

# Survival with Surgery is Superior to Survival Without Surgery in Breast Cancer Patients Aged 85 Years or Older: A Retrospective Study

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## Research

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# Abstract

**Background:** Surgical treatment of breast cancer patients aged 85 years or older is still controversial.

**Methods:** A series of surgically treated breast cancer patients aged 85 years or older was evaluated. The clinicopathological features and outcomes of these patients were compared with the features and outcomes of breast cancer patients in the same age group who were managed without surgery.

**Results:** A total of 45 patients (75%) received surgical treatment, and 15 patients (25%) were managed without surgery. The differences between ages, tumor status, nodal status, stage and immunopathological status of the patients undergoing and not undergoing surgery were not significant. Significantly more patients treated by surgery underwent systemic treatment than patients managed without surgery ( $P=0.004$ ). The three-year disease-free survival rate of patients treated by surgery was higher than that of the patients managed without surgery (90.6% vs 67.5%, respectively;  $P<0.001$ ).

**Conclusions:** The surgical treatment of breast cancer patients aged 85 years or older is warranted. This outcome was achieved with the use of hormonal therapy.

## 1. Background

The Japanese population is aging rapidly. In 2020, individuals aged 75 years or older accounted for 14.9% of the Japanese population [1], and that figure is expected to increase to 26.9% in 2060 [2]. In addition, the incidence of breast cancer has been increasing, and breast cancer is the leading neoplasm affecting Japanese women [3]. Therefore, it is likely that the number of elderly women with breast cancer will increase rapidly, and that an increasing number of elderly patients will require breast cancer treatment.

Surgery is essential for treating breast cancer; it can cure many breast cancer patients without the need for adjuvant therapies [4]. Significant data from many randomized trials have led to the increasing use of surgery for early breast cancer [5, 6]. However, most of the randomized trials recruited younger patients who would be not considered elderly. Hence, the benefits of surgery for elderly patients with breast cancer are unknown. Although retrospective studies older breast cancer patients have been conducted [7–10], the postoperative outcomes of extremely old patients with breast cancer remain unclear.

To determine whether breast cancer surgery for extremely old patients is warranted, the clinicopathological features and outcomes of these patients were compared with the features and outcomes of breast cancer patients in the same age group who were managed without surgery.

## 2. Methods

We searched the surgical and pathological databases of our institution. The study inclusion criteria were as follows: patients with a breast cancer that was histologically confirmed between 2010 and 2019 and

aged 85 years or older at the time of diagnosis. Exclusion criteria were as follows: distant metastatic disease and lost to follow-up just after the diagnosis.

The following information was obtained from the patients' medical charts: age, sex, chief complaint, comorbidities, information on systemic therapy and radiation therapy, histopathological characteristics of the tumor, and survival status. For patients who underwent surgery, data on surgical procedures, anesthesia, and postoperative complications were also obtained. Histopathological data were obtained from the surgical specimens of the patients undergoing surgery and from the biopsy specimens of the patients treated without surgery. The primary lesion in the breast and the stage were categorized according to the TNM classification. Nodal status was classified according to the presence or absence of metastasis. The survival event was defined as the occurrence of distant metastasis or death due to any cause.

The distributions of ages were compared by the Mann Whitney U test. The categorical data were compared by the Fisher exact test. The Kaplan-Meier method was used to estimate survival rates. The log rank test was used to evaluate the difference between the survival rates of the 2 patient groups.  $P < 0.05$  was considered significant. The statistical package R v4.0.3 (R Foundation for Statistical Computing, Vienna, Austria; ISBN 3-900051-07-0; <http://www.R-project.org>) was used for statistical analysis.

### **3. Results**

From 2010 to 2019, 60 breast cancer patients aged 85 years or older were treated in our department. Of these 60 patients, the surgical and pathological databases identified 45 patients who underwent surgery and 15 who were managed without surgery.

