Radiation Therapy for Positive Surgical Margins in Women ≥ 70 Years with Stage I, Estrogen Receptor-positive Breast Cancer

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Abstract. *Background/Aim:* A re-excision for positive margin(s) following a lumpectomy for invasive breast cancer is a standard recommendation. However, for elderly women with stage I estrogen receptor-positive (ER+) tumors, who may be at higher surgical risk, whether radiation therapy without re-excision will be adequate is not known. *Patients and Methods:* We evaluated a cohort of 53,950 women aged ≥ 70 years with Stage I, ER+ breast cancer who had lumpectomy and anti-hormone therapy diagnosed between 2004 and 2011 in the National Cancer Data Base. Patients were divided into four groups: 1) negative margins without radiation (XRT), 2) negative margins with XRT, 3) positive margins without XRT, and 4) positive margins with XRT. Clinicopathological and sociodemographic variables were compared among these groups. Univariable and multivariable analysis were employed. *Results:* The 5-year overall survival (OS) rates for the groups were as follows: 1) negative margins without radiation (XRT); 77.1%, 2) negative margins with XRT; 90.0%, 3) positive margins without XRT; 62.9%, and 4) positive margins with XRT; 86.8% ($p < 0.0001$). Significant predictors ($p < 0.01$) of OS include treatment groups, age, income status, facility type, facility location, tumor size, tumor grade, and comorbidities. *Conclusion:* Radiation therapy for positive surgical margins without re-excision may be a viable option for elderly women with stage I, ER+ tumor treated with lumpectomy and hormonal therapy.

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Complete resection of the primary breast tumor with negative margins is a cornerstone of managing breast cancer (1). However, up to 18% of patients undergoing a breast-conserving therapy (BCT) for breast cancer have positive surgical margins (2). Positive margins portend an increased risk of ipsilateral breast tumor recurrence (IBTR) and possibly worsened survival (3-5) and mitigating this risk generally requires either a re-excision and/or postoperative radiation (RT). For elderly patients, especially those who are frail, another trip to the operating room to re-excite the positive tumor bed can expose the patient to the potential risk of anesthesia and surgery. Whether post-operative radiation therapy without the need for a re-excision can adequately address positive surgical margins following a lumpectomy in the elderly patient is not known. Given the dearth of data on this important but not so uncommon situation, we sought to evaluate the role of postoperative radiation among elderly patients (age ≥ 70 years) with incompletely resected T1, hormone-positive breast cancer who received anti-hormonal therapy.

Patients and Methods

Data source. The nationally recognized National Cancer Data Base (NCDB) is a joint project of the Commission of Cancer (CoC) of the American College of Surgeons and the American Cancer Society. More than 1,500 CoC-accredited facilities contribute clinical information to the database. Approximately 70% of newly-diagnosed cancer cases in the U.S and 30 million historical records are captured in the database. Access to NCDB was awarded to the investigators after having successfully applied for the NCDB Participant User File (PUF). The data sets in the PUF were de-identified and were in compliant with the privacy requirements of the Health Insurance Portability and Accountability Act (HIPAA). The study was exempted from Institutional Review Board (IRB) approval by the Louisiana State University Health Sciences Center-Shreveport.

Study population. A total of 53,950 diagnosed ER+ breast cancer cases from 2004 to 2011 among women aged ≥ 70 years, clinical

stage I (T1N0M0), who underwent breast conserving therapy (BCT) and received anti-hormonal therapy were analyzed to determine the impact of radiation therapy (RT) on survival outcome for those individuals with positive surgical margins. For our study, margin status was classified using the surgical margins variable in the NCDB PUF dataset. No residual tumor was classified as negative surgical margin, and positive surgical margins included residual tumor, microscopic residual tumor, and macroscopic residual tumor. All individuals with indeterminate margin status, unknown margins, or no surgery of the primary site were not considered in the survival analysis. Patients were classified into four major groups: 1) negative margins without radiation (XRT), 2) negative margins with XRT, 3) positive margins without XRT, and 4) positive margins with XRT.

According to the NCDB's PUF dictionary, facility type was classified as 1) community cancer program, 2) comprehensive community cancer program, 3) academic research program, and 4) others (6). Community cancer programs are those that treat between 100 and 500 newly diagnosed cancer patients each year, and patients may be referred to another facility for part of their diagnosis or treatment (6). Comprehensive community cancer programs are those that treat more than 500 newly diagnosed cancer patients each year (6). Academic and research institutions are those that treat more than 500 newly diagnosed cancer patients each year while offering postgraduate medical education programs (6).

