Original Article

Omission of Radiation Therapy After Breast-Conserving Surgery in the United States

A Population-Based Analysis of Clinicopathologic Factors

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BACKGROUND: Radiation therapy (RT) after breast-conserving surgery (BCS) is associated with a significant reduction in ipsilateral breast tumor recurrence and breast cancer mortality rates in patients with early stage breast cancer. The authors of this report sought to determine which patients with breast cancer do not receive RT after BCS in the United States. **METHODS:** The Surveillance, Epidemiology, and End Results registry was used to determine the rates of RT after BCS for women with stage I through III breast cancer in the United States from 1992 through 2007. A multivariate analysis was performed to identify independent predictors of omission of RT. **RESULTS:** In total, 294,254 patients with invasive, nonmetastatic breast cancer were identified who underwent surgery from 1992 through 2007. Most patients (57%) underwent BCS; among those, 21.1% did not receive RT after BCS. The omission of RT increased significantly from 1992 (15.5%) to 2007 (25%). The receipt of RT also decreased significantly for patients with increased cancer stage, age <55 years, high-grade tumors, large tumors, positive or untested lymph node status, African American or Hispanic race, and negative or unknown estrogen receptor status. Significant geographic variation was observed in the rates of RT after BCS. **CONCLUSIONS:** The omission of RT after BCS was more common in recent years, especially among women who had an increased risk of breast cancer recurrence. This trend represents a serious health care concern because of the potential increased risk of local recurrence and breast cancer mortality. *Cancer* **2012;118:2004-13.** *© 2011 American Cancer Society.*

KEYWORDS: breast cancer, radiation, mastectomy, trends, population.

INTRODUCTION

In 1990, the National Institutes of Health Consensus Development Conference recommended breast-conserving surgery (BCS) plus radiation therapy (RT) as the preferred treatment for stage I and II breast cancer.[1] This recommendation was based on the results from randomized trials indicating equivalent overall survival rates for BCS plus RT and mastectomy.[2,3] Several randomized trials have demonstrated that local recurrence rates are significantly higher for patients who undergo BCS without RT.[2,4-9] The overview analysis from the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) recently reported that breast cancer mortality rates also were significantly higher for patients who did not receive RT after BCS.[10]

The patterns of surgical treatment for stage I and II breast cancer changed after the National Institutes of Health Consensus Conference.[11,12] By using a population-based cancer registry, Lazovich et al reported a significant increase in BCS rates after 1990.[12] In that study, the use of RT after BCS increased from 73.1% during 1983 to 1985 to 81.5% during 1990 to 1995. However, in a recent study using the Surveillance, Epidemiology, and End Results (SEER) registry, Freedman et al reported that the use of RT after BCS decreased significantly from 79.4% during 1988 to 66.4% in 2004; however, the factors associated with the omission of RT after BCS were not reported in their study.[13]

RT therapy may not be necessary for all patients after BCS, particularly those with favorable clinicopathologic characteristics, such as older age, low-grade tumors, small tumor size, positive estrogen receptor (ER) status, and negative

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axillary lymph nodes. Conversely, women with adverse patient and tumor characteristics may be harmed by the omission of RT. The objective of the current study was to determine which patients do not receive RT after BCS in the United States. If high-risk patients are not receiving RT after BCS, then strategies should be developed to ensure adequate local therapy for more patients.

MATERIALS AND METHODS

We used the SEER cancer registry database to examine trends in the surgical treatment of incident breast cancer.[14] We determined the rates of mastectomy, BCS alone, and BCS plus RT between 1992 and 2007 among women with nonmetastatic, invasive breast cancer (stages I-III). In the SEER database, the treatment planned is recorded as the first course of treatment (http://training.seer.cancer.gov/treatment [Accessed April 11, 2011]). In the case of RT for women who receive chemotherapy, SEER codes treatment as RT recommended unknown, as delivered, or as RT. Before 1998, treatments were included within 4 months of diagnosis; however, after 1998, every treatment was included within 1 year if there was no disease recurrence or progression.

We included women who were between ages 18 years and 79 years at diagnosis with unilateral, invasive breast cancer. We excluded women who did not undergo mastectomy or BCS. We also excluded women with bilateral or unstaged breast cancer; with unknown tumor size, grade, or laterality; women who were tested for lymph node status with no results reported; unknown radiation status; and those who were diagnosed by death certificate or at autopsy or whose deaths were reported only by a nursing home. We limited our analysis to 14 SEER registries that had adequate information on all variables. The step-wise ascertainment of our study cohort is listed in Table 1.

Trends in treatment rates over time were evaluated using the Cochran-Armitage test for trend. The null hypothesis tested is that there is no linear decrease in RT use over time. Multivariate logistic regression models were constructed to predict BCS versus mastectomy and BCS plus RT versus BCS alone while controlling for patient age, race, year of diagnosis, cancer stage, tumor size, tumor grade, ER status, lymph node status, histology, and registry. Model diagnostic tools included the Hosmer-Lemeshow goodness-of-fit test and classification[15] (for classification tables, see Table 2).

