EJMA

DOI: 10.14744/ejma.269117
EJMA 2025;5(3):117–125

Research Article

Is Young-Onset Breast Cancer a Distinct Clinical Entity?

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Abstract

Objectives: Women under 40 are not included in routine screening programs, which may delay early detection. This study aimed to evaluate the clinicopathological characteristics, treatment patterns, and survival outcomes of young breast cancer (BC) patients.

Methods: This retrospective study included 140 premenopausal women aged 18–40 years diagnosed with BC between January 2018 and December 2023. Medical records were reviewed for histopathological features, treatments, and survival data. Patients were divided into very young (≤35 years) and young (>35 years) groups.

Results: Of 140 patients, 55.7% were very young and 44.3% were young. Most cases were symptom-detected (97.9%). Invasive ductal carcinoma predominated in both groups. Grade 2 and 3 tumors were observed in 42.9% and 27.9% of cases, respectively (p=0.005). Estrogen and progesterone receptor negativity rates were 21.4% and 30%. Early-stage disease was more frequent in the young group, while advanced tumors and node positivity were higher in very young patients. Adjuvant chemotherapy rates were similar, but anthracycline-based regimens were more common in very young patients. Mean disease-free and overall survival were 124 and 170 months.

Conclusion: Young BC patients present with more advanced disease and unfavorable prognostic features. The lack of routine screening remains a critical issue, and larger prospective studies are needed.

Keywords: Breast cancer, Clinicopathological features, Young-onset

Cite This Article: *Şenel HT, Akdeniz A, Ebinç S. Is Young-Onset Breast Cancer a Distinct Clinical Entity? EJMA 2025;5(3):117–125.*

Among all cancer types affecting women, breast cancer (BC) ranks first in terms of incidence and second only to lung cancer as a cause of cancer-related mortality.[1] In the adolescent and young adult (AYA) population—defined as individuals between 15 and 39 years of age—BC is also the most frequently diagnosed malignancy, representing roughly 5.6% of all invasive breast tumors.[2] When BC occurs in younger women, it tends to display more aggressive pathological features, such as larger tumor dimensions, poor differentiation, a greater likelihood of lymph node metastasis, overexpression of human epidermal growth factor receptor 2 (HER2), and a lack of hormone receptor expression.[3] Although different age thresholds have been used, "young" patients are most frequently defined as those under 40 years of age.[4]

AYA women are more likely than their older counterparts to carry inherited genetic mutations that predispose them to cancer, to be diagnosed with larger tumors, to present with unfavorable biological markers, and to have worse clinical outcomes [2]. Delayed diagnosis is common in this population, partly due to low clinical suspicion and the lack of routine screening programs.[5,6] Mammography, for instance,

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Submitted Date: May 7, 2026 **Accepted Date:** June 15, 2026

has not proven cost-effective in this age group.[7] According to data from the National Cancer Database, women under 35 years of age often present with more advanced disease and experience lower 5year survival rates.[8] They are also more frequently diagnosed with aggressive molecular subtypes, including triple-negative and HER2-positive breast cancer.[9] Pathogenic variants in *BRCA1*, *BRCA2*, or *TP53* are found in nearly 50% of AYA women.[10] For those with *BRCA1/2* mutations, risk-reducing bilateral salpingooophorectomy is advised after the completion of childbearing, and PARP inhibitors have emerged as a promising therapeutic option.[11,12]

While chemotherapy protocols do not differ substantially across age groups, young women present unique clinical challenges.[13] Most are of reproductive age, and cancer treatments can adversely affect fertility. Consequently, it is essential to discuss fertility preservation strategies before initiating systemic therapy.[13–15] In this context, early-stage detection and the use of less aggressive treatment regimens are particularly important. The present study therefore aimed to describe the clinicopathological features, treatment approaches, and survival outcomes of young patients diagnosed with breast cancer.

