



# Lumpectomy with or without Irradiation in Women 70 Years of Age or Older with the Early Breast Cancer

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## OBJECTIVE

The incidence of breast cancer increases with age. The treatment of elderly breast cancer patients is not standardized.

## METHODS

A total of 70 patients aged 70 years and older who were diagnosed with histopathologically T1-2 breast cancer between June 2005 and August 2021 were retrospectively evaluated. All patients underwent breast-conserving surgery. The patient groups who received and did not receive adjuvant radiotherapy were compared. The primary endpoint of the study was ipsilateral breast tumor recurrence-free survival. The study's secondary endpoints were breast cancer-specific survival and distant metastasis-free survival.

## RESULTS

The median age was 73 (70-82). Adjuvant radiotherapy was applied in 53 patients (75.7%). Radiotherapy application decreased with age (70-76 years vs. 77-82 years) ( $p=0.023$ ). The median follow-up was 42 months (3-169). Five patients had ipsilateral breast recurrence during the follow-up, one patient had regional recurrence (axilla), three patients had distant metastases, and nine died. Two of the patients died of breast cancer, and seven patients died from other causes. There were no differences in recurrence and death rates in patients who received and did not receive radiotherapy. Median overall survival was 119 months (94-145) in the radiotherapy arm and 141 months (136-167) in the non-irradiated arm; the 5-year OS was 81% and 100%, respectively ( $p=0.078$ ). The 5-year BCSS was 97% in the radiotherapy group and 100% in the non-irradiated group ( $p=0.222$ ); PFS 83% and 84% ( $p=0.622$ ); IBTRFS 87% and 100% ( $p=0.113$ ); and DMFS 93% and 100%, respectively ( $p=0.275$ ). A statistically significant association was found between hormonal subtypes and DMFS. Five-year DMFS was 67% in triple (-) group, 93% in HR (+) HER2 (-) group, and 100% in HER2 (+) group ( $p=0.036$ ).

## CONCLUSION

Radiotherapy usage decreased with age. There were no differences in recurrence and death rates in patients who received and did not receive radiotherapy. Most of the deaths were due to causes other than breast cancer.

**Keywords:** Breast cancer; elderly; lumpectomy; radiotherapy.

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## Introduction

The incidence of breast cancer increases with age. Approximately 33% of breast cancer patients are over

70.[1] The definition of elderly women is a debate. In general, the age of 70 is taken as the threshold value. [2] The treatment of elderly breast cancer patients is not standardized. Elderly patients are not adequately repre-

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sented in studies. Local control rates are much higher in elderly patients who underwent surgical resection than in elderly patients who did not (43.5% vs. 1.9%). [3] Therefore, surgery is the standard treatment. Apart from surgery, axilla sampling and radiotherapy treatments could be reduced according to patient age and survival expectations.[4] Randomized studies showed that radiotherapy after breast-conserving surgery reduced ipsilateral recurrence but had no significant effect on survival.[5-7] In long-term results, local control rates were found to be similar in patients over 65 years of age who received and did not receive radiotherapy.[8]

There are many studies on omitting radiotherapy after breast-conserving surgery in elderly patients. However, it is not clear, in which patient's radiotherapy can be omitted. Our study retrospectively evaluated T1-2 N0 breast cancer patients aged 70 years and older. We investigated the clinical effects of radiotherapy omission after breast-conserving surgery in these patients. The study's primary endpoint was ipsilateral breast tumor recurrence-free survival (IBTRFS). The study's secondary endpoints were breast cancer-specific survival (BCSS) and distant metastasis-free survival (DMFS).

## Materials and Methods

### Ethical Approval

The Clinical Research Ethics Committee of our institute reviewed and approved this retrospective study. As this was a retrospective study, it was exempt by the Institutional Review Board from the need for informed consent. All procedures performed in studies involving human participants were by the Helsinki declaration.

### Patient Selection

A total of 70 patients aged 70 years and older who were diagnosed with histopathologically T1-2 breast cancer between June 2005 and August 2021 were retrospectively evaluated. All patients underwent breast-conserving surgery. Patients with clinically and pathologically no lymph node metastases and no distant metastases (DM) were included in the study. Patients with pure in situ carcinoma, positive surgical margins, and bilateral breast cancer were excluded from the study. Follow-up information was acquired from treatment files and telephone calls.