Table 1. Stepwise Cohort Ascertainment

Step	Total No.	No. of Cases Excluded (%)
Start: Female breast cancer cases diagnosed 1973-2007	965,306	
After excluding cases diagnosed before 1992	722,927	242,379 (25.11)
After excluding patients aged <18 y or >79 y at diagnosis	640,270	82,657 (11.43)
After excluding in situ cases	519,606	120,664 (18.85)
After excluding stage IV cases	496,082	23,524 (4.53)
After excluding cases with unknown stage	452,263	43,819 (8.83)
After excluding cases diagnosed in nursing home, by autopsy, or on death certificate	451,378	885 (0.20)
After excluding cases with unknown tumor size	447,303	4075 (0.90)
After excluding cases with unknown node positivity	442,532	4771 (1.07)
After excluding cases from Alaska and Rural Georgia registries	441,058	1474 (0.33)
After excluding histologies other than SEER codes 8500, 8501, 8503, 8504, 8520-8524	401,509	39,549 (8.97)
After excluding cases with unknown grade	367,597	33,912 (8.45)
After excluding all surgeries other than BCS or mast	362,391	5206 (1.42)
After excluding cases from Kentucky	348,483	13,908 (3.84)
After excluding cases without microscopic confirmation	348,482	1 (0)
After excluding bilateral cases or those with unknown laterality	348,468	14 (0)
After excluding cases which were not a first primary	300,364	48,104 (13.80)
After excluding cases from Louisiana in 2005	299,585	779 (0.26)
After excluding cases with unknown radiation	294,254	5331 (1.78)
After excluding cases with unknown race (multivariate analysis)	292,878	1376 (0.47)

Abbreviations: BCS, breast-conserving surgery; SEER, Surveillance, Epidemiology and End Results.

Survival was calculated in months from diagnosis to death. To determine cancer-specific survival, women who died of causes other than cancer were censored at the time of death. Kaplan-Meier techniques were used to compare unadjusted survival curves. Cox proportional hazards modeling was used to evaluate the impact of RT after BCS on survival while controlling for other factors, such as age, tumor characteristics, and geography.

Table 2. Classification Tables With Cutoff

Actual	No. Predicted 0	1	Percentage Correct
Logistic regression model predicting BCS[a]			
Y=0	81,362	44,638	64.6
Y=1	57,407	114,757	66.7
Percentage correctly classified			65.8
Logistic regression model predicting RT[b]			
Y=0	24,152	10,876	68.9
Y=1	54,559	77,291	58.6
Percentage correctly classified			60.8

Abbreviations; BCS, breast-conserving surgery; RT, radiation therapy.
[a] Hosmer Lemeshow chi-square statistic, 32.71 ($P \leq .0001$ [classification table with cutoff, $P = .600$]). Y = 0: mastectomy; Y = 1: BCS.
[b] Hosmer Lemeshow chi-square statistic, 46.69 ($P \leq .0001$ [classification table with cutoff, $P = .800$]). Y = 0: no RT; Y = 1: RT.

We conducted a series of analyses to assess whether our analytic decisions impacted our final results. For example, we examined whether grouping patients with unknown RT as "no RT" or removing them from the analysis changed the results; we observed no differences in the results, so we excluded those patients with unknown radiation status. Likewise, we evaluated registries that were added to the SEER database in 2000 to ensure that care practice in these registries did not impact trend evaluation, and the results were similar with and without these registries included in the analysis.

RESULTS

We identified 294,254 patients with invasive, nonmetastatic breast cancer who underwent surgery from 1992 through 2007. Most patients (57%) underwent BCS, and 43% underwent mastectomy. Patient and tumor characteristics are listed in Table 3. In multivariate analysis, the use of BCS, compared with mastectomy, increased significantly for women with a recent year of diagnosis, early stage breast cancer, age <70 years, low-intermediate tumor grade, small tumor size, lymph node-negative or not tested status, nonlobular histology, non-Hispanic white or African American race, and ER-positive breast cancer (Table 4). We observed considerable geographic variation in BCS rates; Iowa had the lowest BCS rate (44.4%), and Connecticut had the highest rate (65.7%) (Table 5).

Among the 167,696 patients treated with BCS, 21.1% did not receive RT after surgery (Table 3). On regression analysis, the use of RT decreased significantly for women who were diagnosed in recent years and for women with increased cancer stage, aged <55 years, high-grade tumors, large tumor size, lymph node-positive or not tested status, African American or Hispanic race, and

Table 3. Comparison of Mastectomy, Breast-Conserving Surgery (BCS) With Radiation Therapy (RT), and BCS Without RT