Facility location was categorized into regions within the United States based on the U. S. Census Regions and Divisions: 1) New England, 2) Mid-Atlantic, 3) South Atlantic, 4) East North Central, 5) East South Central, 6) West North Central, 7) West South Central, 8) Mountain, and 9) Pacific.

Race/ethnicity was categorized as White, Black, American Indian/Aleutian or Eskimo, Asian or Pacific Islander, and Others. Insurance status was classified as 1) uninsured, 2) private insurance/managed care, 3) Medicaid, 4) Medicare, and 5) other governmental insurance. Median household income level was classified as 1) <\$38,000, 2) \$38,000-\$47,999, 3) \$48,000-\$62,999, 4) ≥ \$63,000. Education level was classified into percentage of adults (age ≥25 years) who did not graduate from high school in the area based on the 2012 American Community Survey data: 1) ≥21%, 2) 13-20.9%, 3) 7-12.9%, 4) <7%. Comorbidity was described by Charlson/Deyo score, which was a weighted sum score based on the Charlson comorbidity score mapping table in the PUF data dictionary. The Charlson/Deyo score was reported as 0, 1 or 2 (7, 8).

Population density was classified as 1) metropolitan with ≥1 million, 2) metropolitan with 250,000 to 1 million, 3) metropolitan with <250,000, 4) urban with ≥20,000 and adjacent to a metropolitan area, 5) urban with ≥20,000 but not adjacent to a metropolitan area, 6) urban with <20,000 and adjacent to a metropolitan area, 7) urban with <20,000 but not adjacent to a metropolitan area, 8) rural with <2,500 and adjacent to a metropolitan area, and 9) rural with <2,500 but not adjacent to a metropolitan area. Great circle distance is measured in miles and defined as being between the patient's residence at diagnosis and the hospital that reported the case.

Statistical analysis. Descriptive statistics of each categorical variable was performed using Chi-square test for categorical data and ANOVA for the numerical variable. The Kaplan–Meier method was used to produce the Kaplan–Meier survival curves. Multivariable proportional hazards regression analysis was used to determine independent significant factors associated with survival, hazard ratios (HR) and confidence intervals (CI). A p -value ≤0.05

was considered statistically significant. Statistical analyses were performed using SAS Version 9.4 statistical software (SAS Institute Inc., Cary, NC, U.S.A., 2013),

Results

The median follow-up time for the entire cohort was 50.1 months. Table I shows the descriptive statistics for the entire cohort. Of note, 75.6% of patients had negative margins with XRT, 20.5% had negative margins without XRT, 2.9% had positive margins with XRT, and 1.0% had positive margins without XRT. Approximately 91% of patients were Caucasian while African-American represented approximately 6% of the population. Comprehensive community cancer center and academic research programs represent approximately 87% of all facility types. South Atlantic region has the highest percentage of cases (21%) while Mountain region has the lowest (4%). Most patients had Medicare (86%) or private insurance (12%), resided in metropolitan region with ≥1 million people (51%), and had zero comorbidity score (83%). Over a third of patients had an annual income of ≥\$63,000 and over 50% had high education.

Those who did not receive radiation therapy tended to be older; almost half of patients in the negative margins without XRT and 63% of patients in the positive margins without XRT were ≥80 years. In contrast, 80% of patients in the negative margins with XRT and 73% of patients in the positive margins with XRT were younger than 80 years of age ($p<0.0001$) (Table II).

Figure 1 shows the Kaplan–Meier overall survival (OS) curve for the entire cohort. Note that the survival curves for those without XRT were significantly lowered than those who had XRT. As expected, the lowest survival rate was observed in the positive margins without XRT group (the 5-year OS was 63%). What is unique is that compared to the negative margins without XRT group, those that had positive margins but received XRT had significantly better OS (87% vs. 77%; $p<0.0001$). In fact, the OS curves were statistically significantly different ($p=0.02$ for the log-rank test) between those that had positive margins with XRT and those that had negative margins with XRT, but the difference was not clinically significant (87% vs. 90%).