Methods

Study Design and Patient Selection

This retrospective investigation included 140 premenopausal women diagnosed with breast cancer between January 2018 and December 2023 at Gazi Yasargil Training and Research Hospital. All patients were aged 18–40 years at diagnosis. We excluded individuals who had either a second primary malignancy or insufficient data in their medical charts. The following clinical and pathological variables were collected from the hospital's electronic health records: age, marital status, smoking history, family history of breast/ovarian cancer, surgical approach, tumor laterality, histological type and grade, *BRCA1/2* mutation status, estrogen/progesterone receptor status, HER2 status, molecular subtype, TNM stage, tumor size, treatments received, recurrence status, last follow-up date, and survival outcomes. Subsequently, the study population was split into two age categories for comparison: very young (≤35 years) and young (>35 years).

Disease staging was determined according to the 8th edition of the American Joint Committee on Cancer (AJCC) tumor–node–metastasis (TNM) classification system. The study was approved by the Ethics Committee of the University of Health Sciences Gazi Yasargil Training and Research Hospital and was conducted in accordance with the Declaration of Helsinki (approval date: 29/09/2023; decision no: 527).

Pathological Evaluation

Immunohistochemical data extracted from pathology reports were used to determine estrogen receptor (ER), progesterone receptor (PR), HER2, and Ki67 expression levels. Positivity for ER and PR was defined as ≥1% nuclear staining on IHC at 10× magnification. For HER2, an IHC score of 3+ was classified as positive; cases with a score of 2+ required confirmation via fluorescence in situ hybridization (FISH) to assess gene amplification. A Ki67 index of ≥15% was considered high.

Tumor molecular subtyping was performed according to the four markers listed above. The luminal A category comprised ER- and/or PR-positive, HER2-negative tumors with a Ki67 ≤14%. Luminal B tumors were ER- and/or PR-positive with a Ki67 >14%, regardless of HER2 status (positive or negative). HER2-positive (HER2-enriched) tumors lacked both ER and PR but expressed HER2. Finally, triple-negative breast cancers were negative for ER, PR, and HER2.

Treatment

Patients were categorized according to the treatments received. Those who underwent neoadjuvant or adjuvant chemotherapy were further stratified based on receipt of anthracycline-based regimens. Hormonal therapy was classified into three groups: tamoxifen alone, aromatase inhibitors alone, or sequential therapy with tamoxifen followed by aromatase inhibitors. Patients who received adjuvant radiotherapy were recorded. Surgical management included breast-conserving surgery (BCS), modified radical mastectomy (MRM), and simple mastectomy (SM). All patients with HER2-positive disease received trastuzumab, and treatment was completed for a duration of one year.

Statistical Analysis

Statistical analysis was performed using SPSS (version 24.0; IBM Corporation, Armonk, NY, USA). Data normality was tested with the Shapiro–Wilk procedure, and Levene's test served to evaluate equality of variances. Student's t-test was applied for continuous data following a normal distribution; otherwise, the Mann–Whitney U test was used. Categorical variables were compared by means of the Pearson chisquare or Fisher's exact test, depending on the expected frequencies. Descriptive statistics for continuous variables are shown as either mean with standard deviation (SD) or median together with the minimum–maximum range. Categorical variables are expressed as counts and percentages (n/%). To assess survival, we used the Kaplan–Meier method, and group differences were tested with the logrank test. DFS was defined as the period from initial diagnosis to the first recurrence, whereas OS was defined as the period from diagnosis to death or last known follow-up. All analy-

ses were performed with a 95% confidence level, and p-values less than 0.05 were considered statistically significant.

Results

A total of 140 patients were included in the study; 78 (55.7%) were aged ≤35 years and 62 (44.3%) were >35 years. The median age at diagnosis was 35 years (range, 19–39). The predominant histological subtype was invasive ductal carcinoma (IDC), accounting for 72.9% (n=112) of cases. Tumor grading revealed 20% grade 1, 42.9% grade 2, and 27.9% grade 3 tumors. Estrogen receptor, progesterone receptor (PR), and HER2 positivity rates were 78.6%, 70%, and 40%, respectively. At diagnosis, 12.9% of patients were stage I, 48.6% stage II, 20.7% stage III, and 17.9% stage IV. A family history of breast and ovarian cancer in first- and second-degree relatives was present in 9.3% and 7.9% of patients, respectively, with no significant differences between age groups (p=0.30 and p=0.53, respectively). *BRCA* mutation status was available for 50 patients; 12.9% harbored a mutation, with similar frequencies between the two age groups (p=1.00). Regarding marital status, 67.1% of patients were married and 30% were single. A significantly higher proportion of patients aged $>$35 years were married compared to those ≤35 years (79% vs. 62.8%, p=0.03, respectively). Diagnosis was predominantly symptom-driven (97.9%), with no difference between age groups (p=0.58).

