



Palliative Local Surgery for Locally Advanced Breast Cancer Depending on Hormone Receptor Status in Elderly Patients

Hong Pan,¹ Kai Zhang,^{2,3} Ming Wang,⁴ Lijun Ling,¹ Wenbin Zhou,¹ Shui Wang¹

Abstract

Many elderly breast cancer patients receive palliative local surgery to control potential physical symptoms and avert potential emotional symptoms. Elderly patients with locally advanced breast cancer were identified in the Surveillance, Epidemiology, and End Results cancer database. Mastectomy strongly improved survival within hormone receptor-negative patients, but lumpectomy and mastectomy were not associated with overall survival within hormone receptor-positive patients.

Background: Many elderly breast cancer patients might just receive palliative local surgery, especially those with locally advanced breast cancer (LABC). However, palliative tumor removal might lead to perioperative residual tumor growth. In this study, we aimed to determine the survival effect of palliative local surgery without definitive axillary surgery for LABC in elderly patients. **Patients and Methods:** Patients age 70 years or older diagnosed with T3/4M0 breast cancer, who received no surgery, mastectomy, or lumpectomy without axillary surgery, were identified in the Surveillance, Epidemiology, and End Results cancer database from 1973 to 2014. The overall survival effect of palliative local surgery was determined by using multivariable Cox regression, and propensity score matching was applied to confirm the results. **Results:** A total of 2616 female breast cancer patients age 70 years or older diagnosed with T3/4M0 (without inflammatory breast cancer) were identified; 1374 received no cancer-directed surgery, 583 received lumpectomy without axillary surgery, and 659 received mastectomy without axillary surgery. Adjusted for potential confounders, both types of palliative local surgeries (lumpectomy: hazard ratio [HR], 0.95; 95% confidence interval [CI], 0.71-1.27; $P = .719$; mastectomy: HR, 0.88; 95% CI, 0.65-1.17; $P = .371$) were not associated with overall survival compared with no surgery within hormone receptor-positive patients. However, mastectomy strongly improved survival within hormone receptor-negative patients. Palliative local surgery did not change the patterns of mortality. **Conclusion:** For elderly patients diagnosed with LABC, not candidates for standard therapies, mastectomy should be recommended as palliative therapy for hormone receptor-negative, but not for hormone receptor-positive patients.

Clinical Breast Cancer, Vol. 19, No. 1, e247-60 © 2018 Elsevier Inc. All rights reserved.

Keywords: Elderly, Hormone receptor, Locally advanced breast cancer, Lumpectomy, Mastectomy

Introduction

Breast cancer remains the most common malignant disease in women. Older women, the fast-growing segment of the population, will represent an increased cohort of breast cancer patients. Approximately 30% of breast cancer cases occur in women older

than the age of 70 years.^{1,2} Previous studies have shown that elderly patients with breast cancer are less likely to receive standard curative therapies, but less aggressive therapies, including lower rates of chemotherapy, endocrine therapy, postmastectomy radiation, axillary lymph node dissection, and even local surgery. This might be

H.P. and K.Z. contributed equally to this work.

Submitted: Jul 22, 2018; Accepted: Sep 21, 2018; Epub: Sep 27, 2018

¹Department of Breast Surgery

²Pancreatic Center and Department of General Surgery, The First Affiliated Hospital with Nanjing Medical University, Nanjing, China

³Pancreas Institute of Nanjing Medical University, Nanjing, Jiangsu, China

⁴Department of Plastic and Burn Surgery, The First Affiliated Hospital with Nanjing Medical University, Nanjing, China

Addresses for correspondence: Shui Wang, MD, PhD, Department of Breast Surgery, The First Affiliated Hospital with Nanjing Medical University, 300 Guangzhou Road, 210029 Nanjing, China. Fax: 0086-25-83718836, Wenbin Zhou, Department of Breast Surgery, The First Affiliated Hospital with Nanjing Medical University, 300 Guangzhou Road, 210029 Nanjing, China. Fax: 0086-25-83718836; e-mail contact: zhouwenbin@njmu.edu.cn; ws0801@hotmail.com