The median survival times for the negative margins with XRT, positive margin with XRT, negative margins without XRT, and positive margins without XRT were 119 months, 119 months, 102 months, and 80 months, respectively ($p<0.0001$). The median follow-up times for the negative margins with XRT, positive margins with XRT, negative margins without XRT, and positive margin without XRT were 52.0 months, 51.3 months, 43.6 months, and 37.9 months, respectively.

Table III summarizes the univariable survival analyses for this population. Significant factors associated with survival

Table I. Demographic and clinical characteristics of elderly patients with stage I, hormone-positive tumors.

Variable	Frequency (percent)	Variable	Frequency (percent)
Total patients	53,950	Facility location	
Surgical margins/XRT group		New England	4,490 (8.3)
Negative margins without XRT	11,031 (20.5)	Mid Atlantic	9,033 (16.7)
Negative margins with XRT	40,807 (75.6)	South Atlantic	11,282 (20.9)
Positive margins without XRT	550 (1.0)	East North Central	11,188 (20.7)
Positive margins with XRT	1,562 (2.9)	East South Central	2,416 (4.5)
Age		West North Central	4,218 (7.8)
70-74	22,263 (41.3)	West South Central	2,748 (5.1)
75-79	17,292 (32.1)	Mountain	2,246 (4.2)
80-84	10,115 (18.8)	Pacific	6,329 (11.7)
85+	4,280 (7.9)	Urban/rural location (2013 in dataset)	
Race/ ethnicity		Metro ≥ 1 million	27,309 (50.6)
White	49,084 (91.0)	Metro 250 k to 1 million	11,823 (21.9)
Black	3,231 (6.0)	Metro <250k	5,636 (10.5)
American Indian, Aleutian, or Eskimo	61 (0.1)	Urban ≥ 20 k adjacent metro	2,205 (4.1)
Asian/Pacific Islander	909 (1.7)	Urban ≥ 20 k not adjacent metro	702 (1.3)
Other or Unknown	665 (1.2)	Urban <20k adjacent metro	2,479 (4.6)
Income		Urban <20k not adjacent metro	1,132 (2.1)
<\$38,000	7,262 (13.5)	Rural <2500 adjacent metro	387 (0.7)
\$38,000-47,999	12,133 (22.5)	Rural <2500 not adjacent metro	439 (0.8)
\$48,000-62,999	15,023 (27.9)	Unknown	1,838 (3.4)
\$63,000 +	18,773 (34.8)	Great circle distance	
Unknown	759 (1.4)	<50 miles	50,711 (94.0)
Education		≥ 50 miles	2,535 (4.7)
$\geq 21\%$	6,145 (11.4)	Unknown	704 (1.3)
13-20.9%	12,303 (22.8)	Comorbidities/Deyo Score	
7-12.9%	19,340 (35.9)	0	44,621 (82.7)
<7%	15,429 (28.6)	1	7,817 (14.5)
Unknown	733 (1.4)	2	1,512 (2.8)
Primary payor		Tumor Size	
Uninsured	139 (0.3)	≤ 0.1 cm	752 (1.4)
Private insurance	6,550 (12.1)	>0.1-0.5 cm	5,346 (9.9)
Medicaid	454 (0.8)	>0.5-1.0 cm	17,933 (33.2)
Medicare	46,118 (85.5)	>1.0-2 cm	28,800 (53.4)
Other government	142 (0.3)	Unknown	1,119 (2.1)
Unknown	547 (1.0)	Grade	
Facility type		Well differentiated	19,834 (36.8)
Community cancer program	6,922 (12.8)	Moderately differentiated	25,592 (47.4)
Comprehensive community cancer center	33,483 (62.1)	Poorly differentiated	5,918 (11.0)
Academic research program	13,451 (24.9)	Undifferentiated, anaplastic	74 (0.1)
Unknown	94 (0.2)	Unknown	2,532 (4.7)
		Chemotherapy	
		None	50,969 (94.5)
		Yes	2,051 (3.8)
		Unknown	930 (1.7)

were surgical margins and receipt of radiation, age, income, insurance status, facility type, facility location, comorbidity index, tumor size, tumor grade, and chemotherapy.