Surgical management included breast-conserving surgery in 44.3%, modified radical mastectomy in 40.7%, and simple mastectomy in 5% of patients. The median tumor size was 30 mm (range, 9–80), with no significant difference between age groups (p=0.75). The median Ki-67 proliferation index was 20%, also comparable between groups (p=0.74).

The frequency of IDC was 76.9% in patients aged ≤35 years and 67.7% in those >35 years (p=0.17). Notably, grade 3 tumors were significantly more common in the younger group (40.8% vs. 17.9%, p=0.005). Estrogen receptor positivity was significantly lower in patients ≤35 years compared to those >35 years (70.5% vs. 88.7%, p=0.009), whereas PR positivity showed a non-significant trend (64.1% vs. 77.4%, p=0.08). HER2 positivity was similar between groups (p=0.53) (Table 1).

Molecular subtype distribution was as follows: luminal B (62.9%), luminal A (17.1%), HER2-enriched (10.7%), and triple-negative (9.3%), with no significant difference between age groups (p=0.06). Tumor T stage distribution was 20.7% T1, 65% T2, 13.6% T3, and 0.7% T4. Among patients $\le$35 years, 80.8% were T1–T2 and 19.2% were T3–T4, compared to 91.9% and 8.1%, respectively, in patients >35 years (p=0.06). Nodal status was N0 in 22.1%, N1 in 49.3%, N2 in 23.6%, and N3 in 5% of patients. Node positivity was observed in 83.3% of patients aged ≤35 years and 71% of those >35 years, without a statistically significant difference (p=0.08). Stage distribution by age group showed no significant differences (Table 2).

Adjuvant chemotherapy was administered to 54.3% of patients, with no difference between age groups (p=0.57). However, anthracycline-based chemotherapy was used significantly more frequently in younger patients (p=0.04). Adjuvant radiotherapy was delivered in 71.4% of cases and hormonal therapy in 79.3%, with no significant differences between groups (p=0.17 and *p*=0.10, respectively) (Table 3).

The mean disease-free survival (DFS) was 124±6.09 months; 125 months in patients ≤35 years and 103 months in those >35 years, with no significant difference (p=0.79). The 3-year DFS rates were 89% and 86%, respectively (Fig. 1). The mean overall survival (OS) was 176±6.00 months; 177 months in the younger group and 122 months in the young group, also without a significant difference (p=0.59). The 3-year OS rates were 90% and 94%, respectively (Fig. 2). The overall recurrence rate was 13.6%, including 2.1% local recurrence and 10% systemic recurrence.

Discussion

This analysis compared two age groups of breast cancer patients (18–40 years): those aged 35 years or younger ("very young") and those older than 35 years ("young"). The primary aim was to assess differences in clinicopathological features and survival outcomes. Our results indicate that the very young subgroup had more aggressive tumor characteristics, particularly a significantly higher frequen-

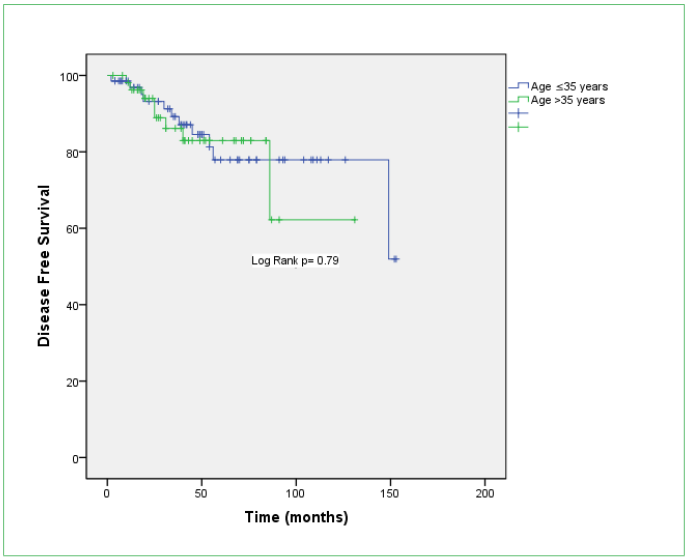

Figure 1. Disease-free survival curve between the ≤35 age group and the >35 age group according to Kaplan–Meier analysis.