Palliative Surgery for LABC in Elderly Patients

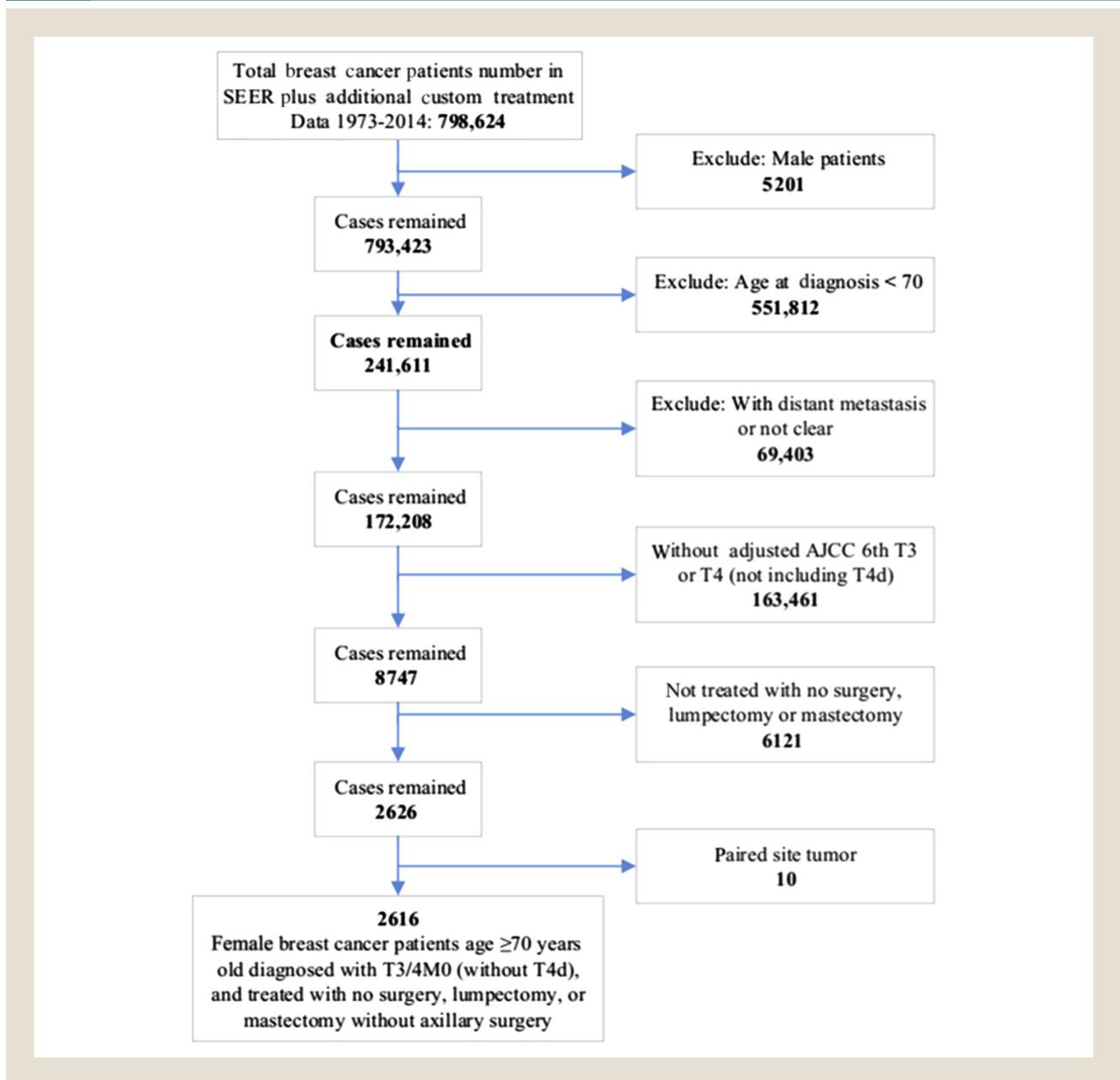
because of their comorbid conditions and short life expectancy, as well as high stage and lack of medical insurance.^{1,3-8}

What we care about is that a great proportion of elderly patients only received palliative local surgery (mastectomy or lumpectomy) without definitive axillary surgery,⁹ including advanced breast cancer patients with fungation, bleeding, and other potential physical symptoms.^{10,11} Moreover, 40% of women older than 70 years and 55% of women older than 80 years are treated with tamoxifen only for their breast cancer, omitting surgery completely in the United Kingdom.^{12,13} Recently, the surgery types and the corresponding survival effects for breast cancer in older women is limited because women older than 70 years have usually been under-represented in most clinical trials.^{3,14-16} The survival effect of palliative local

surgery without axillary surgery for locally advanced breast cancer (LABC) in elderly patients is still unclear.

Apart from controlling physical symptoms, local surgery was reported to avert potential emotional symptoms, reduce overall tumor burden, and remove drug-resistant clones, thus might improve survival.¹⁷ Therefore, palliative local surgery seems therapeutic for a proportion of elderly patients diagnosed with LABC. However, there is increasing evidence that tumor removal might lead to perioperative residual tumor growth without systemic therapy, which was associated with tissue trauma, wound formation, inflammation, and immunosuppression.¹⁸⁻²¹ A high probability remains that residual tumor exists after palliative local surgery for LABC, and few of these elderly patients receive systemic therapy.

Figure 1 Flow Diagram of Study Eligibility and Exclusion Criteria



Abbreviations: AJCC = American Joint Commission on Cancer; SEER = Surveillance, Epidemiology, and End Results.

Table 1 Basic Information Characteristics of Enrolled Patients

Characteristic	No Surgery	Lumpectomy	Mastectomy	P
Entire Cohort	1374	583	659	
Age at Diagnosis				.003
70-79 y	491 (35.7)	190 (32.6)	188 (28.5)	
80-89 y	631 (45.9)	263 (45.1)	310 (47.0)	
90 y or older	252 (18.3)	130 (22.3)	161 (24.4)	
Year of Diagnosis				<.001
1973-1997	359 (26.1)	209 (35.8)	268 (40.7)	
1998-2014	1015 (73.9)	374 (64.2)	391 (59.3)	
Race				<.001
White	1036 (75.4)	515 (88.3)	554 (84.1)	
Black	245 (17.8)	42 (7.2)	64 (9.7)	
Other	93 (6.8)	26 (4.5)	41 (6.2)	
Marital status				.192
Not married	152 (11.1)	60 (10.3)	78 (11.8)	
Married	268 (19.5)	131 (22.5)	112 (17.0)	
Other	954 (69.4)	392 (67.2)	469 (71.2)	
Insurance				<.001
No	7 (0.5)	1 (0.2)	0 (0)	
Yes	605 (44.0)	158 (27.1)	183 (27.8)	
Unknown	762 (55.5)	424 (72.7)	476 (72.2)	
Histology				<.001
Ductal	789 (57.4)	385 (66.0)	394 (59.8)	
Lobular	166 (12.1)	102 (17.5)	152 (23.1)	
Other/unknown	419 (30.5)	96 (16.5)	113 (17.1)	
T Stage				<.001
T3	364(26.5)	228(39.1)	300(45.5)	
T4	1010(73.5)	355(60.9)	359(54.5)	
Tumor Size				.009
≤20 mm	44 (3.2)	24 (4.1)	11 (1.7)	
20-50 mm	24 (1.7)	67 (11.5)	52 (7.9)	
>50 mm	423 (30.8)	130 (22.3)	176 (26.7)	
Unknown	883 (64.3)	362 (62.1)	420 (63.7)	
Tumor Grade				<.001
Well	88 (6.4)	83 (14.2)	58 (8.8)	
Moderately	350 (25.5)	190 (32.6)	230 (34.9)	
Poorly or undifferentiated	380 (27.7)	200 (34.3)	239 (36.3)	
Other/unknown ^a	557 (40.5)	110 (18.9)	132 (20.0)	
N Stage				<.001
0	504 (36.7)	384 (65.9)	428 (64.9)	
1	408 (29.7)	37 (6.3)	85 (12.9)	
2-3	188 (13.7)	21 (3.6)	27 (4.1)	
Unknown	274 (19.9)	141 (24.2)	119 (18.1)	
Hormone Receptor Status				<.001
Positive	734 (53.4)	364 (62.4)	375 (57.0)	
Negative	173 (12.6)	76 (13.0)	102 (15.5)	
Other/unknown ^a	467 (34.0)	143 (24.5)	182 (27.6)	
Chemotherapy				<.001
Yes	237 (17.2)	42 (7.2)	55 (8.3)	
No	1137 (82.8)	541 (92.8)	604 (91.7)	

Palliative Surgery for LABC in Elderly Patients

Table 1 Continued

Characteristic	No Surgery	Lumpectomy	Mastectomy	P
Radiation				<.001
Yes	224 (16.3)	140 (24.0)	107 (16.2)	
No	1150 (83.7)	443 (76.0)	552 (83.8)	

Data are presented as n (%).

