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RESEARCH

PROGNOSTIC FACTORS AND SURVIVAL OF ELDERLY WOMEN WITH BREAST CANCER AGED ≥70 YEARS

Abstract

Introduction: In the treatment of geriatric patients with breast cancer, each patient should be treated according to his/her specific disease, performance status, and biological age. In this study, we aimed to investigate prognostic factors affecting survival in women aged ≥70 years of age and older with breast cancer.

Materials and Method: A total of 148 female patients aged ≥70 years who were admitted to the University of Health Sciences Istanbul Training and Research Hospital Radiation Oncology clinic between 2011 and 2017 were evaluated.

Results: Age (p<0.001), tumor diameter (p<0.001), operability (p<0.001), tumor stage (p<0.001), lenfovascular invasion (p=0.045), estrogene receptor positivity (p=0.002), progesterone receptor positivity (p=0.046), metastasis (p<0.001), Ki 67 ≥ 14 ratio (p=0.035), Charlson comorbidity index (p=0.005), and radiotherapy applicability (p=0.023) were significantly associated with overall survival. Multivariate cox regression analysis revealed that age (HR=1.126, 95% CI=1.048–1.210, p<0.001), estrogene receptor positivity (HR=3.701, 95% CI=1.286–0.652, p=0.015), and presence of metastasis (HR=0.210, 95% CI=0.051-0.863, p=0.030) were independent prognostic factors.

Conclusion: According to our clinical experiences, the treatment approach for healthy elderly women with recently diagnosed breast cancer is similar to that for young women, i.e., surgery, axillary evaluation, radiotherapy, and systemic adjuvant therapy (depending on tumor properties and recurrence risk). In elderly breast cancer patients, ER positivity, absence of distant metastasis, and age younger than < 79 years old have been identified as independent prognostic factors that positively affect survival.

Keywords: Breast cancer; Survival; Prognosis; Aged.

ARAŞTIRMA

YETMİŞ YAŞ VE ÜZERİ MEME KANSERLİ YAŞLI KADINLARDA PROGNOSTİK FAKTÖRLER VE SAĞKALIM

Öz

Giriş: Meme kanseri olan geriatrik hastaların tedavisinde, her hasta kendi hastalığına, performans durumuna ve biyolojik yaşına göre tedavi edilmelidir. Bu çalışmada, meme kanserli, ≥70 yaş ve üstü yaşlı kadınlarda sağkalımı etkileyen prognostik faktörleri araştırmayı amaçladık.

Gereç ve Yöntem: 2011-2017 yılları arasında Sağlık Bilimleri Üniversitesi İstanbul Eğitim ve Araştırma Hastanesi Radyasyon Onkolojisi kliniğine başvuran, yaşları ≥70 ve üstünde olan toplam 148 kadın hasta değerlendirildi.

Bulgular: Yaş (p<0.001), tümör çapı (p<0.001), ameliyat edilebilme (p<0.001), tümör evresi (p<0.001), lenfovasküler invazyon varlığı (p=0.045), östrojen reseptörü pozitifliği (p=0.002), progesteron reseptör pozitifliği (p=0.046), metastaz varlığı (p<0.001), Ki 67 ≥ 14 oranı (p=0.035), Charlson komorbidite indeksi (p=0.005) ve radyoterapi uygulanabilirliği (p=0.023) genel sağkalım ile anlamlı olarak ilişkiliydi. Çok değişkenli cox regresyon analizi yaş (HR=1.126, 95% CI=1.048–1.210, p<0.001), östrojen reseptör pozitifliği (HR=3.701, 95% CI=1.286–0.652, p=0.015) ve metastaz varlığının (HR=0.210, 95% CI=0.051-0.863, p=0.030) bağımsız prognostik faktörler olduğunu gösterdi.

Sonuç: Klinik deneyimlerimize göre, yeni teşhis edilmiş meme kanseri olan sağlıklı yaşlı kadınlar için tedavi yaklaşımı; cerrahi, aksiller değerlendirme, radyoterapi ve sistemik adjuvan tedavi (tümör özelliklerine ve nüks riskine bağlı olarak) yani genç kadınlardakine benzerdir. Yaşlı meme kanseri hastalarında ER pozitifliği, uzak metastaz olmaması ve yaşın 79'dan daha genç olması sağkalımı olumlu etkileyen, bağımsız prognostik faktörler olarak tespit edilmiştir.

Anahtar Sözcükler: Meme kanseri; Sağkalım; Prognoz; Yaşlı.

