ORIGINAL ARTICLE

TREATMENT OUTCOMES IN BREAST CANCER PATIENTS AGED 65 AND ABOVE

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Abstract

Introduction: Despite the increasing number of elderly patients with breast cancer, optimal treatment options remain limited. This study aims to evaluate the clinical characteristics, treatment approaches, and survival outcomes of the patient group aged 65 and above who were treated for breast cancer at our clinic.

Materials and Methods: The data of breast cancer patients aged 65 and above who received treatment and follow-up at our clinic between 2012 and 2018 were retrospectively analyzed. Overall survival and disease-free survival analyses were performed using Kaplan-Meier analysis, and comparisons were conducted using the log-rank test.

Results: A total of 108 elderly female patients with breast cancer were included in the study. The median follow-up duration was 79.75 months (6.64 years), with a maximum follow-up of 133.49 months (11.12 years). At the end of this period, 88 patients (81.48%) were still alive. The 3-year overall survival rate was 93.5%, and the 5-year overall survival rate was 86.1%. The 3-year disease-free survival rate was 91.6%, and the 5-year disease-free survival rate was 88.7%.

Conclusion: When making treatment decisions for elderly breast cancer patients, factors such as performance status, comorbidities, toxicity, and post-treatment quality of life should be carefully considered alongside age. Treatment decisions should be based on comprehensive evaluations taking these factors into account.

Keywords: Breast Neoplasms; Treatment Outcome; Aged; Mastectomy; Drug Therapy; Radiotherapy.

CORRESPONDANCE

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INTRODUCTION

Breast cancer is the predominant form of malignancy globally and exhibits the highest fatality rate among females. It ranks fifth in cancer-induced mortality across various tumor categories (1). As the population ages, the number of elderly individuals diagnosed with breast cancer has been increasing (2). The average age of breast cancer onset is around 61 years, with 45% of newly diagnosed breast cancer patients being aged 65 and above (3,4). Advanced age is considered a risk factor for breast cancer (5). In elderly patients, the diagnosis of breast cancer often occurs at a later stage, leading to 48% of patients being diagnosed with metastatic disease. Limited data is available to establish the standard treatment approach for elderly breast cancer patients. Despite comprising a significant proportion (40%) of cases, tumor biology and optimal treatment remain uncertain. The scarcity of randomized trials demonstrating the safety and efficacy of adjuvant therapies complicates treatment decision-making. Although the American Society of Clinical Oncology (ASCO) and the International Society of Geriatric Oncology (SIOG) encourage research in this age group, the conducted studies account for only 4% of the total (6,7,8). The discrepancy between chronological age and functional age should be taken into account when making treatment decisions, as it is an essential factor to consider. After diagnosis, a comprehensive geriatric assessment should be conducted for these patients. This approach allows for a more accurate evaluation of treatment tolerability, the need for hospitalization, and survival outcomes affected by comorbidities.

The aim of this study is to evaluate the clinical characteristics, treatment approaches, and survival outcomes of the patient group aged 65 and above who were treated for breast cancer at our clinic. Additionally, the study aims to contribute to the existing literature on elderly breast cancer patients.

MATERIAL AND METHODS

This retrospective study was conducted at a radiation oncology center in Turkey and approved by the local ethics committee (Approval No: E-19-2690, dated 09/05/2019). Data of breast cancer patients aged 65 and above, who underwent treatment and follow-up at the Department of Radiation Oncology between 2012 and 2018, were retrospectively examined. Patient information was collected from medical records, hospital information systems, and through telephone communication with the patients. Histopathological characteristics, stages, types of treatment, hormone receptor status, recurrence, metastasis information, and dates of follow-up visits were retrospectively recorded. This retrospective study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of our hospital.

A total of 108 breast cancer patients aged 65 and above were included in the study. The median age of the patients was 70 years (ranging from 65 to 90). The most common histopathological type was invasive ductal carcinoma, with the majority having grade 2 tumors. The patients were staged according to the AJCC staging system. Hormone receptor positivity was prevalent among the patients. The histopathological characteristics of the patients are presented in Table 1. Among them, 59 patients underwent breast-conserving surgery, while 49 patients underwent mastectomy. Axillary evaluation was performed for all patients surgically. Adjuvant chemotherapy consisted of 4 cycles of doxorubicin and cyclophosphamide (AC) followed by 12 weeks of paclitaxel. Neoadjuvant chemotherapy was administered to 18 patients with locally advanced disease.

