *Discover Oncology*. 2024;15(1):1-14.
14. Anders CK, Hsu DS, Broadwater G, et al. Young age at diagnosis correlates with worse prognosis and defines a subset of breast cancers with shared patterns of gene expression. *Journal of clinical oncology*. 2008;26(20):3324-3330.
15. Cancello G, Maisonneuve P, Rotmensz N, et al. Prognosis and adjuvant treatment effects in selected breast cancer subtypes of very young women (< 35 years) with operable breast cancer. *Annals of oncology*. 2010;21(10):1974-1981.
16. Oflazoglu U, İriağaç Y, Küçükzeybek Y, et al. Prognostic Value of De-Ritis Ratio in Adolescents and Young Adult Patients with Breast Cancer. *Acta Oncologica Turcica*. 2020;53:37-45.
17. Partridge AH, Hughes ME, Warner ET, et al. Subtype-dependent relationship between young age at diagnosis and breast cancer survival. *Journal of Clinical Oncology*. 2016;34(27):3308-3314.