The patient groups who received and did not receive radiotherapy were compared in terms of age, tumor size, grade, histological subtype, Estrogen receptor (ER), Progesterone receptor (PR), Human epidermal growth

factor receptor (HER-2) status, hormonal subtype, chemotherapy, and endocrine therapy. The hormonal subtype was analyzed in three groups as Hormone Receptor (HR) (+) HER-2 (-), HER2 (+), and Triple (-).

### Statistical Analysis

The Statistical Package for the Social Sciences Inc., Chicago, IL 22 software was used for statistical analysis. The conformity of the variables to the normal distribution was tested. Since the numerical variables showed non-normally distribution, they were expressed as median (range), while categorical variables were presented as absolute values and percentages. We assessed differences between continuous and categorical variables by the Mann-Whitney U-test and the Chi-square test.

Ipsilateral breast tumor recurrence (IBTR) was defined as the local in the ipsilateral breast; regional recurrence as the regional tumors in the axilla, internal mammary, supraclavicular area, or infraclavicular area. Metastases of other sides were defined as DM.

Kaplan-Meier curves for overall survival (OS), BCSS, progression-free survival (PFS), IBTRFS, and DMFS were plotted. P-value was set at <0.05 for statistical significance. While comparing the survival rates of patients in the radiotherapy and non-irradiated groups, log-rank analysis was used.

## Results

A total of 70 patients aged 70 years and older who were diagnosed histopathologically with T1-2 breast cancer between June 2005 and August 2021 were included in the study. All patients underwent breast-conserving surgery. Patients without lymph node metastases and DM were included in the study. Patients with pure in situ carcinoma, positive surgical margins, and bilateral breast cancer were excluded from the study.

The median age was 73 (70-82). Fifty patients (71.4%) had T1 and 20 patients had T2 (28.6%) tumors. The axillary staging was performed in 62 patients (88.5%); 75.8% of the patients who had an axillary evaluation underwent SLND. Adjuvant radiotherapy was applied in 53 patients (75.7%), chemotherapy in 16 patients (22.9%), and hormonal therapy in 59 patients (84.3%).

Radiotherapy application decreased with age (70-76 years vs. 77-82 years) ( $p=0.023$ ).

There were no differences between the patient groups who received and did not receive radiotherapy in terms of tumor size ( $\leq 2$  cm vs.  $> 2$  cm), grade, pathological subtype, ER, PR, HER2 receptor status, chemo-

**Table 1** Clinicopathologic characteristics of the patients

Parameters	Overall (n=70)		Radiotherapy+(n=53)		Radiotherapy-(n=17)		p
	Median (min-max)		Median (min-max)		Median (min-max)		
	n	%	n	%	n	%	
Age	73	70-82	73	70-82	74	70-81	0.211
Age							
70-76	55	78.6	45	84.9	10	58.8	<b>0.023</b>
77-82	15	21.4	8	15.1	7	41.2	
Tumor size	1.8 cm (0.6-5)		1.9 cm (0.6-5)		1.7 cm (0.8-5)		0.880
Surgery							
BCS only	8	11.4	3	5.7	5	29.4	<b>0.023</b>
BCS+ALND	15	21.4	13	24.5	2	11.8	
BCS+SLND	47	67.1	37	69.8	10	58.8	
Axillary staging							
Yes	62	88.6	50	94.3	12	70.6	<b>0.007</b>
No	8	11.4	3	5.7	5	29.4	
Histological grade							
1	10	14.3	8	15.1	2	11.8	0.480
2	30	42.9	22	41.5	8	47.1	
3	20	28.6	17	32.1	3	17.6	
Unknown	10	14.3	6	11.3	4	23.5	
Pathology							
IDC	50	71.4	39	73.6	11	64.7	0.481
Others	20	28.6	14	26.4	6	35.3	
ER							
Negative	9	12.9	7	13.2	2	11.8	0.877
Positive	61	87.1	46	86.8	15	88.2	
PR							
Negative	17	24.3	14	26.4	3	17.6	0.463
Positive	53	75.7	39	73.6	14	82.4	
HER2							
Negative	58	82.9	44	83	14	82.4	0.949
Positive	12	17.1	9	17	3	17.6	
Alt gruplar							
HR+HER2-	54	77.1	40	75.5	14	82.4	0.420
HER2+	11	15.7	8	15.1	3	17.6	
Triple-	5	7.1	5	9.4	0		
LVI							
Negative	47	67.1	34	64.2	13	76.5	0.347
Positive	23	32.9	19	35.8	4	23.5	
T							
1	50	71.4	37	69.8	13	76.5	0.597
2	20	28.6	16	30.2	4	23.5	
Chemotherapy							
Yes	16	22.9	14	36.4	2	11.8	0.211
No	54	77.1	39	73.6	15	88.2	
Endocrine treatment							
Yes	59	84.3	44	83	15	88.2	0.607
No	11	15.7	9	17	2	11.8	