^aIncludes “unknown,” “borderline,” and “not 1990+ breast” estrogen receptor and progesterone receptor status.

Moreover, breast cancer is a heterogeneous disease, and hormone receptor-positive patients show completely different biological characteristics and clinical outcomes compared with hormone receptor-negative patients. The effects of mastectomy and lumpectomy on hormone receptor-positive and -negative patients might be different in elderly patients.

In the present study, we aimed to determine the survival effect of palliative local surgery (mastectomy and lumpectomy) without definitive axillary surgery for LABC in elderly patients by using the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) cancer database.²² Importantly, the effects of palliative mastectomy or lumpectomy on survival outcomes of hormone receptor-positive or -negative patients were also investigated separately.

Patients and Methods

Data Source

The SEER Program 1973 to 2014 Research Plus Additional Custom Treatment Data (www.seer.cancer.gov): incidence - yr1973_2014.seer9 - BREAST, released April 2017, on the basis of the November 2016 submission.

Study Sample

From 1973 through 2014, 241,650 women age 70 years or older were diagnosed with breast cancer in the SEER cohort. The clinical exclusion criteria were as follows: distant metastasis or not clear (n = 71,652); without adjusted American Joint Commission on Cancer (AJCC) sixth edition T3 or T4 (not including T4d; n = 163,461); not treated with surgery, lumpectomy, or mastectomy without axillary surgery (n = 6121); paired site tumor (n = 10), leaving 2616 who met all our clinical criteria (Figure 1).

Treatment-Related Variables

Surgery was determined from SEER (no surgery: site-specific surgery [1973-1997 varying detail according to year and site] codes 00, 01, 02, 03, 04, 05, 06, and 07 before 1988 and RX Summ-Surg Prim Site [1998+] code 00 since 1988; lumpectomy: site-specific surgery [1973-1997 varying detail according to year and site] code 10 before 1988 and RX Summ-Surg Prim Site [1998+] codes 20, 21, 22, 23, and 24 with EOD (SEER Extent of Disease, 1988: Codes and Coding Instructions) 10—number of lymph nodes examined code 00 since 1988; mastectomy: site-specific surgery [1973-1997 varying detail according to year and site] code 40 before 1988 and RX Summ-Surg Prim Site [1998+] codes 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and 75 with EOD 10—number of lymph nodes examined code 00 since 1988). On the basis of these codes, all included patients did not receive any axillary surgery. Treatment with radiation was determined

using SEER claims (procedure codes 1-6). Treatment with chemotherapy was determined from SEER claims (code 1). Adjuvant endocrine therapy was not reported.

Patient and Tumor-Related Variables

Patient characteristics included age at diagnosis, race, year of diagnosis, marital status, and insurance status. Tumor characteristics as reported by SEER included size, Grade, histology, AJCC T3 and T4 disease, AJCC N stage, and laterality. Margin status and lymph–vascular space invasion were not reported. For estrogen receptor and progesterone receptor, code 1 and code 2 were recognized as positive and negative, respectively. Hormone receptor-negative was defined as estrogen receptor- and progesterone receptor-negative; and hormone receptor-positive was defined as estrogen receptor- and/or progesterone receptor-positive.

Clinical Outcome

The primary outcome was overall survival (OS) estimated using the Kaplan–Meier method. Breast cancer-specific mortality was not included as an outcome because of its questionable validity as reported by SEER.^{3,4,23-25}

Statistical Analysis

Unadjusted associations of variables among no surgery, lumpectomy, and mastectomy groups were tested using Pearson χ^2 . For survival analysis, the Kaplan–Meier method was applied for every variable as in univariate analysis; then, variables, with a P value < .05 in the univariate analysis were further involved in the multivariate analysis using a Cox proportional hazards model. The hazard ratio (HR) with 95% confidence interval (CI) was estimated using a Cox regression model for OS. Propensity score matching was applied to confirm the survival effect of palliative local surgery compared with no surgery. The annual mortality rate of these patients was estimated according to life tables and shown in line graph form. All statistical analyses were performed using software (Stata version 11.0; StataCorp, College Station, TX), and a significant difference was concluded for P < .05.

Results

Baseline Characteristics

A total of 2616 female breast cancer patients age 70 years or older diagnosed with T3/4M0 (without inflammatory breast cancer) from 1973 to 2014 were identified (Table 1). The mean age of enrolled patients was 83.1 years (SD, 7.4). Five- and 10-year OS rates were 24.7% and 7.4%. Of these 2616 patients, 1374 did not receive breast cancer-directed surgery, 583 received lumpectomy without definitive axillary surgery, and 659 received mastectomy without axillary surgery. Clinical T4 and node-positive disease was associated with refusal of cancer-directed surgery; more hormone receptor-positive patients