All patients received adjuvant radiotherapy using the Varian Trilogy therapy unit. Hormone therapy, predominantly aromatase inhibitors, was administered to all hormone receptor-positive patients. Herceptin was given to patients with Her2 positive receptor types. The detailed primary

Table 1. Histopathologic features of patients

	Number of cases	Percent
Histopathology		
Invasive ductal carcinoma	85	7.8
Invasive lobular carcinoma	4	3.7
Mucinous	7	6.5
DCIS	5	4.6
Papiller	3	2.8
Other	4	3.6
Grade		
1	31	28.7
2	47	43.5
3	30	27.8
T stage		
is	5	4.6
1	36	33.3
2	48	44.4
3	9	8.3
4	10	9.3
N stage		
0	47	43.5
1	38	35.2
2	15	13.9
3	8	7.4
LVI		
Yes	34	31.5
No	74	68.5
PNI		
Yes	32	29.6
No	76	70.4
HR status		
Positive	92	85.2
Negative	16	14.8
Margin status		
Positive	2	1.9
Negative	106	98.1
HER2		
Positive	14	13
Negative	94	87
Triple negative	10	9.3
Ki 67- median (min-max)		13 (80-1)

DCIS: Ductal carcinoma in situ
LVI: Lymphovascular invasion
PNI: Perineural invasion
HR: Hormone receptor

treatment characteristics of the patients are presented in Table 2. The median follow-up period was 79.75 months (6.64 years), with a maximum follow-up of 133.49 months (11.12 years). At the end of this period, 88 patients (81.48%) were still alive.

Statistical Analysis: SPSS Statistics version 26.0 (IBM Corp., Armonk, New York) was used for the statistical analysis of the data. Patient characteristics and numerical variables were evaluated and presented in tabular form using descriptive statistics. Survival outcomes were examined using life tables. Overall survival and disease-free survival analyses between groups were performed using Kaplan-Meier analysis, and comparisons were made using the log-rank test. A p-value of ≤0.05 was considered statistically significant.

RESULTS

A total of 108 elderly female patients with breast cancer were included in the study. The median age of the patients was 70 (range: 65-90), and the mean age was 70.84±4.65. The median follow-up duration was 79.75 months (6.64 years), with a maximum follow-up of 133.49 months (11.12 years). At the end of this period, 88 patients (81.48%) were alive.

The most common histopathological type observed in the patients was invasive ductal carcinoma (78.7%), followed by mucinous carcinoma. Early-stage disease accounted for the majority of cases. The number of patients with pathological T2 stage was 48 (44.4%), while 36 patients (33.3%) had T1 stage, and 5 patients were diagnosed with ductal carcinoma in situ. The majority of patients were N0, accounting for 43.5%. Thirty-four patients had positive lymphovascular invasion (LVI). The hormone receptor positivity rate among the patients was 85.2%. Both hormone receptor-positive and HER2-positive patients accounted for 13% of the cases. There were 10 patients with triple-negative breast cancer.