BCS: Breast conserving surgery; ALND: Axillary lymph node dissection; SLND: Sentinel lymph node dissection; IDC: Infiltrative ductal carcinoma; ER: Estrogen receptor; PR: Progesterone receptor; HER 2: Human epidermal growth factor receptor 2; HR: Hormone receptor, LVI: Lymphovascular invasion

**Table 2** Clinical outcome: Recurrence and death

Parameters	Radiotherapy + (n=53)		Radiotherapy - (n=17)		p
	n	%	n	%	
	Ipsilateral breast tumor recurrence	5	9.4	0	
Regional recurrence (axilla)	0		1	5.9	0.075
Distant metastasis	3	5.7	0		0.316
Death					
Breast cancer specific	2	3.8	0	0.416	
Other causes	7	13.2	1	5.9	0.409

therapy, and endocrine therapy. All the triple-negative patients underwent radiotherapy. The proportion of patients without axillary staging was 5.7% in the radiotherapy group and 29.4% in the non-irradiated group ( $p=0.007$ ). The clinicopathologic characteristics of the patients are summarized in Table 1.

The median follow-up was 42 months (3-169). Five patients had ipsilateral breast recurrence during the follow-up, one patient had regional recurrence (axilla), three patients had DM, and nine patients died. Two of the patients died of breast cancer, and seven patients died from other causes (One COVID-19 infection, one diabetic coma, two secondary neoplasms, and three dementia). There were no differences in recurrence and death rates in patients who received and did not receive radiotherapy. Clinical outcomes of the patients are given in Table 2.

Median OS was 119 months (94-145) in the radiotherapy arm and 141 months (136-167) in the non-irradiated arm; the 5-year OS was 81% and 100%, respectively ( $p=0.078$ ). The 5-year BCSS was 97% in the radiotherapy group and 100% in the non-irradiated group ( $p=0.222$ ); PFS 83% and 84% ( $p=0.622$ ); IBTRFS 87% and 100% ( $p=0.113$ ); and DMFS 93% and 100%, respectively ( $p=0.275$ ). Survival rates of the patients are given in Table 3.

At the end of the analysis, tumor size, ER, PR, HER2 receptor status, LVI, T1 versus T2, chemotherapy, and endocrine therapy did not affect OS, BCSS, PFS, IBTRFS, and DMFS. A statistically significant association was found only between hormonal subtypes and DMFS. Five-year DMFS was 67% in triple (-) group, 93% in HR (+) HER2 (-) group, and 100% in HER2 (+) group ( $p=0.036$ ) (Fig. 1).