Table 2 Predictive Factors for Overall Survival in Multivariable Cox Regression

Characteristic	Adjusted Hazard ratio	95% CI	P
Age at Diagnosis			
70-79 y	Reference		
80-89 y	1.71	1.35-2.18	<.001
90 y or older	2.35	1.79-3.09	<.001
Race			
White	Reference		
Black	1.02	0.79-1.32	.852
Other	0.69	0.47-1.02	.060
Histology			
Ductal	Reference		
Lobular	1.01	0.80-1.28	.906
Other/unknown	1.23	0.90-1.68	.194
T Stage			
T3	Reference		
T4	1.16	0.91-1.48	.233
Tumor Size			
≤20 mm	Reference		
20-50 mm	0.97	0.66-1.43	.890
>50 mm	1.12	0.76-1.67	.556
Tumor Grade			
Well	Reference		
Moderately	1.03	0.76-1.39	.862
Poorly or undifferentiated	1.61	1.17-2.20	.003
N Stage			
0	Reference		
1	1.23	0.97-1.57	.094
2-3	1.39	0.95-2.04	.085
Hormone Receptor Status			
Negative	Reference		
Positive	0.50	0.39-0.64	<.001
Chemotherapy			
No	Reference		
Yes	0.86	0.63-1.17	.344
Radiation			
No	Reference		
Yes	0.52	0.39-0.70	<.001
Surgery			
No surgery	Reference		
Lumpectomy	0.85	0.65-1.10	.222
Mastectomy	0.74	0.57-0.96	.022

Bold values represent $P < .05$.

received lumpectomy; chemotherapy use was more preferred among patients in the no surgery group; and more patients in the lumpectomy group received radiation.

Overall Survival After Palliative Local Surgery

The median OS was 23 months (95% CI, 21-26 months) in the no surgery group, 38 months (95% CI, 34-44 months) in the lumpectomy group, and 31 months (95% CI, 29-33 months) in the mastectomy group. Adjusted for potential confounders, lumpectomy was

not associated with improved all-cause mortality compared with no surgery (HR, 0.85; 95% CI, 0.65-1.10; $P = .222$); but mastectomy, with 5- and 10-year OS of 25.4% and 7.2%, respectively, could significantly improve the OS (HR, 0.74; 95% CI, 0.57-0.96; $P = .022$), compared with 18.1% and 4.1% in patients without surgery. Furthermore, radiation use was significantly associated with reduced risk of death (HR, 0.52; 95% CI, 0.39-0.70; $P < .001$), whereas chemotherapy use was not (HR, 0.86; 95% CI, 0.63-1.17; $P = .344$). As expected, hormone receptor-positive status strongly predicted

Palliative Surgery for LABC in Elderly Patients

Table 3 Subgroup Analysis of Predictive Factors for Overall Survival in Multivariable Cox Regression Depending on Hormone Receptor Status

Characteristic	Hormone Receptor-Positive			Hormone Receptor-Negative		
	Adjusted Hazard Ratio	95% CI	P	Adjusted Hazard ratio	95% CI	P
Age at Diagnosis						
70-79 y	Reference			Reference		
80-89 y	2.01	1.51-2.69	<.001	1.19	0.73-1.95	.475
90 y or older	2.94	2.14-4.03	<.001	1.35	0.73-2.50	.346
Race						
White	Reference			Reference		
Black	0.98	0.71-1.33	.878	0.83	0.48-1.44	.511
Other	0.69	0.44-1.06	.093	0.65	0.26-1.63	.361
Histology						
Ductal	Reference			Reference		
Lobular	1.02	0.80-1.31	.857	1.10	0.50-2.45	.809
Other/unknown	1.21	0.80-1.83	.370	1.18	0.69-2.01	.538
T Stage						
T3	Reference			Reference		
T4	1.09	0.82-1.45	.553	1.51	0.91-2.52	.111
Tumor Size						
≤20 mm	Reference			Reference		
20-50 mm	1.02	0.67-1.55	.914	0.88	0.29-2.67	.818
>50 mm	1.11	0.72-1.71	.628	1.34	0.44-4.10	.610
Tumor Grade						
Well	Reference			Reference		
Moderately	1.04	0.76-1.42	.817	0.30	0.06-1.43	.132
Poorly or undifferentiated	1.74	1.26-2.42	.001	0.41	0.09-1.80	.239
N stage						
0	Reference			Reference		
1	1.12	0.84-1.49	.430	1.54	0.92-2.60	.101
2-3	1.71	1.11-2.64	.015	0.69	0.30-1.62	.398
Chemotherapy						
No	Reference			Reference		
Yes	1.11	0.75-1.66	.604	0.51	0.30-0.86	.011
Radiation						
No	Reference			Reference		
Yes	0.44	0.31-0.64	<.001	0.62	0.36-1.06	.080
Surgery						
No surgery	Reference			Reference		
Lumpectomy	0.95	0.71-1.27	.719	0.50	0.27-0.94	.032
Mastectomy	0.88	0.65-1.17	.371	0.45	0.26-0.79	.006

Bold values represent $P < .05$.

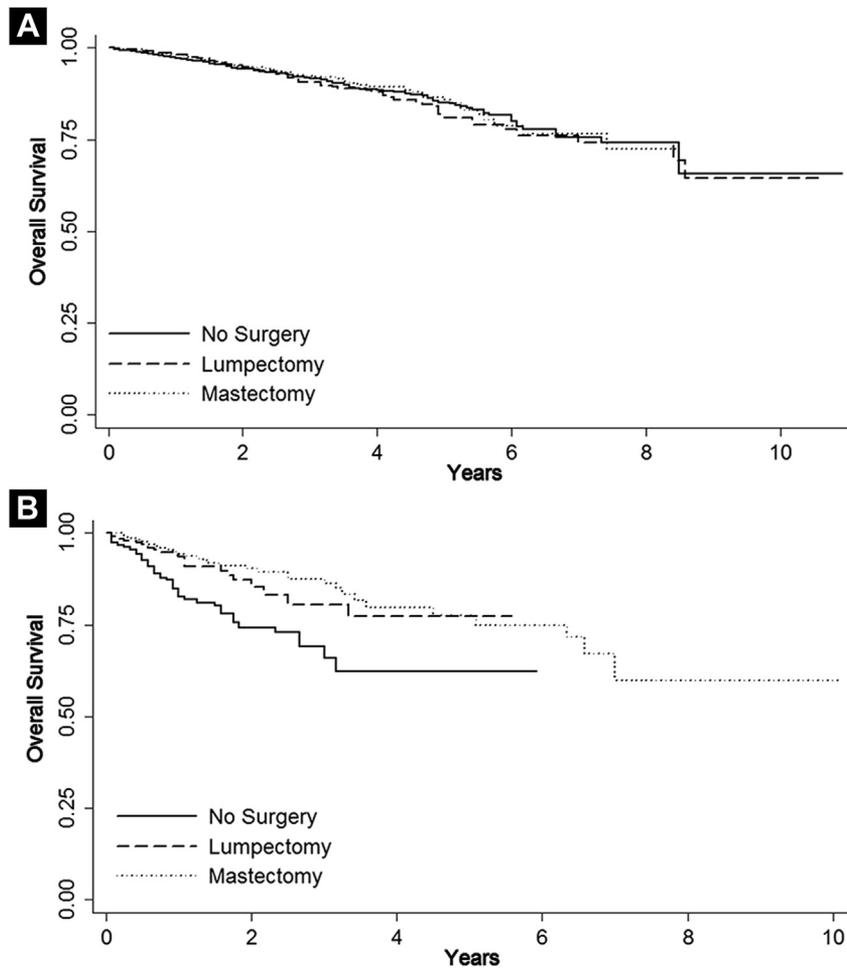
better survival (HR, 0.50; 95% CI, 0.39-0.64; $P < .001$). Older age at diagnosis and high tumor grade were significantly associated with decreased survival (Table 2).