INTRODUCTION

The incidence of breast cancer, the most common malignancy in women, is increasing with age (1). Approximately three-fourth of patients diagnosed with breast cancer comprises postmenopausal women. One out of eight women (12.5%) undergoes breast cancer at least once in the entire life. Cancer treatment in elderly patients is essentially difficult in clinical oncology. Performance, life expectancy and accompanying diseases in elderly patients with breast cancer are the factors that can be used to effectively determine treatment. Despite the significant representations of populations with breast cancer, elderly women with breast cancer are widely excluded from the standard medical treatment or are probably suggested with less effective treatment options (1,2). It is important to take into account the chronological age, potential risks against absolute benefits, treatment tolerance, patient preference, possible side effects of treatment and life expectancy in the treatment of older patients with breast cancer (3). Therefore, we aimed to describe our treatment practices in elderly women with breast cancer.

MATERIALS AND METHOD

Between 2011 and 2017, 148 female patients aged ≥70 years who were admitted to the Radiation Oncology Clinic of the Istanbul Training and Research Hospital were evaluated. The last follow-up was conducted in December 2017. The period from disease-free survival (DFS) until metastasis or local recurrence was observed; overall survival (OS) was assessed as the time until death. Exclusion criteria were as follows: patients who were previously diagnosed with other types of cancer, patients who were diagnosed with ductal carcinoma in situ (DCIS), male sex, and patients aged <69 years. In accordance with the Declaration of Helsinki, this retrospective study was approved by the ethics committee of our hospital (2019/1889).

Statistical analyses

Using descriptive data analysis, the average, standard deviation, median, lowest, highest, frequency, and ratio were obtained. The Kolmogorov Smirnov test was used to measure variable distributions. The Mann–Whitney U test was used for quantitative analysis of independent data, which were then assessed using the chi-square test. The Fisher's test was used when the chi-square test conditions were not provided. Survival analysis was performed using log-rank test for univariate analysis and Cox model for multivariate analysis. The SPSS 22.0 program was used in all analyses. A p value of <0.05 was considered statistically significant.

RESULTS

All the patients enrolled in this study primarily complained of a mass in the breast. The most common histologic type was invasive ductal carcinoma 111 (75%) patients, followed by mucinous carcinoma 13 (8%), invasive lobular carcinoma 8 (6%), mixed type 5 (4%), invasive micropapillary carcinoma 4 (3%), apocrine carcinoma 3 (2%), metaplastic carcinoma 2 (1%), and neuoroendocrine carcinoma 2 (1%) (p=0.715). In both the groups, the most common location of metastasis was bone 7 (44%) patients, followed by the lung 5 (31%), liver 2 (13%), and brain 2 (13%). Baseline characteristics of patients and analysis results are shown in Table 1.

When the groups were divided according to ages, i.e., 70–79 and >80 years, Charlson Comorbidity index (CCI) and radiotherapy (RT) were found to be statistically significant. Median follow-up was 30±24.33 months (95% CI 31.0–40.0) in 70-79 years group and 25.5±19.72 months (95% CI 22.4–36.1) in >80 years patients (p=0.231). There was no statistically significant difference in regard to osteoporosis or osteopenia in patients with bone mineral density measured (p=0.407) (Table 2).

Table 1. Baseline characteristics of patient groups and difference analysis results.

Variable	Exitus (n=31/%)	Alive (n=117/%)	p
Age (mean±sd)	78.00±6.42	73.00±4.13	<0.001
Tumour diameter Mean±sd	3.00±1.70	2.00±1.39	<0.001
Histology			
IDC	21 (68)	90 (77)	
ILC	1 (2)	7 (6)	0.301
Others	9 (30)	29 (17)	
Operation			
Mastectomy	20 (65)	48 (41)	
BCS	5 (16)	61 (52)	<0.001
Biopsy	6 (19)	8 (7)	
Histological grade			
1	1 (3)	15 (13)	
2	17 (55)	75 (64)	0.059
3	13 (42)	27 (23)	
Nuclear grade			
1	2 (6)	17 (15)	
2	16 (52)	74 (63)	0.067
3	13 (42)	26 (22)	
LVI			
Present	17 (55)	41 (35)	0.045
Absent	14 (45)	76 (65)	
PNI			
Present	9 (29)	18 (15)	0.080
Absent	22 (71)	99 (85)	
Receptor status			
ER (+)	18 (58)	98 (84)	0.002
ER (-)	13 (42)	19 (16)	
PgR (+)	24 (77)	106 (91)	0.046
PgR (-)	7 (23)	11 (9)	
Cerb-B2 (+)	7 (23)	15 (13)	0.174
Cerb-B2 (-)	24 (77)	102 (87)	
Radiotherapy			
Yes	21 (68)	100 (85)	0.023
No	10 (32)	17 (15)	