The clinical and histopathological characteristics of these 60 patients are summarized in Table 1. The median age of each group of patients was 87 years. The most common finding at presentation was a breast lump, and the second-most common finding was nipple discharge. All the patients were women. The most frequent comorbidities were hypertension, diabetes mellitus, and hyperlipidemia.

Table 1  
Clinical characteristics of the study patients

		Total		Surgery		No surgery		
No. of patients		60		45		15		
Median age (years)		87		87		87		P = 0.2154
Sign/Symptom	Lump	49	(82%)	36	(80%)	13	(87%)	
	Nipple discharge	6	(10%)	4	(9%)	2	(13%)	
	Nipple erosion	1	(2%)	1	(2%)	0	(0%)	
	Pain	1	(2%)	1	(2%)	0	(0%)	
	No symptoms	3	(5%)	3	(7%)	0	(0%)	
Comorbidity	Hypertension	23	(38%) <sup>§1</sup>	19	(42%) <sup>§1</sup>	4	(27%) <sup>§1</sup>	
	Diabetes mellitus	9	(15%) <sup>§1</sup>	9	(20%) <sup>§1</sup>	0	(0%) <sup>§1</sup>	
	Hyperlipidemia	8	(15%) <sup>§1</sup>	8	(18%) <sup>§1</sup>	0	(0%) <sup>§1</sup>	
	Asthma	3	(5%) <sup>§1</sup>	3	(7%) <sup>§1</sup>	0	(0%) <sup>§1</sup>	
	Metachronous breast cancer	2	(3%) <sup>§1</sup>	1	(2%) <sup>§1</sup>	1	(7%) <sup>§1</sup>	
	Arrythmia	2	(3%) <sup>§1</sup>	1	(2%) <sup>§1</sup>	1	(7%) <sup>§1</sup>	
	Spinal stenosis	2	(3%) <sup>§1</sup>	2	(4%) <sup>§1</sup>	0	(0%) <sup>§1</sup>	
	Others <sup>§2</sup>	13	(22%) <sup>§1</sup>	7	(16%) <sup>1</sup>	6	(40%) <sup>§1</sup>	
	None	11	(18%) <sup>§1</sup>	7	(16%) <sup>§1</sup>	4	(27%) <sup>§1</sup>	
The percentage in parenthesis represents the ratio in each group.								
§ 1 Each patient has a different number of comorbidities. Therefore, these percentages do not add up to 100%.								
§ 2 Others include the following conditions: Brain stroke, Gastric cancer, Chronic obstructive pulmonary disease, Dementia, Hepatitis type-C, Cardiac failure, and Scleroderma in patients undergoing surgery; Bladder cancer, Cerebral aneurysm, Colon cancer, Depression, and Hyperuricemia in patients not undergoing surgery.								

The histopathological data are summarized in Table 2. The differences between the histopathological features of the patients undergoing and not undergoing surgery with regard to T factor, nodal status, stage, types of tumors, estrogen receptor (ER) expression, progesterone receptor expression, and human epidermal growth factor receptor 2 expression were not significant.