Table 1. Demographic and pathological characteristics

Feature	Category	Overall (n=140)	≤35 years (n=78)	>35 years (n=62)	p
Family history of breast cancer	Yes	13 (9.3%)	9 (11.5%)	4 (6.5%)	0.30
	No	127 (90.7%)	69 (88.5%)	58 (93.5%)	
Family history of ovarian cancer	Yes	11 (7.9%)	5 (6.4%)	6 (9.7%)	0.53
	No	129 (92.1%)	73 (93.6%)	56 (90.3%)	
Marital status	Married	94 (67.1%)	47 (60.3%)	47 (75.8%)	0.03
	Single	42 (30.0%)	29 (37.2%)	13 (21.0%)	
	Divorced	4 (2.9%)	2 (2.6%)	2 (3.2%)	
Initial presentation	Symptomatic	137 (97.9%)	77 (98.7%)	60 (96.8%)	0.58
	Screening	3 (2.1%)	1 (1.3%)	2 (3.2%)	
Smoking status	Active Smoker	15 (10.7%)	12 (15.4%)	3 (4.8%)	0.12
	Passive Smoker	21 (15.0%)	12 (15.4%)	9 (14.5%)	
	Non-Smoker	104 (74.3%)	54 (69.2%)	50 (80.6%)	
Tumor localization	Right	84 (60.0%)	44 (56.4%)	40 (64.5%)	0.29
	Left	52 (37.1%)	32 (41.0%)	20 (32.3%)	
	Bilateral	4 (2.9%)	2 (2.6%)	2 (3.2%)	
Histological subtype	IDC	102 (72.9%)	60 (76.9%)	42 (67.7%)	0.17
	ILC	5 (3.6%)	1 (1.3%)	4 (6.5%)	
	Other	32 (22.9%)	16 (20.5%)	16 (25.8%)	
	Unknown	1 (0.7%)	1 (1.3%)	0 (0.0%)	
Histological grade	G1	28 (20.0%)	12 (15.4%)	16 (25.8%)	0.005
	G2	60 (42.9%)	30 (38.5%)	30 (48.4%)	
	G3	39 (27.9%)	29 (37.2%)	10 (16.1%)	
	Unknown	13 (9.3%)	7 (9.0%)	6 (9.7%)	
Lymphovascular invasion	Negative	81 (57.9%)	45 (57.7%)	36 (58.1%)	0.12
	Positive	43 (30.7%)	26 (33.3%)	17 (27.4%)	
	Unknown	16 (11.4%)	7 (9.0%)	9 (14.5%)	
Perineural invasion	Negative	108 (77.1%)	59 (75.6%)	49 (79.0%)	0.12
	Positive	16 (11.4%)	12 (15.4%)	4 (6.5%)	
	Unknown	16 (11.4%)	7 (9.0%)	9 (14.5%)	
Estrogen receptor	Negative	30 (21.4%)	23 (29.5%)	7 (11.3%)	0.009
	Positive	110 (78.6%)	55 (70.5%)	55 (88.7%)	
Progesterone receptor	Negative	42 (30.0%)	28 (35.9%)	14 (22.6%)	0.08
	Positive	98 (70.0%)	50 (64.1%)	48 (77.4%)	
HER2 status	Negative	84 (60.0%)	45 (57.7%)	39 (62.9%)	0.53
	Positive	56 (40.0%)	33 (43.3%)	23 (37.1%)	

IDC: Invasive ductal carcinoma; ILC: Invasive lobular carcinoma; HER2: Human epidermal growth factor receptor 2.

cy of grade 3 tumors and a lower rate of estrogen receptor (ER) positivity. Despite these adverse pathological findings, no significant differences were observed between the two groups in terms of diseasefree survival (DFS) or overall survival (OS). Although the younger cohort showed a tendency toward more frequent lymph node involvement and more advanced disease stages, these differences did not achieve statistical significance. Taken together, these findings suggest that while younger age at diagnosis is linked to more aggressive tumor biology, it does not necessarily