Subgroup Analysis According to Hormone Receptor Status

Because of completely different biological characteristics and clinical outcomes, subgroup analysis was performed according to different hormone receptor status (Table 3). Within hormone

receptor-positive patients, advancing age, poorly or undifferentiated tumor, and node stage 2/3 were significantly associated with decreased survival using traditional multivariable Cox regression. Furthermore, radiation use could also strongly improve survival (HR, 0.44; 95% CI, 0.31-0.64; $P < .001$). However, both types of palliative local surgeries (lumpectomy: HR, 0.95; 95% CI, 0.71-1.27; $P = .719$; mastectomy: HR, 0.88; 95% CI, 0.65-1.17; $P = .371$) were not associated with survival compared with no surgery (Figure 2).

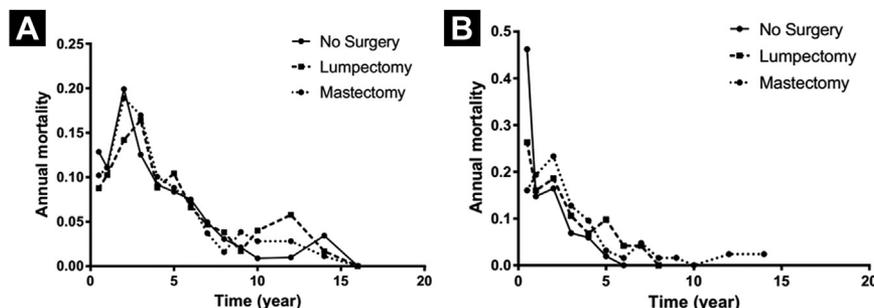
Figure 2 Adjusted Kaplan–Meier Overall Survival Curves for Patients Treated With No Surgery, Lumpectomy, and Mastectomy Without Axillary Surgery Stratified According to Hormone Receptor Status: (A) Hormone Receptor-Positive, and (B) Hormone Receptor-Negative



Different to hormone receptor-positive patients, chemotherapy use could improve the OS (HR, 0.51; 95% CI, 0.30-0.86; $P = .011$) in hormone receptor-negative patients in multivariable

Cox regression, but radiation use had a borderline statistical significance to improve survival (HR, 0.62; 95% CI, 0.36-1.06; $P = .080$). Interestingly, both types of palliative local surgeries

Figure 3 Annual Mortality From Enrolled Elderly Patients Who Underwent No Surgery, Lumpectomy or Mastectomy, Diagnosed With (A) Hormone Receptor-Positive and (B) Negative Locally Advanced Breast Cancer



Palliative Surgery for LABC in Elderly Patients

(lumpectomy: HR, 0.50; 95% CI, 0.27-0.94; $P = .032$; mastectomy: HR, 0.45; 95% CI, 0.26-0.79; $P = .006$) were associated with improved survival compared with no surgery (Figure 2). Other clinical variables, including age at diagnosis, tumor size, node status, tumor grade, clinical T4, and histology, were not associated with OS (Table 3).

To avoid potential selection bias and imbalance of clinical characteristics, propensity score matching analysis was performed to confirm our results. After 1:1 propensity score matching for age, race, T stage, N stage, tumor size, Grade, histology chemotherapy recode, and radiation recode, 144 and 32 pairs of patients were identified in hormone receptor-positive and -negative patients in a comparison of no surgery with lumpectomy, respectively (see Supplemental Table 1 in the online version). In the comparison of no surgery and mastectomy (see Supplemental Table 2 in the online version), 152 and 41 pairs of patients were identified in hormone receptor-positive and -negative groups. Characteristics between these groups were well balanced. The results were consistent with multivariable Cox regression, except for the association of lumpectomy with improved survival in hormone receptor-negative patients ($P = .365$).

Annual Mortality of Patients Without Radiation and Chemotherapy

To expeditiously the effect of palliative local surgery on all-cause mortality and natural history of LABC, annual mortalities of enrolled patients without radiation and chemotherapy in different surgery types were calculated (Figure 3). Within hormone receptor-positive patients, annual mortalities in the 3 groups were similar, and 2 peaks were observed, with a first at the second to third years and a second at the 9th through the 14th years. Lumpectomy and mastectomy were not associated with improved OS using multivariable Cox regression (see Supplemental Table 3 in the online version). Within hormone receptor-negative patients, annual mortalities decreased gradually with a peak at the first through third years. In all, lumpectomy ($P = .034$) and mastectomy ($P = .012$) significantly improved OS within hormone receptor-negative patients (see Supplemental Table 3 in the online version).