Table 2  
Histopathological characteristics of the study patients

		Total		Surgery		No Surgery				
T factor	Tis	7	(12%)	6	(13%)	1	(7%)	P = 0.5226		
	T1	24	(40%)	20	(44%)	4	(27%)			
	T2	22	(37%)	14	(31%)	8	(53%)			
	T3	1	(2%)	1	(2%)	0	(0%)			
	T4b	6	(10%)	4	(9%)	2	(13%)			
Nodal status	Negative	44	(73%)	35	(78%)	9	(60%)	P = 0.1947		
	Positive	16	(27%)	10	(22%)	6	(40%)			
Stage	0	6	(10%)	5§1	(11%)	1	(7%)	P = 0.4373		
	1	22	(37%)	18	(40%)	4	(27%)			
	2A	17	(28%)	13	(29%)	4	(27%)			
	2B	7	(12%)	3	(7%)	4	(27%)			
	3A	1	(2%)	1	(2%)	0	(0%)			
	3B	5	(8%)	3	(7%)	2	(13%)			
	3C	2	(3%)	2	(4%)	0	(0%)			
	Histology	DCIS	9	(15%)	6§1	(13%)	3		(20%)	P = 0.728
		IDC	48	(80%)	36	(80%)	12		(80%)	
ILC		3	(5%)	3	(7%)	0	(0%)			
ER	Positive	53	(88%)	38	(84%)	15	(100%)	P = 0.176		
	Negative	7	(12%)	7	(16%)	0	(0%)			
PgR	Positive	48	(80%)	34	(76%)	14	(93%)	P = 0.262		
	Negative	12	(20%)	11	(24%)	1	(7%)			
HER2	Positive	7	(12%)	7	(16%)	0	(0%)	P = 0.381		
	Negative	52	(87%)	37	(82%)	15	(100%)			
	Undetermined	1	(2%)	1	(2%)	0	(0%)			
The percentage in parenthesis represents the ratio in each group.										
§ 1 There was one DCIS case which had a positive lymph node.										

	Total	Surgery	No Surgery
DCIS: ductal carcinoma in situ			
IDC: invasive ductal carcinoma			
ILC: invasive lobular carcinoma			
ER: estrogen receptor			
PgR: progesterone receptor			
HER2: human epidermal growth factor receptor 2			

The surgical data are summarized in Table 3. Sixteen of the 45 (35.6%) surgery patients did not undergo axillary surgery. Local anesthesia was used for 11 of 45 (24.4%) patients. No in-hospital deaths were recorded. Postoperative complications, which consisted of skin necrosis and wound infections, were seen in 7 of 45 (15.6%) patients.

Table 3  
Surgical characteristics of the surgery patients

Surgery	Tumorectomy	2	(4%)
	Bp	12	(27%)
	Bp + SN	4	(9%)
	Bp + AX	2	(4%)
	Bt	2	(4%)
	Bt + SN	13	(29%)
	Bt + AX	10	(22%)
Anesthesia	Local	11	(24%)
	General	34	(76%)
Postoperative course	Hospital death	0	(0%)
	Postoperative complications <sup>§1</sup>	7	(16%)
§ 1 Postoperative complication comprised skin necrosis and wound infections.			
Bp: partial mastectomy; Bt: mastectomy; SN: sentinel node biopsy; AX: axillary dissection			

The types of systemic and radiation therapies are summarized in Table 4. Although all 15 patients not undergoing surgery had ER-positive breast cancer, only 33% of them received endocrine therapy. The difference between the proportion of patients undergoing surgery who received endocrine therapy versus the proportion of patients not undergoing surgery who received endocrine therapy was significant ( $P =$

0.003). None of the patients received cytotoxic chemotherapy. Only 5 of the 45 patients undergoing surgery received radiation therapy. Two of them received radiation therapy for breast conserving surgery and 3 of them had post-mastectomy radiation therapy. None of the patients not undergoing surgery received radiation therapy.

Table 4  
The distribution of systemic and radiation therapy in the study patients

		Total		Surgery		No Surgery		
Systemic therapy	Endocrine therapy	41	(68%)	36	(80%)	5	(33%)	P = 0.003
	None	19	(32%)	9	(20%)	10	(67%)	
Radiation therapy	Yes	5	(8%)	5	(11%)	0	(0%)	P = 0.318
	No	55	(92%)	40	(89%)	15	(100%)	

The survival curves of the 60 study patients stratified according to with/without surgery are shown in Fig. 1. The median follow-up time was 40 months. The three-year overall survival rate of the patients undergoing surgery was significantly higher than the survival rate of the patients not undergoing surgery (90.6% vs 67.5%, P = 0.001).

