

PROFILES AND PREDICTIVE FACTORS IN YOUNG AGE BREAST CANCER PATIENTS (RETROSPECTIVE STUDY)

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GENÇ YAŞTAKİ MEME KANSERLİ HASTALARIN PROFİL VE PREDİKTİF FAKTÖRLERİ

ÖZET

Amaç: Genç meme kanserli hastalar hastalığın seyri, biyolojik davranış farklılıkları, prognostik faktör özelliklerinin değişik olması nedeni ile özel olarak incelenmesi gereken bir konudur.

Hastalar ve Yöntem: 1997–2005 yılları arasında tedavi edilen 1300 meme kanserli olgu incelendi. 133 olgu (%10) 35 yaş ve altındaydı. Bu olgular evre, nodal durum, cerrahi teknik, adjuvant ve neo-adjuvan tedaviler, ER/PR durumu, grade, lenfatik ve vasküler invazyon, intraduktal komponent, histolojik tip, yerel nöks, metastaz, mortalite, hastaliksız ve toplam sağ kalım süreleri ve etkili prediktif faktörler yönünden 35 yaş üzeri hastalar ile karşılaştırıldılar.

Bulgular: 35 yaş ve altındaki olgularda evre, nodal tutulum, lenfatik ve vasküler invazyon, ER/PR negatifliği daha yüksek oranda bulundu. Bu olgularda yerel nöks ve mortalite oranları yüksek, hastaliksız ve toplam sağ kalım süreleri düşük bulundu. Kuvvetli prediktif faktörler evre, grade ve nodal tutulumdu.

Sonuç: Görülmektedir ki genç meme kanserli olgularda prognoz daha kötü seyretmektedir. Ülkemizde görülen genç meme kanserli olguların özellikleri diğer ülkeler ile benzerdir.

Anahtar sözcükler: prognoz, rekürens, metastaz, cerrahi, kemoterapi

ABSTRACT

Young breast cancer patients have been examined specifically according to the progress of disease, biological behavior differences, and manifestation of various characteristics of prognostic factors. A total of 1300 breast cancer patients, treated between the years 1997 and 2005, were enrolled in the study. Of those patients, 133 were aged 35 years or younger (10%). They were then compared with women older than 35 years in relation to stage, nodal state, surgical technique, adjuvant and neo-adjuvant therapies, ER/PR status, grade, lymphatic and vascular invasion, intraductal component, histological type, local-recurrence, metastasis, mortality, disease-free survival and overall survival rates and predictive factors. In patients aged 35 years or younger, stage, nodal involvement, lymphatic and vascular invasion, ER/PR negativity resulted with higher ratios. In this patient group, local-recurrence and mortality rates were increased while overall survival and disease-free survival decreased. The strong predictive factors observed in the study include stage, grade, and nodal status.

These outcomes demonstrate that breast cancer in young patients possess worse prognoses. The characteristics of young breast cancer patients in Turkey are similar to that of other countries.

Key words: prognosis, recurrence, metastasis, surgery, chemotherapy

Factors efficacious over prognosis of breast cancer are crucial in disease treatment choice and its progress. Although opinions for many factors have been definite, there are prognostic factors that are still under dispute. In patients with breast cancer, age is a prognostic factor one that is debatable. The opinion of accepting young age as a risk factor has been gradually emphasized. In addition to this, other prognostic characteristics of young patients, biological differences due to patient and tumor, and different treatment alternatives in young patients bring about this issue as another subject of debate retrospectively (1-4). Furthermore, young patient profile and characteristics may differ as a result of genetic, socio-economical and geographical factors.

In this study we sought to demonstrate the profile of young patients with breast cancer in the West-Anatolian region of Turkey. Patients comprising the study group included a mixed European and Asian population with varying socio-economical statuses.

Materials and methods

from a total of 1300 cases that underwent breast carcinoma treatment between the years 1997 and 2005, 133 cases, aged 35 years and younger, were included in the study. The variables choice of surgery, adjuvant therapies (radiation therapy, chemotherapy, hormonal therapy), stage distribution, nodal status, grade, histological type, neo-adjuvant chemotherapy, ER/PR status, lymphatic

and vascular invasion, intraductal component, metastasis, local recurrence, exitus, disease free and overall survival were compared between age groups ≤ 35 years and > 35 years (young age versus older age breast cancer group). Pathological evaluation was processed by H&E staining, and ER/PR evaluations were assessed by the Ventana-Benchmark immunohistochemical automatic system. A modified Bloom-Richardson scale was used for classification purposes. Predictive factors were examined from aspects of local-recurrence, metastasis and mortality rates. Outcomes were statistically calculated using z-tests and multi-variety regression analyses. A chi-square test was employed to confirm statistical significance. Disease-free survival and overall survival were estimated and plotted using the Kaplan-Meier method. Group differences in survival time were tested using log-rank tests. A p -value of < 0.05 was considered statistically significant. SPSS for Windows (version 13.0, SPSS Inc., Chicago, IL, USA) was used for all statistical analyses.