Table 2. Molecular subtypes, tumor (t) stage, and nodal (n) stage

Feature	Category	Overall (n=140)	≤35 years (n=78)	>35 years (n=62)	P
Molecular subtype	Luminal A	24 (17.1%)	10 (12.8%)	14 (22.6%)	0.06
	Luminal B	88 (62.9%)	47 (60.3%)	41 (66.1%)	
	HER2 positive	15 (10.7%)	10 (12.8%)	5 (8.1%)	
	Triple negative	13 (9.3%)	11 (14.1%)	2 (3.2%)	
Tumor (T) Stage	T1	29 (20.7%)	15 (19.2%)	14 (22.6%)	0.06
	T2	91 (65.0%)	48 (61.5%)	43 (69.4%)	
	T3	19 (13.6%)	14 (17.9%)	5 (8.1%)	
	T4	1 (0.7%)	1 (1.3%)	0 (0.0%)	
Nodal (N) Stage	N0	31 (22.1%)	13 (16.7%)	18 (29.0%)	0.08
	N1	69 (49.3%)	40 (51.3%)	29 (46.8%)	
	N2	33 (23.6%)	20 (25.6%)	13 (21.0%)	
	N3	7 (5.0%)	5 (6.4%)	2 (3.2%)	

HER2: Human epidermal growth factor receptor 2.

lead to worse survival. This may reflect the effectiveness of current multimodal treatment protocols in offsetting the impact of unfavorable tumor features.

Breast cancer is responsible for a significant proportion of cancers diagnosed in adolescents and young adults.[16] Compared to older patients, this population typically presents with more aggressive disease and a poorer prognosis.[17] This unfavorable pattern is associated with a higher prevalence of adverse features, including high histological grade, ER negativity, and HER2 positivity.[16] Moreover, aggressive subtypes like triplenegative and HER2-positive breast cancer occur more frequently in younger women and are commonly detected at later stages.[9]

A family history of BC is a well-established risk factor and has gained further importance with the identification of hereditary genetic mutations.[18] McAree et al.[19] reported that 27.1% of patients aged 18–40 years had a family history of breast or ovarian cancer. Similarly, another study reported a family history rate of 37%.[20] In a cohort of 628 patients under 40, the prevalence of breast or ovarian cancer history was 31%.[21] In contrast, our study observed considerably lower rates: 9.3% for breast cancer and 7.9% for ovarian cancer family history. Pathogenic variants in *BRCA1* and *BRCA2* are well-established genetic risk factors, conferring a lifetime breast cancer risk of approximately 72% and 69%, respectively.[22] In a large cohort study by Copson

Tablo 3. Neoadjuvant therapy, adjuvant chemotherapy, and adjuvant radiotherapy

Feature	Category	Overall (n=140)	≤35 years (n=78)	>35 years (n=62)
Neoadjuvant therapy	No	79 (56.4%)	46 (59.0%)	33 (53.2%)
	Yes	61 (43.6%)	32 (41.0%)	29 (46.8%)
Neoadjuvant anthracycline-based therapy	Yes	55 (39.3%)	28 (35.9%)	27 (43.5%)
	Non- anthracycline -based	6 (4.3%)	4 (5.1%)	2 (3.2%)
	No Therapy	79 (56.4%)	46 (59.0%)	33 (53.2%)
Adjuvant chemotherapy	No	64 (45.7%)	34 (43.6%)	30 (48.4%)
	Yes	76 (54.3%)	44 (56.4%)	32 (51.6%)
Adjuvant anthracycline -based therapy	Yes	53 (38.0%)	35 (44.9%)	18 (29.0%)
	Non- anthracycline -based	23 (17.0%)	10 (12.8%)	13 (22.6%)
	No Therapy	64 (45.0%)	33 (42.3%)	31 (50.0%)
Adjuvant radiotherapy	No	37 (26.4%)	24 (30.8%)	13 (21.0%)
	Yes	100 (71.4%)	52 (66.7%)	48 (77.4%)
	Unknown	3 (2.1%)	2 (2.6%)	1 (1.6%)