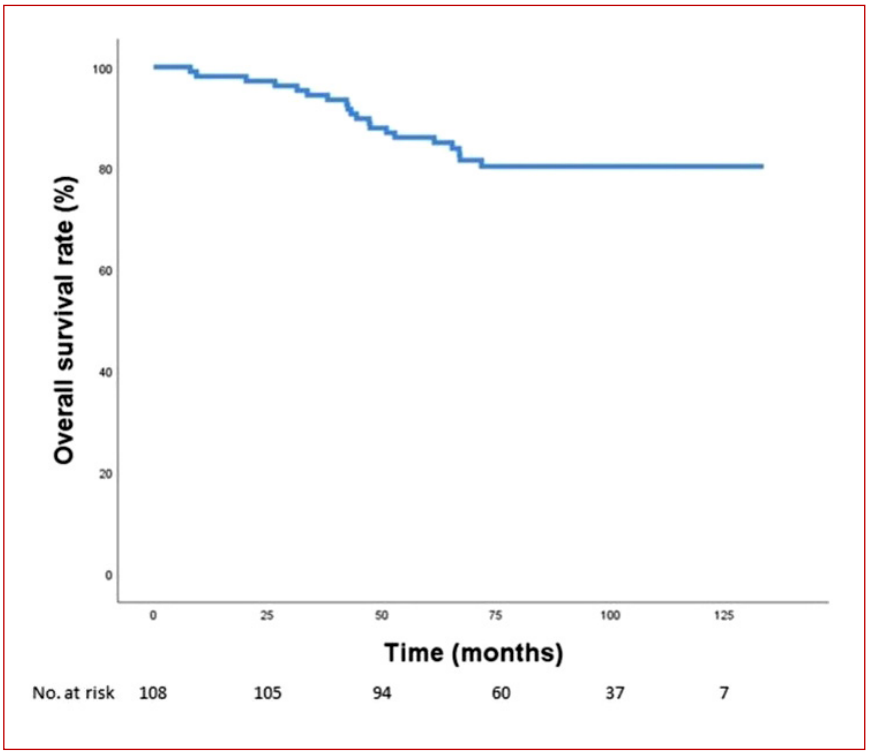

Figure 1. Overall survival (OS) analysis of 65 years of age and older breast cancer patients

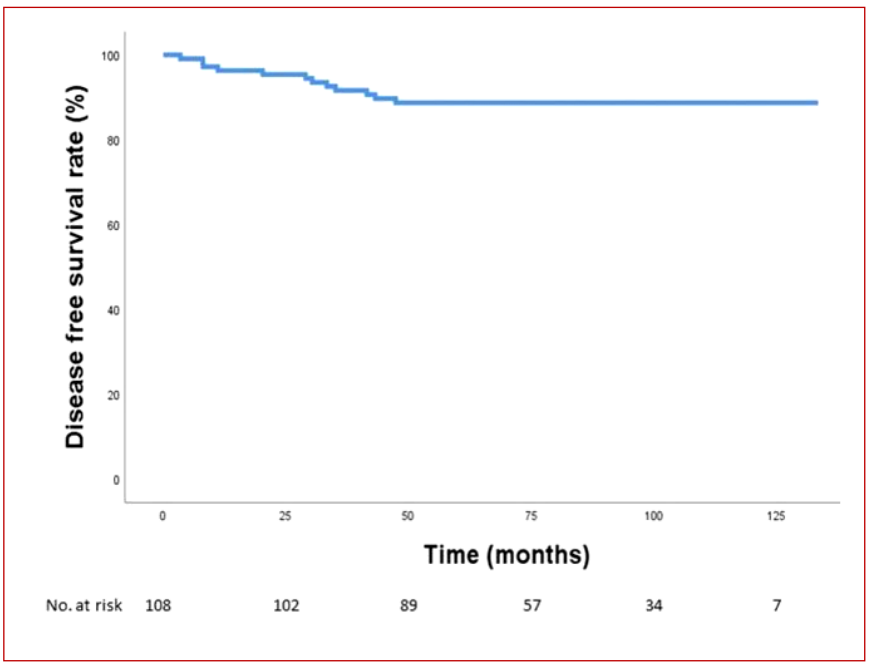

Figure 2. Disease-free survival (DFS) analysis of 65 years of age and older breast cancer patients

A total of 59 patients underwent breast-conserving surgery, while 49 patients underwent mastectomy. Sentinel lymph node biopsy (SLNB) was performed on 45 patients (41.7%), and axillary lymph node dissection (ALND) was performed on 48 patients (44.4%). The majority of patients received adjuvant chemotherapy, which consisted of 4 cycles of doxorubicin and cyclophosphamide (AC), followed by 12 weeks of paclitaxel. For locally advanced cases, 18 patients received neoadjuvant chemotherapy followed by surgery and radiotherapy. All patients who received breast-conserving surgery received a total of 50 Gy radiation to the whole breast and 10 Gy additional dose to the tumor bed, while seven patients received an additional 16 Gy dose to the tumor bed. Postmastectomy radiotherapy was administered to patients with T3-T4 or N2-N3 disease, delivering 50 Gy to the entire chest wall and regional lymph nodes. Hormone receptor-positive patients received hormone therapy, predominantly with aromatase inhibitors. All patients with HER2-positive tumors received trastuzumab.

The 3-year overall survival (OS) rate was 93.5%, and the 5-year OS rate was 86.1% (Figure 1).

Disease-free survival (DFS) at 3 years was 91.6%, and at 5 years it was 88.7% (Figure 2). Among the 20 patients who died, 11 died from causes unrelated to cancer. The median age at diagnosis for non-cancer-related deaths was 76 (range: 69-84), and the median OS was 44.4 months (95% CI: 33.71-56.93). For patients who died due to cancer, the median age at diagnosis was 71 (range: 66-90), and the median OS was 43.2 months (95% CI: 25.66-56.99).