Results

Young age breast cancer patients (≤ 35 years) were 10% (133/1300) in total. The median follow-up time was 58 months, and the median age of the patients was 31.2 years of age (age range between 21 to 35 years). The older age breast cancer group (> 35 years) had a median follow-up time of 62 months and a median age of 54.3 years (age range between 35 and 92 years).

Modified radical mastectomy and breast-conservation were not statistically significant in either age group. For the inoperable patients in the study, no statistical significance was found between groups. Simple mastectomy was found to be statistically significant and carried out more frequently in the older age ($p < 0.01$).

For adjuvant treatments, chemotherapy and radiation therapy were administered more in the young age breast cancer group (100/133, $p < 0.01$; 41/133, $p < 0.05$, respectively), whereas hormone therapy was administered more in the older age breast cancer group ($p < 0.05$). FEC (endoxan, fluorouracil, epirubicin) was the most common chemotherapy regimen administered to young age breast cancer group and was statistically more frequent than the older age breast cancer group ($p < 0.05$).

According to stage distribution, 0, 1, 2A, 2B, 3B and 4 did not show significant difference between both groups. Only stage 3A cases were observed more frequently in the young age breast cancer group (28/133, $p < 0.01$).

When nodal status was examined, number of N0 patients was observed more at older age breast cancer group ($p < 0.01$). N1 patient ratios did not differ between the two groups. Number of N2 patients were more in the young age breast cancer group (31/133, $p < 0.01$).

Patients with bilateral breast cancer did not show statistically significant difference between the two groups.

Table 1. Statistical differences between age ≤ 35 and age > 35 patient groups.

		Age ≤ 35	Age > 35
Simple Mastectomy	-	(6)-4,5 %	$p < 0.01$
Chemotherapy	$p < 0.01$	(100)-75,2 %	-
Radiotherapy	$p < 0.05$	(41)-30,8 %	-
Hormonotherapy	-	(74)-55,6 %	$p < 0.05$
Stage 3A	$p < 0.05$	(28)-21 %	-
Nodal Status N0	-	(50)-37,6 %	$p < 0.01$
Nodal Status N2	$p < 0.01$	(31)-23,3 %	-
Inflammatory Cancer	-	(1)-0,7 %	$p < 0.01$
Invasive Ductal Cancer	$p < 0.05$	(111)-83,4 %	-
Lymphatic Invasion	$p < 0.01$	(51)-38,3 %	-
Vascular Invasion	$p < 0.05$	(27)-20,3 %	-
ER/PR Negativity	$p < 0.05$	(32)-24 %	-
Local Recurrence	$p < 0.01$	(9)-6,7 %	-
Mortality	$p < 0.01$	(26)-19,5 %	-

Table 2. Overall and disease-free survival rates for age ≤ 35 and all aged patients.

	Age ≤ 35	All aged patients
Overall survival	% 91.7	% 95
Disease-free survival	% 86.4	% 91

According to grades, no significant difference was found between the two groups.

Furthermore, no significant difference was found with respect to metastasis, therefore, as expected, metastatic disease was not more frequent in young age breast cancer patients.

Mortality was observed at a significantly higher rate in the young age breast cancer group (26/133, $p < 0.01$).

Inflammatory breast cancer was observed less frequently in young age breast cancer group ($p < 0.01$).

No significant difference was found in the distribution of the in situ, lobular, medullary and mucinous histological types. Invasive ductal carcinoma (IDC) was observed more frequently in the young age breast cancer group (111/133, $p < 0.05$).

Neo-adjuvant chemotherapy administration rates did not show a significant difference between both groups.

In the young age breast cancer group, lymphatic invasion (51/133, $p < 0.01$) and vascular invasion (27/133, $p < 0.05$) were observed more frequently. IDC observation rate showed no significant difference.

Hormone receptor negativity (ER/PR) was observed more frequently in young age breast cancer group patients (32/133, $p < 0.05$).

Table 3. Predictive factors for mortality, local recurrence and metastasis.

	<i>Local recurrence</i>	<i>Stage 3</i>	<i>Grade 2/3</i>	<i>Node positivity</i>	<i>IDC</i>	<i>Vascular invasion</i>
Mortality	p<0.01	p<0.01	p<0.05	p<0.01	-	-
Local Recurrence	-	-	p<0.05	p<0.01	p<0.01	p<0.01
Metastasis	p<0.01	p<0.01	p<0.05	p<0.01	-	-

Local-recurrence rate was significantly higher in young age breast cancer group (9/133, p<0.01) (Table 1).

In the young age breast cancer group, median survival was 53.5 months and the overall survival was 91.7%. In our entire age patient-based cohort (1330 cases), the survival rate was calculated as 95%. Poorer survival was observed in young age breast cancer group. In the younger patients, disease-free survival was 86.4%, as patient-based cohort resulted with a 91% disease-free survival (Table 2).