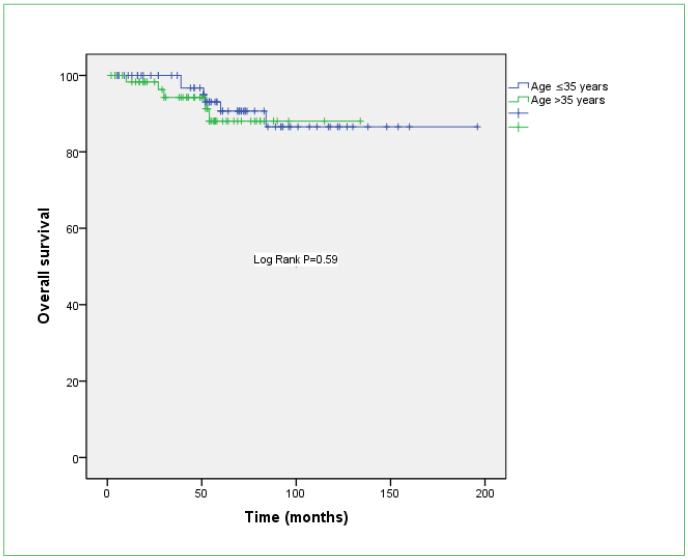

Figure 2. Overall survival curve between the ≤35 age group and the >35 age group according to Kaplan–Meier analysis.

et al.[23], *BRCA1/2* mutations were identified in 12 of 2,733 women under age 40. In our study, the mutation rate was 12.9%, which appears higher than previously reported series, although this finding should be interpreted with caution given the limited number of patients who underwent genetic testing. Individuals with *BRCA1/2* mutations are more likely to have a family history of early-onset breast or ovarian cancer; therefore, genetic testing and counseling should be strongly considered, particularly in patients with a relevant family history.[24]

Regarding sociodemographic characteristics, 30% of patients were single, 67.1% were married, and 2.9% were divorced. The proportion of married individuals was significantly higher in the young patients subgroup compared to very young patients (p=0.03). This finding has important implications for multidisciplinary management, particularly regarding psychosocial support. Furthermore, since many patients are within their reproductive years, marital status may also influence fertility preservation strategies and the management of treatment-related complications.

Since women under age 40 are not routinely included in population-based screening programs, BC in this group is more often diagnosed at a symptomatic stage. Avci et al.[20] reported that 62.9% of patients presented with a palpable mass. Similarly, another study found that 24.2% of patients aged 40–70 years were diagnosed through screening.[25] Consistent with the literature, 97.9% of patients in our cohort were diagnosed based on symptoms, while only 2.1% were detected through screening. These findings highlight the need for increased awareness and the development of tailored early detection strategies in younger populations.

With respect to tumor laterality, previous studies have reported right breast involvement in 59.7% of cases,[26] while two other studies demonstrated rates of 50.6% and 44.8%, respectively.[27,28] In our cohort, 60% of tumors were localized in the right breast, consistent with the existing literature.

Regarding histological subtype, IDC has been reported as the predominant subtype, with a frequency of 86% in one study.[20] Similarly, Ozmen reported that, in a large cohort of 11,385 patients, an IDC rate of 79% was observed.[29] In our study, IDC was observed in 72.9% of patients, with rates of 76.9% in the very young group and 67.7% in the older young group (p=0.17). Although no statistically significant difference was observed between age groups, the distribution and frequency of histological subtypes in our cohort were consistent with previously published data.

Avci et al.[20] reported grade 2 and grade 3 tumors in 44.3% and 43.2% of patients, respectively. The rate of grade 3 disease was 42.9% in very young patients and 43.5% in young patients. Another study reported a grade 3 tumor rate of 60% in patients under 40 years, compared to 48% in those aged ≥40 years.[29] Similarly, Copson et al.[30] demonstrated that 59% of tumors were grade 3 in patients younger than 40 years. In contrast, in a cohort of patients aged 45–69 years, grade 2 and grade 3 tumors were observed in 33% and 13% of cases, respectively.[31] Multiple studies have consistently shown that higher tumor grade is associated with poorer prognosis.[32] In our study, 42.9% of patients had grade 2 disease and 27.9% had grade 3 disease. Notably, the proportion of grade 3 tumors was significantly higher in very young patients compared to young patients (40.8% vs. 17.9%, p=0.005). These findings are consistent with the literature, indicating that younger patients tend to present with higher-grade tumors, while lower-grade tumors become more prevalent with increasing age. Furthermore, the higher frequency of grade 3 tumors in very young patients supports the concept that breast cancer diagnosed at an earlier age is associated with more aggressive tumor biology and a poorer prognostic profile.