Variable	Exitus (n=31/%)	Alive (n=117/%)	p
Chemotherapy			
Yes	13 (42)	62 (53)	0.274
No	18 (58)	55 (47)	
Ki67 ratio			
0-14	19 (61)	47 (40)	0.035
>14	12 (39)	70 (60)	
Stages			
1	3 (10)	31 (27)	
2	11 (35)	61 (52)	<0.001
3	11 (35)	22 (19)	
4	6 (20)	3 (2)	
Metastases			
Present	11 (35)	5 (4)	<0.001
Absent	20 (65)	112 (96)	
Additional illness			
Present	22 (71)	82 (70)	0.924
Absent	9 (29)	35 (30)	

sd: standart deviation, IDC: Invasive ductal carcinoma, ILC: Invasive lobular carcinoma, BCS: Breast conserving surgery, LVI: Lenfovascular invasion, PNI: Perineural invasion, ER: Estrogen receptor, PgR: Progesterone receptor

Table 2. Group analysis according to age.

Variable	Age 70–79 years(n/%)	Age >80 years(n/%)	p
Charlson Comorbidity Index			0.002
1–2 points	94 (83)	18 (53)	
3–4 points	15 (13)	12 (35)	
>5 points	5 (4)	4 (12)	
BMD			0.407
Osteopenia	23 (31)	5 (22)	
Osteoporosis	52 (69)	18 (78)	
Radiotherapy schema			0.011
Absent	17 (15)	10 (29)	
50 Gy	31 (27)	15 (44)	
60 Gy	40 (35)	5 (15)	
Hypofraction	23 (20)	2 (6)	
Palliative	3 (3)	2 (6)	

BMD: Bone mineral density

Table 3. Results of univariate cox regression analysis.

Univariate analysis	95% CI	HR	p
Age	1.076–1.206	1.139	<0.001
Tumor diameter	1.242–1.875	1.526	<0.001
LVI	1.116–4.624	2.272	0.024
ER	0.137–0.577	0.281	0.001
PgR	0.139–0.771	0.328	0.011
Radiotherapy	0.266–1.214	0.569	0.145
Stage	1.649–3.657	2.456	<0.001
Operation	1.602–4.685	2.739	<0.001
Metastases	2.711–1.944	5.690	<0.001
Ki 67 ratio	0.385–1.697	0.808	0.573
CCI	0.592–1.234	0.854	0.402

LVI: Lenfovascular invasion, ER: Estrogene receptor, PgR: Progesterone receptor, CCI:Charlson comorbidity index.

Table 4. Results of multivariate cox regression analysis.

Multivariate analysis	95% CI	HR	p
Age	1.048–1.210	1.126	0.001
Tumor diameter	0.827–1.470	1.103	0.506
LVI	0.268–1.424	0.617	0.258
ER	1.286–0.652	3.701	0.015
PgR	0.189–2.508	0.688	0.571
Stage	0.415–2.579	1.034	0.943
Operation	0.077–2.312	0.422	0.320
Metastases	0.051–0.863	0.210	0.030
Metastases	2.711–1.944	5.690	<0.001
Ki 67 ratio	0.385–1.697	0.808	0.573
CCI	0.592–1.234	0.854	0.402

LVI: Lenfovascular invasion, ER: Estrogene receptor, PgR: Progesterone receptor

The univariate analysis revealed that age, tumor diameter, LVI, ER positivity, PgR, tumor stage, operation, and metastasis were statistically significant (Table 3).

The multivariate analysis revealed that ER positivity, age, and presence of metastasis were independent prognostic factors (Table 4).

DISCUSSION

Increasing age is the main risk factor for breast cancer. The incidence of breast cancer increases in elderly women up to the age of 80 years but reaches a plateau at the age of 80–85 years (4). In our clinic, 10% of all patients with breast cancer are aged ≥70 years. Elderly women do not meet the criteria for inclusion in clinical trials owing to the existence of comorbidities. Therefore, no evidence-based guidelines are available for the treatment of this group of patients (3, 5).

The most common breast cancer occurring in elderly patients is invasive ductal cancer (76%). Moreover, invasive lobular carcinoma accounts for 5.6% of elderly breast pathologies (6). The most common breast cancer in our study is similar to that reported in the literature, i.e., invasive ductal carcinoma (75%) and invasive lobular carcinoma (6%). Age does not affect the histological characteristics of breast cancer. Lobular, mucinous, and papillary carcinomas are also more common in elderly women (7). A study reported that mucinous carcinomas were observed in 4%–6% of patients with breast cancer aged >75 years (7). In our study, this carcinoma was observed in a relatively high proportion of patients (8%).

Surgery assumes a serious role for the treatment of breast cancer. Advanced age may be a primary factor of death in elderly patients with breast cancer. It also increases morbidity and mortality rates associated with surgery (8). Mastectomy was the classic treatment option for elderly patients in the past years. Currently, breast-conserving surgery (BCS) is in the foreground for the treatment of breast cancer (8). In the present study, modified radical mastectomy was performed in patients aged ≥80 years and BCS in those aged <79 years.