**Table 3** Survival rates of the patients

Parameters	Radiotherapy+ (n=53)	Radiotherapy- (n=17)	p
	Survival rate (%)	Survival rate (%)	
5 year OS	81	100	0.078
5 year CSS	97	100	0.222
5 year PFS	83	84	0.622
5 year LRFS	87	100	0.113
5 year DMFS	93	100	0.275

OS: Overall survival; CSS: Cause-specific survival; PFS: Progression-free survival; LRFS: Local recurrence-free survival; DMFS: Distant metastasis-free survival

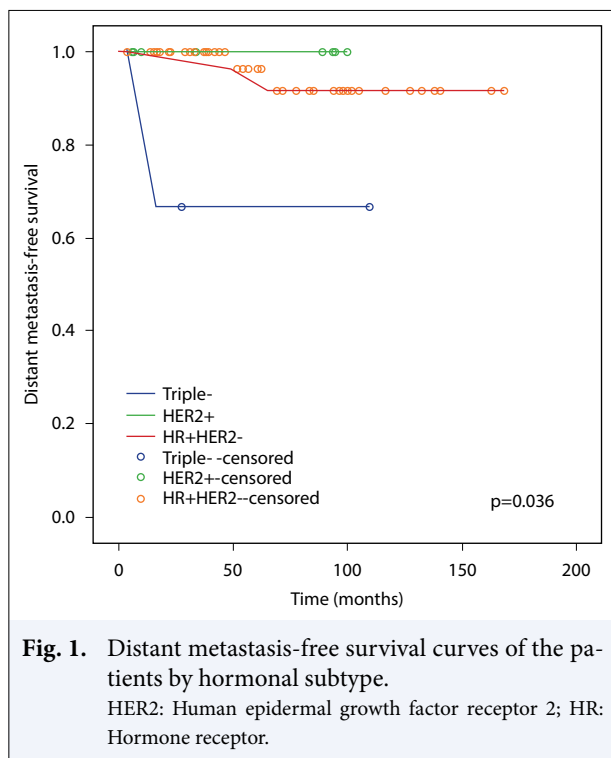
## Discussion

As age progresses, breast cancer-specific mortality decreases non-breast cancer-related mortality increases. [6] Post-operative complication rates also increase.[9] In these patients, possible side effects of radiotherapy such as cardiac toxicity should also be considered due to comorbid conditions.

In our study, 11.4% of the patients did not undergo axillary surgery. Similar outcomes were seen in clinical node-negative elderly breast cancer patients with and without axillary surgery. In the study of Martelli et al., after a median follow-up of 15 years, they found breast cancer-specific mortality similar in both groups. [10] Better quality of life was noted in patients who did not undergo axillary surgery. It has also been reported that sentinel lymph node biopsy could be omitted in elderly patients.[11] In a study conducted with patients, over 70 years of age who underwent breast-conserving surgery and did not undergo axillary surgery or radiotherapy, after a median follow-up of 60 months, no significant differences in local recurrence, distant metastasis, and breast cancer cancer-specific death were observed. IBTR rate was 1.6% in these patients and 5.3% in the others.[4]

In our study, the proportion of patients without axillary staging was 5.7% in the radiotherapy group and 29.4% in the non-irradiated group ( $p=0.007$ ). This situation makes us think that axillary surgery and radiotherapy were applied to patients who were thought to be in the high-risk group. However, our study found no relationship between radiotherapy application and factors other than age associated with local recurrence or survival.

In our study, 75.7% of the patients received radiotherapy. Soulos et al. showed that the rate of radiotherapy after breast-conserving surgery in patients aged 70



years and older with T1N0M0 breast cancer was 79% before and 75% after the Cancer and Leukemia Group B C9343 study.[12] In another study conducted with patients over the age of 70, the rate of application was found to be 75%. In this study, as in our study, radiotherapy usage decreased with age.[13]

The 5-year OS was 81% and 100%, respectively ( $p=0.078$ ). The 5-year BCSS was 97% in the radiotherapy group and 100% in the non-irradiated group ( $p=0.222$ ); PFS 83% and 84% ( $p=0.622$ ); IBTRFS 87% and 100% ( $p=0.113$ ); and DMFS 93% and 100% , respectively ( $p=0.275$ ). The rate of DMFS was significantly lower in the triple-negative group. Five-year DMFS was 67% in triple (-) group, 93% in HR (+) HER2 (-) group, and 100% in HER2 (+) group ( $p=0.036$ ). After a median follow-up of 42 months (3-169), five patients had ipsilateral breast recurrence, one patient had regional recurrence (axilla), three patients had DM, and nine patients died. Two of the patients died of breast cancer, and seven patients died from other causes (One COVID-19 infection, one diabetic coma, two secondary neoplasms, and three dementia). There were no differences in recurrence and death rates in patients who received and did not receive radiotherapy. Of the patients who died, 77.8% died from causes other than breast cancer. Our findings are compared with the results in the literature below.