In a study of patients under 40 evaluating receptor status, ER negativity was reported in 33.7% and HER2 positivity in 24% of cases.[30] In another study comparing very young and young patient groups, ER negativity rates were 38.8% and 21.6%, respectively, while PR negativity rates were 49.1% and 35.3%, with significantly higher hormone receptor negativity in the very young group (p<0.001 and p=0.0010, respectively).[8] Similarly, another study reported ER negativity in 39%, PR negativity in 43%, and HER2 positivity in 26% of patients under 40.[29] Poorolajal et al.[33] demonstrated that patients with ER-negative and

HER2-positive tumors had shorter survival than those with ER/PR-positive, HER2-negative disease. Furthermore, ER-positive tumors have been associated with improved five-year OS compared to ER-negative tumors.[30] In studies including older patient populations, ER and PR negativity rates were lower. For example, one study reported ER negativity in 14.2% and PR negativity in 20.4% of patients over 40,[34] while another study found both ER and PR negativity rates to be 25.9%.[35] In our cohort, 21.4% of patients were ER-negative and 30% were PR-negative, while HER2 positivity was observed in 40%. When stratified by age, ER negativity was significantly higher in the very young group compared to the young group (29.5% vs. 11.3%, p=0.005). Progesterone receptor negativity was also more frequent in the very young group (35.9% vs. 22.6%), although this difference did not reach statistical significance (p=0.08). The higher prevalence of hormone receptor negativity and relatively elevated HER2 positivity in younger patients supports the association between younger age and more aggressive tumor biology, and is consistent with previously reported findings.

Ozmen[29] reported molecular subtype distributions in patients under 40 as 56% luminal A, 18.5% luminal B, 8% HER2-positive, and 17% triple-negative. In the same study, among patients older than 40, 64% were luminal A and 14% were luminal B. In another cohort of patients under 40, subtype distribution was reported as 33% luminal A, 35% luminal B, 11% HER2-positive, and 21% triple-negative.[36] In studies including patients over 40, luminal A, luminal B, HER2-positive, and triple-negative subtypes were observed in 33%, 44%, 9.4%, and 13.5% of cases, respectively.[37] Furthermore, Sweeney et al.[38] demonstrated that the luminal B subtype was 2.48 times more frequent than luminal A in patients younger than 40. In our study, molecular subtype distribution was 17.1% luminal A, 62.9% luminal B, 10.7% HER2-positive, and 9.3% triple-negative. The relatively lower proportion of the favorable prognostic luminal A subtype, together with the predominance of luminal B tumors, supports the notion that younger patients tend to have more aggressive tumor biology. These findings are consistent with the literature and may partly explain the comparatively poorer prognosis observed in younger BC populations.

Since women under 40 are not routinely included in screening programs, BC in this population is often diagnosed at a symptomatic and more advanced stage. In the analysis by Avci et al.[20], 12.9% of patients under 40 had T3–T4 tumors and 61% were node-positive; in patients ≤35 years, these rates were 13.7% and 59.1%, respectively. Another study reported stage distribution as 2.5% stage I, 20.5% stage II, 55% stage III, and 22% stage IV.[39] Several studies have consistently shown that younger women tend to present with larger tumors, higher rates of lymph node involvement, and consequently more advanced-stage disease.[2,20,29] In our study, most patients presented with a palpable mass, and the proportion of T2 tumors was 65%. T3 and T4 tumors accounted for 13.6% and 0.7%, respectively, while in the very young subgroup, the proportion of T3–T4 tumors was 19.2%. The overall rate of node-positive disease was 77.9%, reaching 83.3% in the very young group. Stage distribution in the entire cohort was 12.9% stage I, 48.6% stage II, 20.7% stage III, and 17.9% stage IV. Although the very young group exhibited numerically higher rates of T3–T4 tumors and nodal involvement compared to the young group, these differences were at the borderline of statistical significance (p=0.06 and p=0.08, respectively). These findings are consistent with prior reports suggesting a tendency toward more advanced disease at presentation in younger patients.