Discussion

To our knowledge, this is the first report about the survival effect of palliative local surgery without axillary surgery in elderly patients diagnosed with LABC. In this population-based cohort study of women with age at 70 years or older diagnosed with T3/4 breast cancer, traditional multivariable Cox regression was first used, and then propensity score matching analysis was applied to confirm the results. Furthermore, patterns of annual all-cause mortality in 3 groups were compared. Our findings help to define appropriate indications for palliative local surgery in elderly patients with LABC to control physical symptoms and avert potential emotional symptoms.

Hormone receptor-positive breast cancer is sensitive to endocrine therapy, and shows better survival than hormone receptor-negative breast cancer.²⁶ In this study, hormone receptor-positive patients, with 5- and 10-year OS of 23.3% and 6.5%, also showed better survival than hormone receptor-negative patients with 5- and 10-year OS of 13.2% and 2.1%. Similar to the previous study,⁴ radiation use, but not chemotherapy, strongly improved survival except for several important clinicopathological features. Interestingly, palliative local

surgery did not improve survival in this subtype of patients. The good survival of elderly patients with hormone receptor-positive LABC receiving endocrine therapy might be contributed to the biological characteristics of this type, although the information of endocrine therapy was unknown. On the basis of our results, lumpectomy, but not mastectomy, should be recommended as palliative surgery in elderly patients with hormone receptor-positive LABC with fewer injuries than mastectomy.

In general, hormone receptor-negative breast cancer shows a more aggressive phenotype than hormone receptor-positive cancer. In this subtype of LABC, endocrine therapy is not suitable, and only a small proportion of patients received chemotherapy and radiation in elderly patients with palliative surgery or no surgery in this study. Because of the relatively small sample size, patients who received radiation had a trend toward improved survival, and several important features were not associated with survival in this subtype. However, chemotherapy and palliative surgery were still associated with improved survival using traditional multivariable Cox regression. Mastectomy still strongly improved OS in propensity score matching analysis. Compared with lumpectomy, patients who received mastectomy might have a higher rate of clear margins for this advanced disease,²⁷ although this is not documented. Total mastectomy is important and should be recommended for these patients without systemic therapy.

Previous studies^{18,19} have reported that surgical injury induces changes at the expression level of genes implicated in metastasis, leading to accelerated postoperative residual tumor growth, which might be associated with the imbalance between growth-inducing and growth-inhibiting factors in the tumor microenvironment.²⁸ In the present study, palliative surgery did not show bad survival effects of these elderly patients with LABC when there was a great chance that residual tumor existed. Different from the previous study,²⁹ the patterns of mortality in 3 groups were almost the same. The transient inflammation and immunosuppression status regarding surgical injury might not have adverse effects on OS in these elderly patients. Interestingly, mastectomy strongly improved OS of these elderly patients with hormone receptor-negative LABC, especially for the first year. The results were further confirmed in patients without radiation and chemotherapy. This benefit might be contributed to reduce tumor burden with recovery of immune response in this subtype of patients.^{17,27,30}

Several limitations of this study should be considered when interpreting these results. First, some pathologic information, including Ki-67 status, HER2 status, and lymphovascular invasion, were not available. Furthermore, endocrine therapy and anti-HER2 therapy were not clear. These treatments might not significantly bias the outcomes because administering these treatments to women is on the basis of the pathological assessment, not the types of surgery.³¹ Our results still represented the real-world situation in this special portion of patients. Second, because of its retrospective design and limitations of this large cancer database, our results should be confirmed in future cohort studies.

Conclusion

For elderly patients diagnosed with LABC who are not candidates for standard therapies, palliative local surgery is recommended to control physical symptoms and avert potential emotional symptoms.

For hormone receptor-positive patients, lumpectomy should be considered as palliative therapy because of no survival benefit of mastectomy with more surgical injuries. However, mastectomy should be recommended first for hormone receptor-negative patients because of definitive survival benefit. Further studies are urgently needed to define optimal treatment strategies for elderly women with different subtypes of LABC.

Clinical Practice Points

- Many elderly breast cancer patients refuse surgery, or receive palliative local surgery.
- To control potential physical symptoms and avert potential emotional symptoms, palliative local surgery is needed for elderly patients diagnosed with LABC.
- However, tumor removal might lead to perioperative residual tumor growth.
- The effects of palliative mastectomy or lumpectomy without axillary surgery on survival outcomes of hormone receptor-positive or -negative patients were not known.
- In this study, using the SEER cancer database, lumpectomy and mastectomy were not associated with overall survival compared with no surgery within hormone receptor-positive patients.
- However, mastectomy strongly improved survival within hormone receptor-negative patients.
- Therefore, for elderly patients diagnosed with LABC, who are not candidates for standard therapies, mastectomy should be recommended as palliative therapy for hormone receptor-negative patients, and lumpectomy for hormone receptor-positive patients.

Acknowledgments

This work was supported by the National Natural Science Foundation of China (81502286, 81502299, 81572607, and 81771953), and a project funded by the Priority Academic Program Development of Jiangsu Higher Education Institutions.

Disclosure

The authors have stated that they have no conflicts of interest.

Supplemental Data

Supplemental tables accompanying this article can be found in the online version at <https://doi.org/10.1016/j.clbc.2018.09.007>.