## 4. Discussion

Our study found that breast cancer surgery for extremely old patients is warranted. This conclusion is based on the finding that a series of surgically treated breast cancer patients aged 85 years or older had a better survival outcome than patients in the same age group who did not undergo surgery for breast cancer.

Although surgery led to a favorable outcome, it is doubtful that surgery is the only reason for the good outcome. Another reason accounting for the better outcome for the patients undergoing surgery is that quite a few patients who did not undergo surgery did not receive hormonal therapy, regardless of the high prevalence of estrogen receptor-positive breast cancer. Therefore, the low frequency of hormonal therapy administration to the patients who did not undergo surgery probably accounts for the apparent better outcome of the patients undergoing surgery. Another reason for the worse outcome of the patients not undergoing surgery is that performance status might have affected the physician's and patient's decision. Safely undergoing surgery requires a good performance status. Furthermore, a poor performance status may result in the avoidance of adequate treatments, including hormonal therapy, by both the physician and patient. More studies are needed to validate the findings of our investigation.

We believe that surgical treatment for elderly patients with breast cancer is extremely safe if their preoperative conditions are appropriately evaluated. In our series, there were no hospital deaths. Although some patients had wound infections and necrosis, none of those postoperative problems were severe.

Results from other single-institution studies on postoperative mortality of elderly patients who undergo breast cancer surgery have been favorable [8, 10].

The evaluation of surgical safety is essential for elderly breast cancer patients. The level of safety depends on the balance between surgical invasiveness and the patient's tolerance of surgery. Surgical treatment for breast cancer is less invasive than other general surgeries and is thus safely performed in many patients. On the other hand, tolerability depends on a patient's comorbidities [11, 12], frailty [13], and physical activity [11]. These 3 factors are closely associated with one another [14].

Considering the low tolerance of some elderly patients being treated for breast cancer, various essential treatments, including axillary surgery, radiation treatment, and adjuvant chemotherapy have been avoided [7, 9]. Several small studies investigated avoiding axillary dissection in clinically node-negative patients with small breast cancers, and reported that the absence of axillary dissection does not affect overall survival [15–17]. However, 5.8–9% of patients developed recurrence involving the axillary lymph nodes. We believe that concomitant axillary surgery is preferable for 2 reasons. One, axillary surgery is not very invasive, and sentinel lymph node biopsy is appropriate for clinically node-negative cases [18]. The second reason is that comorbid diseases may weaken the general condition of an elderly patient during the interval between the initial surgery and potential axillary recurrence. This interval to recurrence has been reported to range from 7 to 157 months [16]; longer intervals can reduce the treatment options, including a second surgery.

Radiation therapy after partial mastectomy tends to be avoided for elderly patients with breast cancer [7], because they are required to visit the hospital every day for several weeks. Although radiation therapy after a partial mastectomy does not seem to affect overall survival [19], the risk of local recurrence is increased in patients who do not undergo radiation therapy [20–22]. Although mastectomy is related to a higher risk of postoperative hemorrhage than is partial mastectomy [23], mastectomy is preferred for patients who want to avoid radiation therapy.

Adjuvant chemotherapy improves the survival outcomes of patients with early breast cancer; however, maintenance of the relative dose intensity is difficult in elderly patients [24–27]. Furthermore, treatment-related mortality increases with age [24]. We believe that adjuvant chemotherapy is not appropriate for patients aged 85 years or older.

## Conclusions

Our study demonstrates that breast cancer surgery for extremely old patients is warranted. The evidence is that a series of surgically treated breast cancer patients aged 85 years or older had a better survival outcome than patients in the same age group who were not managed by surgery. More studies are needed to reveal the association between elderly breast cancer patients and favorable postoperative survival.

# Abbreviations

**CI**

Confidence Interval

**ER**

Estrogen Receptor

**PgR**

Progesterone Receptor

**DCIS**

ductal carcinoma in situ

**IDC**

invasive ductal carcinoma

**ILC**

invasive lobular carcinoma

**Bp**

partial mastectomy

**Bt**

mastectomy

**SN**

sentinel node biopsy

**AX**

axillary dissection

# Declarations

## **Ethics approval and consent to participate**

This study was approved by our institutional ethics board (RK-200908-11). This study was performed in accordance with the principles of the Declaration of Helsinki.