In the study by Wang et al.[40], neoadjuvant therapy, adjuvant chemotherapy, adjuvant radiotherapy, and hormonal therapy rates were 38.1%, 89.7%, 27.4%, and 34.3%, respectively. In our cohort, 43.6% received neoadjuvant chemotherapy, 54.3% adjuvant chemotherapy, 71.4% adjuvant radiotherapy, and 79.3% adjuvant hormonal therapy. The relatively frequent use of both neoadjuvant and adjuvant treatments in younger patients is consistent with previous studies, which suggest that more intensive treatment strategies are often required in this population to reduce mortality and recurrence risk [40]. In our study, 37.9% of patients received anthracycline-based adjuvant chemotherapy. Notably, anthracycline use was significantly higher in the very young group compared to the young group (77.8% vs. 56.3%, p=0.04). This finding likely reflects the more aggressive tumor biology observed in younger patients and the consequent need for more intensive systemic therapy, consistent with the existing literature.

The main limitations of our study include its retrospective design and relatively small sample size. Consequently, subgroup analyses for all variables could not be performed with sufficient statistical power. Additionally, due to the limited number of events during follow-up, median survival outcomes could not be reliably estimated. The retrospective nature also precluded a comprehensive evaluation of established breast cancer risk factors. Furthermore, the heterogeneity of molecular subtypes among very young patients may contribute to variability in histopathological characteristics, potentially influencing stage at presentation and treatment outcomes. Despite these limitations, our study highlights important histopathological differences and treatment patterns in young BC patients. Since this population often presents with aggressive disease and is excluded from routine

screening, careful attention to these features is critical. Raising awareness and considering more intensive treatments could improve outcomes in this group.

Conclusion

In conclusion, this study shows that younger breast cancer patients frequently present with laterstage disease and a higher number of poor prognostic features. The ongoing debate about excluding this age group from standard screening protocols continues to lack resolution. Additionally, because few studies have focused specifically on this population, there is a clear need for wellpowered prospective research to develop standardized screening and treatment strategies for young women with breast cancer.

Disclosures

Ethics Committee Approval: All analyses were performed in accordance with the principles of the Declaration of Helsinki. Approval was obtained from the ethics committee of Gazi Yasargil Training and Research Hospital for the study (approval date: 29/09/2023; decision no: 527).

Informed Consent: All authors of the manuscript titled: 'Is Young-Onset Breast Cancer a Distinct Clinical Entity?' certify that they qualify for authorship because of substantial contribution to the work submitted. The authors undersigned declare that this manuscript has not been published nor is under simultaneous consideration for publication elsewhere. The authors agree to transfer the copyright to the 'Eurasian Journal of Medical İnvestigation' to be effective if and when the manuscript is accepted for publication and that the manuscript will not be published elsewhere in any other language without the consent of the Eurasian Journal of Medical İnvestigation. The final form of the manuscript has been seen and approved by all authors.

Conflict of Interest: The authors declare that they have no conflict of interest.

Financial Disclosure: This study was not supported by any organization or entity. The authors have no financial involvement with any organization or entity. No writing assistance was utilized in the production of this manuscript.

Use of AI for Writing Assistance: The authors declare that no artificial intelligence–assisted technologies were used in the preparation of this manuscript.

Authorship Contributions: Concept – HTŞ, NA, SE; Design – HTŞ, NA; Supervision – HTŞ; Materials – HTŞ, NA, SE; Data collection &/or processing – HTŞ; Analysis and/or interpretation – NA, SE, HTŞ; Literature search – NA, HTŞ; Writing – HTŞ, NA, SE; Critical review – HTŞ, NA, SE.

Acknowledgement: This article has not previously been published elsewhere as a partial or complete text and article is not under review or publication in any other journal. The Authors grants the Publisher the sole and exclusive license of the full copyright in the Contribution, which license the Publisher hereby accepts.

Peer-review: Externally peer-reviewed.

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