Three patients experienced local recurrence (2.7%) at the 8th, 11th, and 47th months, all of whom had received breast-conserving surgery. None of these patients had positive surgical margins, and two of them had triple-negative tumors. All three patients are currently alive without disease after receiving adjuvant chemotherapy and undergoing treatment for local recurrence.

Table 2. Treatment characteristics of patients

	Number of cases	Percent
Type of surgery		
Breast conserving surgery	59	54.6
Mastectomy	49	45.4
Regional lymphatics		
SLND	45	41.7
ALND	48	44.4
SLND+ALND	15	13.9
Neoadjuvant chemotherapy		
Yes	18	16.7
No	90	83.3
Adjuvant chemotherapy		
Yes	62	57.4
No	46	42.6
Trastuzumab		
Yes	13	12
No	95	88
RT treatment dose		
50	50	46.3
60	51	47.2
66	7	6.5
Lymphatic irradiation		
Yes	59	54.6
No	49	45.4
Hormone therapy		
Yes	92	85.2
No	16	14.8

SLND: Sentinel lymph node dissection
ALND: Axillary lymph node dissection

Eight patients (7.4%) developed distant metastasis, and all of them had a fatal outcome. The median time to distant metastasis was 31.85 months (range: 3.52-43.20). In patients with distant metastasis, the median survival after metastasis detection was 9.46 months (range: 1.31-28.06).

Table 3. Trastuzumab, TNB and HT features; recurrence and death status according to adjuvant CT in T1-2 N0 staged patients

	Adjuvant CT group	No CT group	Total
Number of cases	15	20	35
Hormone therapy			
Yes	12	20	32
No	3	0	3
Trastuzumab	0	0	0
Triple negative	2	0	2
Recurrence			
Local	2	0	2
Distant	0	1	1
Death			
Cancer related	0	1	1
Other causes	2	1	3

CT: Chemotherapy

Subgroup analysis was performed on a total of 35 patients, including 15 who received adjuvant chemotherapy and had T1-2 and N0 disease. A comparison of the chemotherapy and non-chemotherapy groups is presented in Table 3.

DISCUSSION

Elderly women constitute a significant portion of breast cancer patients. However, there is a scarcity of research data specifically focusing on this age group, leading to uncertainties in treatment options. Geriatric assessments, which evaluate the tolerability of different treatments for elderly patients, are still not widely used in clinical practice. In our study, we examined the tumor characteristics and treatments of 108 breast cancer patients aged 65 and above. All patients were able to undergo surgery, chemotherapy, and radiotherapy treatments. Consistent with the literature, the most common histopathological type observed was invasive ductal carcinoma (IDC) (9,10). The majority of patients were hormone receptor (HR) positive. In elderly breast cancer patients, the tumor biology predominantly consists of HR-positive, HER2-negative, and low Ki67 proliferation index patients (11,12,13). In our study, similarly to the literature, we observed a high number of HR-positive patients and a low number of HER2-positive patients.

In our study, all patients underwent surgical treatment. Various retrospective studies have shown that treatment approaches vary according to age, and less aggressive treatment options are chosen for elderly patients. Aggressive treatments are also avoided due to concerns about tolerability in these patients. In the past, the traditional treatment for geriatric patients was radical or modified radical mastectomy. Nowadays, breast-conserving surgery (BCS) has become prominent, although it is less preferred by patients due to the necessity of adjuvant treatments (14,15,16). In our study, 54.6% of the patients underwent BCS, while 45.4% underwent mastectomy. Patients tolerated the surgical treatment well, and there were no delays in initiating adjuvant treatments.

After surgical treatment, our patients received adjuvant chemotherapy based on tumor size and lymph node involvement. The ongoing randomized study by The Early Breast Cancer Trialist's Collaborative Group (EBCTCG) aims to investigate the effects of chemotherapy and hormone therapy on recurrence and 15-year survival. However, the study primarily includes patients aged between 60-69, and the number of patients aged 70 and above is limited (17). Therefore, although the effectiveness of treatment may be similar, the low number of older patients is concerning. Age alone should not be a barrier to receiving chemotherapy. The decision should be based on the patient's performance status and comorbidities (18,19) In our study, adjuvant chemotherapy was administered to 62 (52.4%) patients, while neoadjuvant chemotherapy was administered to 18 (16.7%) patients.