## **Consent for publication**

Under the regulation of our institutional ethics board, informed consent was obtained in the form of an opt-out system on the web-site. Patients who declined were excluded from the study.

## **Availability of data and materials**

The datasets used and/or analyzed in the current study are available from the corresponding author upon reasonable request.

## **Competing interests**

The authors declare that they have no competing interests.

## Funding

There is no source of funding to be declared.

## Authors' contributions

KE, SF, KH, SM, FN and YH collected the data and contributed to drafting the manuscript.

KE and KT drafted the manuscript.

All authors read and approved the final manuscript.

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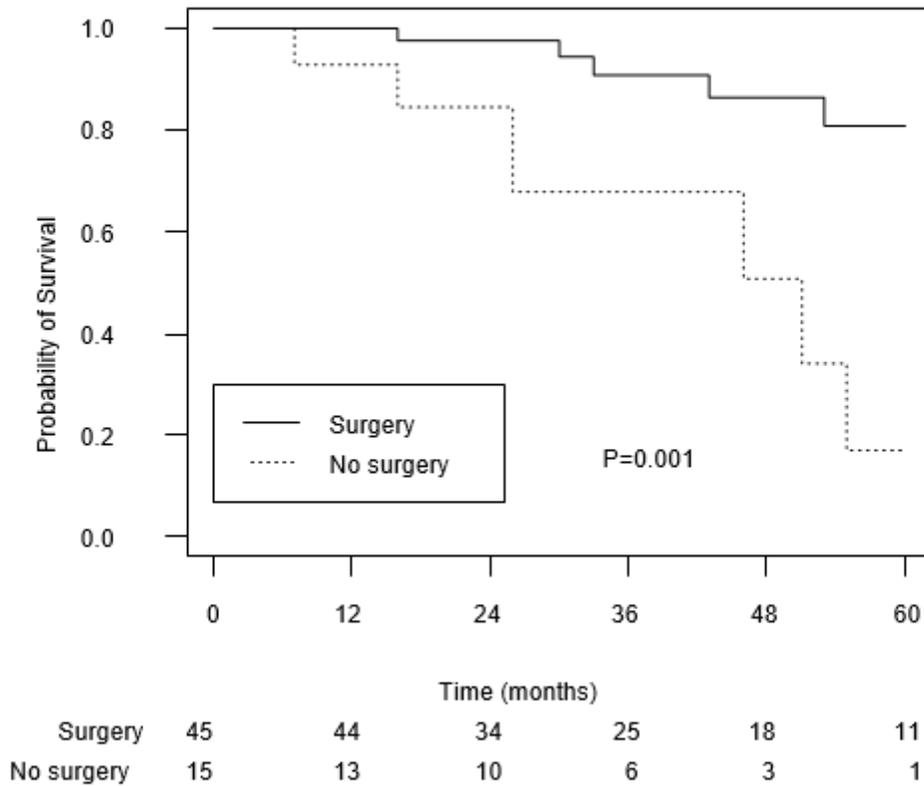
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## Figures

**Survival of elderly breast cancer patients stratified according to surgery or no surgery**



**Figure 1**

The survival curves of the 60 breast cancer patients aged 85 years or older, stratified according to receiving or not receiving surgical treatment. The estimated 3-year survival rates were 90.6% (95% confidence interval [CI] 80.9%-100%) with surgery and 67.5% (95% CI 45.7-99.7%) without surgery. The difference between the survival curves was significant ( $P < 0.001$ ). The solid line denotes the patients undergoing surgery, and the dotted lines indicate the patients not undergoing surgery. The numbers placed at the bottom of the figure indicate the number of patients at risk in each group.