References

- Gennari R, Curigliano G, Rotmensz N, et al. Breast carcinoma in elderly women: features of disease presentation, choice of local and systemic treatments compared with younger postmenopausal patients. *Cancer* 2004; 101:1302-10.
- Kimmick GG, Balducci L. Breast cancer and aging. Clinical interactions. *Hematol Oncol Clin North Am* 2000; 14:213-34.
- Elkin EB, Hurria A, Mitra N, Schrag D, Panageas KS. Adjuvant chemotherapy and survival in older women with hormone receptor-negative breast cancer: assessing outcome in a population-based, observational cohort. *J Clin Oncol* 2006; 24:2757-64.
- Smith BD, Haffty BG, Hurria A, Galusha DH, Gross CP. Postmastectomy radiation and survival in older women with breast cancer. *J Clin Oncol* 2006; 24:4901-7.
- Yancik R, Wesley MN, Ries LA, Havlik RJ, Edwards BK, Yates JW. Effect of age and comorbidity in postmenopausal breast cancer patients aged 55 years and older. *JAMA* 2001; 285:885-92.
- Javid SH, He H, Korde LA, Flum DR, Anderson BO. Predictors and outcomes of completion axillary node dissection among older breast cancer patients. *Ann Surg Oncol* 2014; 21:2172-80.
- Eaker S, Dickman PW, Bergkvist L, Holmberg L, Uppsala/Orebro Breast Cancer Group. Differences in management of older women influence breast cancer survival: results from a population-based database in Sweden. *PLoS Med* 2006; 3:e25.
- Gaitanidis A, Alevizakos M, Tsalikidis C, Tsaroucha A, Simopoulos C, Pitiakoudis M. Refusal of cancer-directed surgery by breast cancer patients: risk factors and survival outcomes. *Clin Breast Cancer* 2018; 18:e469-76.
- Sun SX, Hollenbeck CS, Leung AM. Deviation from the standard of care for early breast cancer in the elderly: what are the consequences? *Ann Surg Oncol* 2015; 22:2492-9.
- Fairweather M, Jiang W, Keating NL, Freedman RA, King TA, Nakhlis F. Morbidity of local therapy for locally advanced metastatic breast cancer: an analysis of the Surveillance, Epidemiology, and End Results (SEER)-Medicare Registry. *Breast Cancer Res Treat* 2018; 169:287-93.
- Badwe R, Hawaldar R, Nair N, et al. Locoregional treatment versus no treatment of the primary tumour in metastatic breast cancer: an open-label randomised controlled trial. *Lancet Oncol* 2015; 16:1380-8.
- Wyld L, Reed M. The role of surgery in the management of older women with breast cancer. *Eur J Cancer* 2007; 43:2253-63.
- Wyld L, Garg DK, Kumar ID, Brown H, Reed MW. Stage and treatment variation with age in postmenopausal women with breast cancer: compliance with guidelines. *Br J Cancer* 2004; 90:1486-91.
- Hutchins LF, Unger JM, Crowley JJ, Coltman CA Jr, Albain KS. Underrepresentation of patients 65 years of age or older in cancer-treatment trials. *N Engl J Med* 1999; 341:2061-7.
- Kunkler IH, Williams LJ, Jack WJ, Cameron DA, Dixon JM, PRIME II investigators. Breast-conserving surgery with or without irradiation in women aged 65 years or older with early breast cancer (PRIME II): a randomised controlled trial. *Lancet Oncol* 2015; 16:266-73.
- Aziz D, Gardner S, Pritchard K, Paszat L, Holloway CM. Selective application of axillary node dissection in elderly women with early breast cancer. *Ann Surg Oncol* 2007; 14:652-9.
- Rashid OM, Nagahashi M, Ramachandran S, et al. Resection of the primary tumor improves survival in metastatic breast cancer by reducing overall tumor burden. *Surgery* 2013; 153:771-8.
- Coffey JC, Wang JH, Smith MJ, Bouchier-Hayes D, Cotter TG, Redmond HP. Excisional surgery for cancer cure: therapy at a cost. *Lancet Oncol* 2003; 4:760-8.
- Al-Sahaf O, Wang JH, Browne TJ, Cotter TG, Redmond HP. Surgical injury enhances the expression of genes that mediate breast cancer metastasis to the lung. *Ann Surg* 2010; 252:1037-43.
- Coussens LM, Werb Z. Inflammation and cancer. *Nature* 2002; 420:860-7.
- Abramovitch R, Marikovsky M, Meir G, Neeman M. Stimulation of tumour growth by wound-derived growth factors. *Br J Cancer* 1999; 79:1392-8.
- Hankey BF, Ries LA, Edwards BK. The Surveillance, Epidemiology, and End Results Program: a national resource. *Cancer Epidemiol Biomarkers Prev* 1999; 8: 1117-21.
- Bach PB, Guadagnoli E, Schrag D, Schussler N, Warren JL. Patient demographic and socioeconomic characteristics in the SEER-Medicare database applications and limitations. *Med Care* 2002; 40(8 suppl), IV-19-25.
- Hoel DG, Ron E, Carter R, Mabuchi K. Influence of death certificate errors on cancer mortality trends. *J Natl Cancer Inst* 1993; 85:1063-8.
- Lu TH, Shih TP, Lee MC, Chou MC, Lin CK. Diversity in death certification: a case vignette approach. *J Clin Epidemiol* 2001; 54:1086-93.
- Yin WJ, Lu JS, Di GH, et al. Clinicopathological features of the triple-negative tumors in Chinese breast cancer patients. *Breast Cancer Res Treat* 2009; 115: 325-33.
- Blanchard DK, Shetty PB, Hilsenbeck SG, Elledge RM. Association of surgery with improved survival in stage IV breast cancer patients. *Ann Surg* 2008; 247: 732-8.
- Karrison TG, Ferguson DJ, Meir P. Dormancy of mammary carcinoma after mastectomy. *J Natl Cancer Inst* 1999; 91:80-5.
- Demicheli R, Valagussa P, Bonadonna G. Does surgery modify growth kinetics of breast cancer micrometastases? *Br J Cancer* 2001; 85:490-2.
- Danna EA, Sinha P, Gilbert M, Clements VK, Pulaski BA, Ostrand-Rosenberg S. Surgical removal of primary tumor reverses tumor-induced immunosuppression despite the presence of metastatic disease. *Cancer Res* 2004; 64:2205-11.
- Mogal HD, Clark C, Dodson R, Fino NF, Howard-McNatt M. Outcomes after mastectomy and lumpectomy in elderly patients with early-stage breast cancer. *Ann Surg Oncol* 2017; 24:100-7.