Therefore, it is worth noting that studies on postoperative radiotherapy after breast-conserving surgery in patients aged 70 and older, with negative lymph nodes and hormone receptor-positive tumors, suggest a reduction in local recurrence rates without significantly affecting overall survival. However, these studies are based on historical series from an era when radiotherapy technology was less advanced and associated with higher side effects (20,21). Clinical trials aim to explore the avoidance of postoperative radiotherapy in elderly breast cancer patients, but definitive indications for such practices are still not well-defined (22).

In our study, we administered whole breast radiotherapy to all patients who underwent breast-conserving surgery, along with an additional boost dose to the tumor bed. For patients who underwent mastectomy, we planned radiotherapy to the chest wall and regional lymph nodes for those with T3-T4 tumors or lymph node positivity. Our patients tolerated radiotherapy well.

In a subgroup analysis of our study, which included 35 early-stage patients with T1-2 and N0 disease, no significant differences were observed in overall survival and disease-free survival between those who received adjuvant chemotherapy and those who did not. Considering the potential toxicity of chemotherapy in elderly patients with early-stage breast cancer, current guidelines recommend systemic adjuvant endocrine therapy for HR-positive patients. The survival benefit of chemotherapy in elderly patients remains uncertain. Therefore, in HR-positive, Her2-negative, lymph node-negative, or limited lymph node involvement (1-3 nodes) cases, prognostic scoring methods like Oncotype Dx or Mammaprint, which assess the risk of recurrence, are utilized. However, their widespread use is hindered by high costs (23).

Among our patients, 11 out of 20 deceased individuals passed away due to non-cancer-related causes, while 8 developed distant metastasis, leading to poor outcomes. The 5-year overall survival rate in our study was 86.1%. In a study by Joana et al., overall survival was evaluated in patients aged 65 and older, revealing a rate of 82.7% (24).

The limitations of our study include the lack of detailed information on comorbidities, data on the duration of hormone therapy in elderly patients, and the absence of comprehensive evaluations of treatment-related side effects as this is a retrospective study. Furthermore, due to the methodology of reaching out to non-responsive patients through telephone contact and gathering information from their relatives, specific details regarding aromatase inhibitors could not be ascertained. Additionally, considering the evolving nature of geriatric patient assessment scores and the ongoing refinement of their role in treatment decisions, our study spanned the past 10 years and treatment decisions were made based on outcomes from studies involving younger breast cancer patients. It's important to highlight that comprehensive information and widespread utilization related to patients' vulnerability scores and concurrent health conditions are even currently lacking.

The strengths of this study lie in its comprehensive evaluation of breast cancer treatment outcomes in a specific age group, shedding light on a population that has been understudied. The inclusion of a significant number of elderly patients and the examination of various treatment modalities, including surgery, chemotherapy, and radiotherapy, contribute to a more holistic understanding of their management. The study's attempt to address the limited research on elderly breast cancer patients and its contribution to the existing literature are also notable strengths. By examining both clinical characteristics and treatment approaches, the study provides valuable insights into the challenges and opportunities in managing breast cancer in this age group. Since the geriatric age group is examined, it is an article that may benefit geriatrics from an oncological point of view.

Importantly, this study underscores the significance of collaborative assessment and treatment decision-making involving both oncologists and geriatricians. The joint evaluation by these specialists is appropriate, as evidenced by the demonstration that while biological age alone may not hold complete significance, elderly patients can tolerate treatments despite their advanced years. Therefore, this research emphasizes the necessity of a nuanced approach that takes into account factors beyond chronological age.

In conclusion, this study not only highlights the importance of considering various factors, including performance status, comorbidities, and post-treatment quality of life, when making treatment decisions for elderly breast cancer patients, but also suggests that collaborative evaluation and treatment decision-making by oncologists and geriatricians would be beneficial. While providing valuable insights, the study also brings attention to the existing gaps in knowledge and the need for further research to optimize treatment strategies for this growing patient population.

CONCLUSION

When making treatment decisions for elderly breast cancer patients, factors such as performance status, comorbidities, toxicity, and post-treatment quality of life should be carefully considered alongside age. Treatment decisions should be based on comprehensive evaluations taking these factors into account.

As future suggestions; retrospective studies may lead to prospective studies and guidelines as they show feasible treatments and tolerability in elderly breast cancer patients.

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