When predictive factors for cancer related mortality were examined for the young age breast cancer group, local-recurrence (p<0.01), stage 3 and 4 (p<0.01), grade 2 and 3 (p<0.05), lymph node involvement (p<0.01) were statistically significant. Very young age (≤30 years) was not found significantly predictive factor for breast cancer. The predictive factors for local-recurrence were intraductal component (p<0.01), grade 2 and 3 (p<0.05), vascular invasion (p<0.01), and lymph node involvement (p<0.01). Stage, lymphatic invasion, very young age (≤30) patients, surgical margin positivity was not found statistically significant. The predictive factors for metastasis were stage 3 disease (p<0.01), grade 2 (p<0.05) and 3 (p<0.01) histology lymph node involvement (p<0.01), and presence of local recurrence (p<0.01) (Table 3).

Discussion

Breast cancer comprises approximately 22% of all cancers observed in females, with 2% of these are patients aged 35 years or younger (1). Young breast cancer patients (≤35 years) are represented by 5-7% in previous studies (2,3). A study conducted in Korea demonstrated that 12.5% of breast cancer cases were young patients (4). The ratio of ≤30 years of age patients was reported as 1% (5). In our study, 10% of our study population consisted of young patients aged ≤35 years.

Nixon and Albain found young aged patients resulted with worse prognosis. In the study by Nixon, worse prognosis was a result of grade 3 tumor, extensive intraductal component, lymph node involvement and necrosis. In Albain's study, nodal status, tumor diameter, BRCA 1 positivity, S phase fraction and p53 abnormality was found higher (2,6,7). However, in a different study, p53 was found to have no relationship with young age (8).

In the studies of MD Anderson Cancer Center, Institute Curie, Milan group and NSABP, prognosis in younger aged patients with breast cancer was found to be worse. As a result, young age is recognized as a prognostic factor.

Various studies have demonstrated age as a prognostic factor, as prognosis and survival have been shown to be worse in the younger (1,2,4-6,9-28).

Being at a young age has been stated as the second most leading risk factor after lymph node involvement (13,15).

In our study, there is significant majority of N0 patients in >35 years of age and N2 patients in ≤35 years age group.

Previous studies have expressed that prognosis at young age has been worse with grade 1 disease less frequently seen in comparison to the higher numbers of high grade, node positivity, and ER negativity. Diagnosis has been delayed in the younger patients due to difficulties, therefore increasing mortality risk (2,9,29).

In a population-based cohort consisting of 452 patients ≤35 years of age, positive family history was found in 34% of the patients, grade 3 was found in 69%, and ER positivity was reported in 52% (7). Hormone receptor-negativity and grade 3 were related to poor survival within the study patients (30). Concurrently, ER/PR negativity was more frequent in the younger aged patients.

Tumor diameter, nodal involvement, positive family history, ER negativity, DNA aneuploidy, lymphatic and vascular invasion were determined as predictive factors of a worse prognosis in younger aged patients (1,7,10,12,15,31-35). Similarly, this study found that lymphatic and vascular invasions were observed more frequently in the younger patients.

Patients in the ≤35 years age group were reported to receive more chemotherapy and less hormonal therapy. Combined use of chemotherapy, LH/RH agonist and tamoxifen was more frequent in younger patients (10, 36). In our study, it was determined that more chemotherapy and less hormonal therapy were administered to young patients.

Medullar carcinoma was found to be the most common histological type in young patients according to one study and invasive ductal carcinoma was reported to be the most frequent type in another study (4,35). With our study, invasive ductal carcinoma was observed significantly more in the younger aged patient group.

Previously, stage 2 disease was generally observed in younger patients. (37). Our cohort breast cancer was more frequently observed in stage 3A.

Furthermore, being at a young age has been reported as a risk factor for local-recurrence after breast conservation. This rate was reported to be between 7.5-35% in numerous studies (13, 32, 33, 36, 38-41). Various studies have demonstrated the 5-year-survival of young aged patients being between 64% and 91%. Young age has been shown to be a strong prognostic factor for survival. Disease-free survival was determined to be worse in younger patients (1,4,10,12,13,15,16,28,37,42,43). However, another study found no difference in the overall and disease-free survival for younger aged patients, thus, outcome explained by a more aggressive treatment (33, 44). In our study, the overall and disease-free survival was worse in younger aged patients.

Tumor diameter, ER negativity, lymphatic and vascular invasion, nodal involvement and metastasis were predictive factors in younger age patients (1). In our study, stage 3-4 diseases, grade 2-3, and nodal involvement have been determined as strong predicative factors for local-recurrence, metastasis, and mortality.

Conclusion

In young breast cancer patients, stage, nodal involvement, lymphatic invasion, vascular invasion and ER/PR negativity were found to be significantly more. Local-recurrence and mortality were observed more frequently in these patients and overall and disease-free survival rates were worse. Stage, grade and nodal status were strong predictive factors. The results demonstrate that young breast cancer patients have worse prognostic factors. The characteristics of breast cancer in younger women living in Turkey are similar to those of other countries.

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