Table IV summarizes the multivariable survival analyses for this cohort. Significant independent factors related to worse survival were positive surgical margins without the receipt of radiation, older age, lower income, facility of non-academic cancer program, facility in the non-pacific or non-mountain area, higher comorbidity score, larger tumor size, and poorly differentiated or undifferentiated histology. Compared to the negative margins without XRT group, those

with positive margins without XRT were 1.56 times as likely to die. In contrast, those with positive margins with XRT had a 36% reduction in risk of dying.

Complete excision of the primary breast tumor before radiation therapy is paramount to optimize local control in breast-conserving therapy (BCT) (9-11). For those with positive margins, a re-excision is recommended since the rate of in-breast tumor recurrence (IBTR) is higher compared

Figure 1. Kaplan–Meier curve for patients aged ≥ 70 years, Stage I, ER+, BCT + hormone treatment population: The 5-year overall survival rates and median survival for the four groups were as follow: 1) negative margins with XRT: 90.0%, 118.8 months; 2) positive margins with XRT: 86.8%, 119.1 months; 3) negative margins without XRT: 77.1%, 101.6 months; and 4) positive margins without XRT: 62.9%, 80.2 months ($p < 0.0001$).

to those with negative margins (12-15). Locoregional recurrences can have an impact on survival; the Early Breast Cancer Trialists Collaborative Group (EBCTCG) reported that one life is saved after 15-year of follow-up for every four local recurrences prevented by 10 years after lumpectomy (10, 15).

Margin width following BCT was a controversial topic. In the past, surgeons and radiation oncologists who have been surveyed tend not to agree on an ideal margin width required following BCT, and consequently, a width ranging anywhere between 2-5 mm was arbitrarily selected. Adding to the confusion is the lack of consensus on what constitutes a positive margin. In February 2014, the Society of Surgical Oncology (SSO) and the American Society of Radiation Oncology (ASTRO) released a guideline to help quell controversy over margin width, which referenced a 2013 meta-analysis also endorsed by the American Society of Clinical Oncology (ASCO) and the American Society of Breast Surgeons (ASBS), which states that no ink on a tumor is an adequate margin post-breast conserving surgery (BCS) for breast cancer patients (1, 15).

Although EBCTCG reported the advantages of adjuvant RT, such advantages were not uniformly observed across all age groups. Women aged < 40 years had a more substantial reduction in recurrence than the older age groups. Consequently, many began to ponder whether adjuvant

radiation can be avoided in a select group of elderly women with favorable breast cancer. Two major randomized trials, the Cancer and Leukemia Group B (CALGB) 9343 trial (16, 17) and PRIME II trial (18), demonstrated no survival advantage with adjuvant RT among elderly women with small estrogen-receptor positive tumors treated with BCT and anti-hormonal therapy. All of these patients had negative margins. This prompted us to ask the question of what to do with those who had positive margins.

Re-excision rates after BCT are reported to be anywhere from 20-60%, depending on various factors such as margin status, age, tumor size, and presence of an *in situ* component (19-22). The decision to subject a patient to a re-excision depends on a number of factors such as patient's age, comorbidity status, life expectancy, extent of excision, extent of margin involvement, tumor characteristics, and whether the patient will receive adjuvant therapies (15). Re-excision, however, does carry some potential disadvantages. Jung *et al.* reported that re-excision delays treatment, increases morbidity, and compromises the aesthetics of the breast (23). Given these disadvantages with re-excision, we began to question whether these patients could adequately be treated with postoperative RT? The National Comprehensive Cancer Network (NCCN) reported that higher radiation boost dose to the tumor bed can be considered in selected cases of BCT with a microscopically focally positive margin in the absence

Table II. Demographic and clinical characteristics of elderly patients with Stage I, hormone-positive tumors by margin/XRT Groups.