Difficulties in providing optimal treatment include treatment effects on the patient's quality of life, reduced life expectancy, reduced intellectual and physical performances, patient preference, and slow disease progression. Elderly women may delay reporting the suspect symptoms and lesions to their physicians. Such symptoms are commonly detected at advanced stages of breast cancer (9). In the present study, tumor diameter was also found to be larger in patients with advanced age.

The prognosis of breast cancer in elderly women considerably varies depending on many factors. The existence of comorbidity frequently involved a decrease in life expectancy and played a vital role in shaping the survival in elderly patients (10, 11). Some studies show that comorbidities are not associated with increased treatment toxicity or disease recurrence in elderly women with good performance status undergoing adjuvant chemotherapy (12). No significant difference was observed regarding the presence of additional comorbidities in our patients. The Charlson comorbidity index (13) revealed statistical significance when our patients were categorized as older, and octogenarians. The multivariate analysis showed that this was not a prognostic factor. Therefore, when creating a geriatric-specific treatment plan, comorbidities, survival, and treatment tolerance should be considered.

Surgical choices for axillary involvement in elderly women are similar to those for young women (14). The risk of local recurrence is low in elderly women, and the advantage of RT may decrease with age after undergoing BCS (15). Therefore, some elderly women may not require adjuvant RT, particularly those aged >70 years with negative nodal disease (clinically or pathologically confirmed) and estrogen receptor-positive breast cancer, tumor diameter <2 cm; therefore, adjuvant endocrine treatment is often

recommended. Excluding RT does not afflict OS but is associated with high breast recurrence (16). For patients aged ≥80 years with lymph node-positive and HR-negative breast cancer, breast RT is recommended because most local recurrences are likely to occur several years after diagnosis. For patients with large lesions and lymph node involvement, regional radiation increases survival, and the benefits of survival are observed 5–10 years after the diagnosis. Life expectancy is not useful for those with recurrence in <5 years (17, 18). RT lymph node-positive and HR-negative elderly patients were included in our study, and no local recurrence was observed in the patients. In elderly patients, hypofractionated RT is preferred. In elderly patients, the efficacy of postmastectomy irradiation has been evaluated; however, no randomized controlled trial has been conducted for the same. In a retrospective analysis, postmastectomy irradiation was associated with improved survival in elderly women with a risk of breast cancer (T3/4 and/or N2/3) (19). Irradiation (postmastectomy and/or breast + boost) was found to be statistically significant for survival in our patients too, and RT toxicities analogous to those observed in younger patients were monitored.

The most common type of breast cancer occurring in elderly patients is higher-grade, hormone receptor-positive invasive ductal cancer (20). In the univariate analyses, ER and PR statuses were statistically significant. However, in the multivariate analyses, only the ER status was identified as an independent prognostic factor.

Tamoxifen is only suitable for women who are at risk of heart complications, osteoporosis, and/or osteopenia, or who cannot tolerate aromatase inhibitors (20). Although the optimum period of using hormonal therapy remains unclear, the treatment has been suggested to be administered for 5 years in elderly women similar to that in young women. However, in selected patients, especially those with high-risk capable tumors, more extended periods of up to 10 years may be appropriate (21). In our patients, aromatase inhibitors were the first choice for hormonal therapy. No significant difference was observed between the two groups in terms of osteopenia or osteoporosis for patients whose bone mineral density was measured.

Our study revealed that the independent prognostic factors were advanced age, ER positivity, and presence of metastasis.

According to our expertise, currently, treatment for elderly patients with breast cancer may be similar to that for young patients. The treatment plan consists of breast and axillary surgeries, systemic chemotherapy, adjuvant RT, and hormonal therapy if patient performance is excellent. If the patient's life expectancy is constrained due to comorbidities, follow-up with hormonal therapy can be advised. In patients with HER-2-positive breast cancer, trastuzumab can be used without systemic chemotherapy. Further clinical studies are required in elderly patients for validating the findings of this study. Moreover, cooperation between oncologists and geriatrists is required.

Due to advanced age, long-term follow-up is not possible. Considering the human life has prolonged, we recommend that elderly patients should be included in clinical trials/studies to establish additional appropriate treatment choices.

CONFLICT OF INTEREST

The authors declare no conflicts of interest associated with this study

Abbreviations:

OS: Overall survival, DFS: Disease-free survival, CCI: Charlson comorbidity index, RT: Radiotherapy, LVI: Lenfovascular invasion, PNI: Perineural invasion, ER: Estrogen receptor, PgR: Progesterone receptor, BCS:Breast conserving surgery

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