Palliative Surgery for LABC in Elderly Patients

Supplemental Data

Supplemental Table 1 Characteristics of Patients in the No Surgery Group and Lumpectomy Group After Propensity Score Matching					
Characteristic	n	No Surgery	Lumpectomy	χ^2	P
Hormone Receptor-Positive					OS = .423
Entire cohort	288	144	144		
Age at diagnosis				1.469	.480
70-79 y	73	37	36		
80-89 y	143	67	76		
90 y or older	72	40	32		
Race				2.561	.278
White	247	120	127		
Black	28	18	10		
Other	13	6	7		
T Stage				0.501	.479
T3	150	72	78		
T4	138	72	66		
Tumor grade				0.902	.637
Well	58	27	31		
Moderately	152	80	72		
Poorly or undifferentiated	78	37	41		
Histology				0.149	.928
Ductal	185	91	94		
Lobular	84	43	41		
Other	19	10	9		
N Stage				a	1.000
0	271	135	136		
1	13	7	6		
2-3	4	2	2		
Chemotherapy				0.000	1.000
Yes	14	7	7		
No	274	137	137		
Radiation				2.798	.094
Yes	53	21	32		
No	235	123	112		
Hormone Receptor-Negative					OS = .365
Entire cohort	64	32	32		
Age at diagnosis				1.525	.467
70-79 y	13	8	5		
80-89 y	31	16	15		
90 y or older	20	8	12		
Race				a	.148
White	55	25	30		
Black	9	7	2		
Other	0	0	0		
T stage				0.000	1.000
T3	40	20	20		
T4	24	12	12		
Tumor grade				a	1.000

Supplemental Table 1		Continued			
Characteristic	n	No Surgery	Lumpectomy	χ^2	P
Well	2	1	1		
Moderately	11	6	5		
Poorly or undifferentiated	51	25	26		
Histology				a	.782
Ductal	45	24	21		
Lobular	2	1	1		
Other	17	7	10		
N stage				a	.043
0	51	22	29		
1	11	9	2		
2-3	2	1	1		
Chemotherapy				0.988	.320
Yes	11	7	4		
No	53	25	28		
Radiation				0.097	.756
Yes	13	7	6		
No	51	25	26		

Abbreviation: OS = overall survival.

^aFisher's exact test.

Palliative Surgery for LABC in Elderly Patients

Supplemental Table 2 Characteristics of Patients in the No Surgery Group and Mastectomy Group After Propensity Score Matching

Characteristic	n	No Surgery	Mastectomy	χ^2	P
Hormone Receptor-Positive					OS = .493
Entire cohort	304	152	152		
Age at diagnosis				1.362	.506
70-79 y	74	40	34		
80-89 y	146	68	78		
90 y or older	84	44	40		
Race				5.567	.062
White	230	112	118		
Black	47	30	17		
Other	27	10	17		
T stage				0.331	.565
T3	163	79	84		
T4	141	73	68		
Tumor grade				0.648	.723
Well	42	20	22		
Moderately	163	85	78		
Poorly or undifferentiated	99	47	52		
Histology				1.327	.515
Ductal	166	88	78		
Lobular	110	51	59		
Other	28	13	15		
N stage				a	.424
0	279	138	141		
1	19	12	7		
2-3	6	2	4		
Chemotherapy				0.070	.791
Yes	15	8	7		
No	289	144	145		
Radiation				2.474	.116
Yes	48	19	29		
No	256	133	123		
Hormone Receptor-Negative					OS = .004
Entire cohort	82	41	41		
Age at diagnosis				1.687	.430
70-79 y	23	13	10		
80-89 y	38	20	18		
90 y or older	21	8	13		
Race				a	.065
White	63	28	35		
Black	14	11	3		
Other	5	2	3		
T stage				0.049	.825
T3	43	21	22		
T4	39	20	19		
Tumor grade				a	.569
Well	1	1	0		
Moderately	15	6	9		
Poorly or undifferentiated	66	34	32		
Histology				a	.367

Supplemental Table 2 Continued

Characteristic	n	No Surgery	Mastectomy	χ^2	P
Ductal	61	33	28		
Lobular	7	2	5		
Other	14	6	8		
N stage				^a	.192
0	66	30	36		
1	14	10	4		
2-3	2	1	1		
Chemotherapy				0.734	.391
Yes	15	9	6		
No	67	32	35		
Radiation				0.265	.607
Yes	20	9	11		
No	62	32	30		

Abbreviation: OS = overall survival.

^aFisher's exact test.

Palliative Surgery for LABC in Elderly Patients

Supplemental Table 3 Subgroup Analysis of Predictive Factors for Overall Survival in Patients Without Chemotherapy and Radiation

Characteristic	Hormone Receptor-Positive			Hormone Receptor-Negative		
	Adjusted Hazard Ratio	95% CI	P	Adjusted Hazard Ratio	95% CI	P
Age at Diagnosis						
70-79 y	Reference			Reference		
80-89 y	1.92	1.39-2.65	<.001	1.45	0.73-2.87	.283
90 y or older	2.61	1.84-3.69	<.001	1.53	0.71-3.31	.278
Race						
White	Reference			Reference		
Black	0.85	0.60-1.22	.381	0.92	0.46-1.87	.828
Other	0.62	0.37-1.02	.060	0.54	0.06-4.49	.567
Histology						
Ductal	Reference			Reference		
Lobular	1.13	0.86-1.49	.367	0.81	0.28-2.31	.694
Other/unknown	1.13	0.69-1.83	.630	1.12	0.61-2.05	.712
T stage						
T3	Reference			Reference		
T4	1.11	0.81-1.52	.513	1.34	0.65-2.76	.423
Tumor Size						
≤20 mm	Reference			Reference		
20-50 mm	1.06	0.66-1.72	.803	0.47	0.14-1.58	.222
>50 mm	1.06	0.65-1.75	.811	0.75	0.22-2.60	.650
Tumor Grade						
Well	Reference			Reference		
Moderately	1.03	0.74-1.44	.847	0.41	0.08-2.03	.272
Poorly or undifferentiated	1.56	1.09-2.21	.014	0.47	0.10-2.11	.325
N Stage						
0	Reference			Reference		
1	1.09	0.79-1.50	.610	1.39	0.69-2.77	.357
2-3	1.69	0.97-2.93	.062	0.91	0.25-3.29	.888
Surgery						
No surgery	Reference			Reference		
Lumpectomy	1.07	0.78-1.48	.683	0.44	0.21-0.94	.034
Mastectomy	0.92	0.67-1.27	.622	0.41	0.20-0.82	.012

Bold values represent $P < .05$.