Variable	Negative margins without XRT N (%)	Negative margins with XRT N (%)	Positive margins without XRT N (%)	Positive margins with XRT N (%)	p-Value
Total patients	11,031 (20.5)	40,807 (75.6)	550 (1.0)	1,562 (2.9)	
Age					<0.0001
70-74	2,484 (22.5)	19,045 (46.7)	89 (16.2)	645 (41.3)	
75-79	3,126 (28.3)	13,550 (33.2)	116 (21.1)	500 (32.0)	
80-84	3,117 (28.3)	6,529 (16.0)	161 (29.3)	308 (19.7)	
85+	2,304 (20.9)	1,683 (4.1)	184 (33.5)	109 (7.0)	
Race/ethnicity					0.07
White	10,013 (91.8)	37,173 (92.2)	484 (89.5)	1,414 (92.1)	
Non-Whites	890 (8.2)	3,133 (7.8)	57 (10.5)	121 (7.9)	
Income					<0.0001
<\$38,000	1,601 (14.7)	5,345 (13.3)	98 (18.0)	218 (14.2)	
\$38,000- 47,999	2,564 (23.6)	9,145 (22.7)	131 (24.0)	293 (19.1)	
\$48,000- 62,999	3,053 (28.1)	11,419 (28.4)	127 (23.3)	424 (27.6)	
\$63,000 +	3,645 (33.6)	14,339 (35.6)	190 (34.8)	599 (39.1)	
Education					<0.0001
≥21%	1,358 (12.5)	4,518 (11.2)	61 (11.2)	208 (13.5)	
13-20.9%	2,575 (23.7)	9,242 (23.0)	148 (27.1)	338 (22.0)	
7-12.9%	3,854 (35.5)	14,769 (36.7)	196 (35.9)	521 (33.9)	
<7%	3,084 (28.4)	11,735 (29.2)	141 (25.8)	469 (30.5)	
Primary payor					<0.0001
Private insurance	1,197 (11.0)	5,082 (12.6)	57 (10.5)	214 (13.8)	
Uninsured/Medicaid/Medicare/Other government	9,738 (89.1)	35,292 (87.4)	488 (89.5)	1,335 (86.2)	
Facility type					<0.0001
Community cancer program	1,412 (12.8)	5,211 (12.8)	78 (14.2)	221 (14.2)	
Comprehensive community cancer center	6,377 (57.9)	25,823 (63.4)	335 (60.9)	948 (60.9)	
Academic research program	3,222 (29.3)	9,704 (23.8)	137 (24.9)	388 (24.9)	
Facility location					<0.0001
New England	1,129 (10.2)	3,200 (7.8)	35 (6.4)	126 (8.1)	
Mid Atlantic	1,661 (15.1)	6,993 (17.1)	89 (16.2)	290 (18.6)	
South Atlantic	2,567 (23.3)	8,263 (20.3)	137 (24.9)	315 (20.2)	
East North Central	2,137 (19.4)	8,651 (21.2)	109 (19.8)	291 (18.6)	
East South Central	597 (5.4)	1,729 (4.2)	27 (4.9)	63 (4.0)	
West North Central	819 (7.4)	3,265 (8.0)	43 (7.8)	91 (5.8)	
West South Central	512 (4.6)	2,111 (5.2)	26 (4.7)	99 (6.3)	
Mountain	441 (4.0)	1,729 (4.2)	20 (3.6)	56 (3.6)	
Pacific	1,168 (10.6)	4,866 (11.9)	64 (11.6)	231 (14.8)	
Urban/rural location					0.29
Metro counties	9,102 (85.7)	33,929 (86.0)	469 (87.8)	1,268 (85.1)	
Urban counties	1,326 (12.5)	4,934 (12.5)	57 (10.7)	201 (13.5)	
Rural counties	192 (1.8)	605 (1.5)	8 (1.5)	21 (1.4)	
Great circle distance					<0.0001
<50 miles	10,265 (94.4)	38,457 (95.5)	527 (96.5)	1,462 (95.2)	
≥50 miles	614 (5.6)	1,828 (4.5)	19 (3.5)	74 (4.8)	
Comorbidities/Deyo Score					<0.0001
0	8693 (78.8)	34,211 (83.8)	402 (73.1)	1315 (84.2)	
1	1873 (17.0)	5,614 (13.8)	117 (21.3)	213 (13.6)	
2	465 (4.2)	982 (2.4)	31 (5.6)	34 (2.2)	
Tumor Size					<0.0001
≤0.1 cm	157 (1.5)	563 (1.4)	9 (1.7)	23 (1.5)	
>0.1-0.5 cm	1,279 (11.8)	3,885 (9.7)	54 (10.1)	128 (8.4)	
>0.5-1.0 cm	3,785 (35.1)	13,597 (34.0)	132 (24.8)	419 (27.6)	
>1.0-2 cm	5,578 (51.7)	21,934 (54.9)	338 (63.4)	950 (62.5)	
Grade					<0.0001
Well differentiated	4,591 (43.5)	14,604 (37.6)	161 (31.4)	478 (32.5)	
Moderately differentiated	4,997 (47.4)	19,522 (50.2)	274 (53.4)	799 (54.3)	
Poorly differentiated or Undifferentiated	961 (9.1)	4,758 (12.2)	78 (15.2)	195 (13.3)	
Chemotherapy					<0.0001
None	10,679 (98.0)	3,8330 (95.7)	530 (97.8)	1,430 (94.5)	
Yes	224 (2.1)	1,732 (4.3)	12 (2.2)	83 (5.5)	