In study C9343, there was no difference in 5-year OS and disease-free survival rates between patients who received and did not receive radiotherapy. The locoregional recurrence rate was 1% in the arm with RT and 4% without RT.[5] In the study containing the long-term follow-up results of this study, after a median follow-up of 12 years, 8% less locoregional recurrence and 7% less IBTR were found in the arm that received radiotherapy. Similar to the previous study, there was no difference in OS and disease-free survival rates.[6]

The Early Breast Cancer Trialists' Collaborative Group 2005 meta-analysis reported a significant reduction in mortality at 15 years with RT, but this only applied if the difference in IBTR was >10%.[14] In most of the studies, the difference in IBTR was below 10%.

We thought that there would be less time for local recurrence with the short life expectancy in elderly patients. However, in our study, the median OS was 119 months (94-145) in the radiotherapy arm and 141 months (136-167) in the non-irradiated arm. Long-term follow-up of the CALBG study found a median survival of 12 years, with IBTR rates still low.[6]

In the PRIME II study, after a median follow-up of 5 years, the absolute risk reduction in ipsilateral tumor recurrence with radiotherapy after breast-conserving surgery was 2.9%. It was stated that there was no survival advantage, and most of the deaths were due to causes other than breast cancer. This study argued that the reduction in absolute risk was low enough for radiotherapy omission.[7]

The German Breast Cancer Group found the ipsilateral breast tumor recurrence rate in the adjuvant endocrine treatment alone arm to be 6% and 2% when radiotherapy was added. Patients aged 45 years and older were included in this study.[15]

Tinterri et al.,[16] after 5 years of median follow-up, the incidence of IBTR was 2.5% in the surgery-only arm and 0.7% in the surgery plus radiotherapy arm. Patients aged 55-75 years who received systemic therapy were included in this study.

Livi et al.[17] found breast relapse rates of 3.4% in the arm that received radiotherapy and 10.6% in the arm that did not. Breast relapse decreased with increasing age (especially over 75). They reported that omission of radiotherapy was safe in breast cancer patients over 75 years of age who underwent T1-2 quadrangectomy.

Despite the differences in design, no study showed significant differences in distant disease-free survival or OS, although all showed some decrease in IBTR with radiotherapy. Differences in local control are primarily due to inclusion criteria.[6]



As a result of these studies, changes were made + in the National Comprehensive Cancer Network guidelines.[18] Despite these changes, one of the reasons why radiotherapy application rates are still high is that with newly developed radiotherapy techniques, patients are treated in a shorter time with fewer side effects. Today, with accelerated partial breast irradiation (APBI), organs at risk are better protected without irradiation of the entire breast. Hypofractionated radiotherapy can be applied in a shorter time cost-effectively.

Studies on breast cancer in female patients aged 65 and over in our country are limited.[19] A review emphasizes that local recurrence decreases with age, and thus, the necessity of radiotherapy in elderly patients is not as clear as in younger patients. However, there are also studies suggesting that elderly patients will benefit more from radiotherapy than younger patients.[20]

One of the limitations of our study is that we did not specify APBI and hypofractionated radiotherapy applications in patients who received radiotherapy. In addition, selection bias cannot be avoided due to the retrospective nature of our study. We did not indicate if radiotherapy omission was the result of the patient's preference or the clinician's guidance.

As a result, in our study, the rate of radiotherapy application in low-risk breast cancer patients over 70 was similar to that in the literature. Radiotherapy usage decreased with age. There were no differences in recurrence and death rates in patients who received and did not receive radiotherapy. Most of the deaths were due to causes other than breast cancer. Comorbidities and the biology of the tumor, not specific breast cancer treatments, dictated death and recurrence rates.

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**Conflict of Interest:** All authors declared no conflict of interest.

**Ethics Committee Approval:** The study was approved by the Muğla Sıtkı Koçman University Medical and Health Sciences Ethics Committee (No: 22, Date: 04/04/2022).

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