Table III. Univariate analysis of factors associated with survival.

Variable	Hazard ratio	95%CI	p-Value
Surgical margins/XRT group			
Negative margins without XRT	1.00		
Negative margins with XRT	0.42	0.40-0.44	<0.0001
Positive margins without XRT	1.79	1.55-2.07	<0.0001
Positive margins with XRT	0.50	0.43-0.57	<0.0001
Age			
70-74	1.00		
75-79	1.59	1.49-1.69	<0.0001
80-84	2.81	2.63-2.99	<0.0001
85+	5.37	5.00-5.76	<0.0001
Race/ethnicity			
White	1.00		
Non-Whites	1.02	0.93-1.11	0.69
Income			
<\$38,000	1.36	1.27-1.46	<0.0001
\$38,000- 47,999	1.28	1.21-1.37	<0.0001
\$48,000- 62,999	1.11	1.04-1.18	0.001
\$63,000 +	1.00		
Education			
≥21%	1.27	1.17-1.38	<0.0001
13-20.9%	1.18	1.10-1.26	<0.0001
7-12.9%	1.16	1.09-1.23	<0.0001
<7%	1.00		
Primary payor			
Private insurance	1.00		
Uninsured/Medicaid/ Medicare/Other government	1.16	1.08-1.25	<0.0001
Facility type			
Community cancer program	1.26	1.17-1.36	<0.0001
Comprehensive community cancer center	1.12	1.05-1.18	0.0001
Academic research program	1.00		
Facility location			
New England	1.24	1.12-1.37	<0.0001
Mid Atlantic	1.13	1.03-1.24	0.01
South Atlantic	1.28	1.18-1.40	<0.0001
East North Central	1.36	1.25-1.48	<0.0001
East South Central	1.33	1.17-1.51	<0.0001
West North Central	1.29	1.16-1.44	<0.0001
West South Central	1.18	1.04-1.34	0.01
Mountain	1.08	0.94-1.24	0.28
Pacific	1.00		
Comorbidities/Deyo Score			
0	1.00		
1	1.74	1.64-1.84	<0.0001
2	3.18	2.88-3.51	<0.0001
Tumor Size			
≤0.1 cm	0.83	0.68-1.02	0.07
>0.1-0.5 cm	0.74	0.68-0.81	<0.0001
>0.5-1.0 cm	0.82	0.78-0.87	<0.0001
>1.0-2 cm	1.00		
Grade			
Well differentiated	1.00		
Moderately differentiated	1.03	0.98-1.08	0.30
Poorly differentiated or Undifferentiated	1.22	1.13-1.31	<0.0001
Chemotherapy			
None	1.00		
Yes	0.72	0.62-0.84	<0.0001

Table IV. Multivariate analysis of factors associated with survival.

Variable	Hazard ratio	95%CI	p-Value
Surgical margins/XRT group			
Negative margins without XRT	1.00		
Negative margins with XRT	0.59	0.56-0.63	<0.0001
Positive margins without XRT	1.56	1.33-1.83	<0.0001
Positive margins with XRT	0.64	0.55-0.75	<0.0001
Age			
70-74	1.00		
75-79	1.54	1.44-1.65	<0.0001
80-84	2.49	2.32-2.67	<0.0001
85+	4.11	3.78-4.46	<0.0001
Race/ethnicity			
White	1.00		
Non-Whites	1.04	0.95-1.15	0.38
Income			
<\$38,000	1.17	1.06-1.29	0.003
\$38,000- 47,999	1.14	1.05-1.23	0.002
\$48,000- 62,999	1.03	0.96-1.10	0.46
\$63,000 +	1.00		
Education			
≥21%	1.04	0.93-1.16	0.53
13-20.9%	0.99	0.91-1.08	0.82
7-12.9%	1.07	1.00-1.15	0.06
<7%	1.00		
Primary payor			
Private insurance	1.00		
Uninsured/Medicaid/ Medicare/Other government	1.02	0.94-1.10	0.69
Facility type			
Community cancer program	1.13	1.04-1.23	0.005
Comprehensive community cancer center	1.14	1.07-1.21	<0.0001
Academic research program	1.00		
Facility location			
New England	1.21	1.09-1.36	0.0007
Mid Atlantic	1.13	1.03-1.25	0.01
South Atlantic	1.18	1.07-1.29	0.0007
East North Central	1.30	1.18-1.43	<0.0001
East South Central	1.21	1.05-1.39	0.008
West North Central	1.24	1.10-1.40	0.0003
West South Central	1.19	1.04-1.37	0.01
Mountain	1.11	0.96-1.29	0.17
Pacific	1.00		
Comorbidities/Deyo Score			
0	1.00		
1	1.66	1.56-1.77	<0.0001
2	2.90	2.61-3.22	<0.0001
Tumor Size			
≤0.1 cm	0.96	0.76-1.22	0.76
>0.1-0.5 cm	0.77	0.71-0.85	<0.0001
>0.5-1.0 cm	0.88	0.83-0.93	<0.0001
>1.0-2 cm	1.00		
Grade			
Well differentiated	1.00		
Moderately differentiated	1.02	0.97-1.08	0.43
Poorly differentiated or Undifferentiated	1.23	1.14-1.34	<0.0001
Chemotherapy			
None	1.00		
Yes	0.93	0.79-1.09	0.34

of an extensive intraductal component (24). However, there is a paucity of data to substantiate this position.

Assersohn *et al.* reported survival outcome of 70 patients with positive margins who received RT instead of re-excision. There was no significant difference in survival between the positive margins plus RT and negative margin groups ($p=0.5$) (25). However, this was a small cohort of patients with both invasive cancer and ductal carcinoma *in situ*. Additionally, the median age was 55, which represents a younger population of patients than ours.

We believe that our study is the largest to evaluate the impact of RT among elderly women with small, hormone-positive tumors who had a positive margin. In our study, we examined 53,950 patients aged ≥ 70 years and divided the cohort into four groups: 1) negative margins with XRT, 2) positive margins with XRT, 3) negative margins without XRT and 4) positive margins with RT. All patients were clinical and pathologic stage I, ER+ tumor and treated with anti-hormone therapy. Surprisingly, we found that RT was adequate to address those with positive margins.

There are several key findings that are worthy of mentioning. Patients with positive margins without RT had a significantly worst survival than the other 3 groups. This suggests that even among elderly patients, breast cancer remains an aggressive disease, despite treatment with anti-hormonal therapy. Another interesting finding is that even among those with negative margins, those that received radiation did better than those that did not. Finally, those that had positive margins and treated with RT, their survivals were comparable to those that had negative margins and treated with RT. These data suggest that receipt of RT imparts a survival advantage and that the decision to forego it should be given serious evaluation.

We have recently reported that outcomes in real-world practice are different than cooperative trials for this population of patients (26). In this study, we found that those who received RT had better survival outcomes than those who did not, revealing a discordant between real-world practice and randomized trials setting. Our explanation was that the advantages in the RT group may not have anything to do with the effect of RT *per se*, but rather due to better adherence to antihormonal therapy. It is likely that the RT group may have had more opportunities to be reminded of the need to be compliant with antihormonal therapy and that receipt of RT serves as a safety valve to ensure compliance with antihormonal therapy (26). We propose that this explanation might partly explain the observations in this current study. What is different between the real-world outcome paper and this paper is that the real-world outcome paper provided a broader, bird's eye view of the practice pattern of RT among elderly women with favorable, small, hormone-positive breast cancer, while this paper specifically focused on the interplay between RT and margin status.

One major limitation of our study is that we do not have information on breast cancer recurrence since such information was not captured in the data base. Whether or not recurrence is a harbinger of a poorer outcome cannot be answer in this study. Additionally, we lack cause-specific survival information.

Conclusion

In summary, RT for positive margins appears to be a viable alternative to re-excision among elderly women with small, hormone-positive breast cancer who received anti-hormone therapy following BCT.

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