Characteristic	Treatment Group, % Mastectomy n = 126,558	BCS and RT, n = 132,342	BCS Alone, n = 35,354[a]
Total percentage of patients	43	45	12 (21.1)
Patient age, y			
18-39	53	35.1	11.9 (25.3)
40-54	43.6	44.2	12.2 (21.6)
55-69	40	48.6	11.4 (19)
≥70	44.2	43	12.8 (22.9)
Stage			
I	29.9	57.6	12.6 (17.9)
II	52.2	35.5	12.3 (25.7)
III	83.9	10.9	5.2 (32.3)
Grade			
Low-intermediate	38.8	49.3	11.9 (19.4)
High	49.8	38	12.2 (24.3)
Tumor size, cm			
<1	29.7	58	12.3 (17.5)
1.0-1.9	32.9	54	13.2 (19.6)
2.0-4.9	53.6	34.6	11.8 (25.4)
≥5.0	84.2	10.4	5.4 (34.2)
Lobular histology			
No	41.7	46.1	12.2 (20.9)
Yes	50.4	38.7	10.9 (22)
Lymph node status			
Negative	35.9	53	11.2 (17.4)
Positive	58.4	30.8	10.8 (26)
Not tested	22.9	42.2	35 (45.3)
Race			
Non-Hispanic white	41.4	47	11.6 (19.8)
African American	45.2	39.1	15.7 (28.6)
American Indian	46.8	42.8	10.4 (19.5)
Asian	50.9	39.8	9.3 (18.9)
Hispanic	47.1	39.3	13.6 (25.7)
Other/unknown	40.6	35.8	23.7 (39.8)
ER status			
Positive	47.7	40	12.3 (23.5)
Negative	40.8	48.1	11.1 (18.8)
Unknown	49.2	33.4	17.4 (34.3)
Year diagnosed			
1992-1997	51.7	40.5	7.8 (16.1)
1998-2002	42.3	45.4	12.3 (21.3)
2003-2007	39.3	46.8	13.9 (22.9)

Abbreviations: ER: estrogen receptor.
[a] Values in parenthesis indicate the proportion of patients who underwent BCS without RT.

Table 4. Multivariate Predictors of Treatment

	BCS vs Mastectomy			BCS: RT vs No RT		
Variable	OR	95% CI	*P*	OR	95% CI	*P*
Year diagnosed						
1992-1997			Ref			Ref
1998-2002	1.640	1.604-1.677	<.0001	0.645	0.619-0.671	<.0001
2003-2007	1.895	1.853-1.938	<.0001	0.535	0.514-0.557	<.0001
Stage						
I			Ref			Ref
II	0.857	0.832-0.883	<.0001	0.806	0.768-0.846	<.0001
III	0.403	0.379-0.427	<.0001	0.727	0.652-0.812	<.0001
Patient age, y						
18-39			Ref			Ref
40-54	1.210	1.171-1.25	<.0001	1.094	1.037-1.153	.001
55-69	1.210	1.171-1.251	<.0001	1.217	1.153-1.284	<.0001
≥70	0.912	0.88-0.944	.0019	1.061	1.001-1.124	.045
Grade						
Low-intermediate			Ref			Ref
High	0.869	0.853-0.885	<.0001	0.908	0.881-0.935	<.0001
Tumor size, cm						
<1			Ref			Ref
1.0-1.9	1.032	1.009-1.056	.006	0.848	0.820-0.877	<.0001
2.0-4.9	0.556	0.540-0.572	<.0001	0.773	0.738-0.809	<.0001
≥5.0	0.181	0.171-0.19	<.0001	0.687	0.623-0.759	<.0001
Lymph node status						
Negative			Ref			Ref
Positive	0.636	0.621-0.653	<.0001	0.777	0.744-0.810	<.0001
Not tested	2.630	2.506-2.760	<.0001	0.255	0.243-0.267	<.0001
Any lobular history						
No			Ref			Ref
Yes	0.683	0.668-0.698	<.0001	0.974	0.939-1.010	.150
Race						
Non-Hispanic white			Ref			Ref
African American	1.049	1.018,1.081	.002	0.800	0.766-0.835	<.0001
Asian	0.550	0.533,0.568	<.0001	1.013	0.958-1.071	.658
Hispanic	0.846	0.822,0.871	<.0001	0.928	0.888-0.970	.001
American Indian	0.893	0.784-1.017	.087	0.909	0.731-1.131	.393
ER status						
Positive			Ref			Ref
Negative	0.957	0.937-0.979	<.0001	0.843	0.814-0.873	<.0001
Unknown	0.734	0.715-0.754	<.0001	0.501	0.482-0.521	<.0001

Abbreviations: BCS, breast-conserving surgery; CI, confidence interval; ER, estrogen receptor; OR, odds ratio; Ref, referent category; RT, radiation therapy.

ER-negative or ER-unknown breast cancer (Table 4). We observed considerable geographic variation in the omission of RT after BCS; Los Angeles had the highest rate (30.5%), whereas Seattle had the lowest rate (8.1%) (Table 5). However, we did not observe any association between mastectomy rates and the omission of RT. Although BCS use increased over the study period, the omission of RT after BCS increased significantly from 15.5% in 1992 to 25% in 2007 ($P < .001$). These trends were observed for all age groups, races, tumor sizes, and lymph node status (Fig. 1). We compared the trends for patients aged <70 years with those for patients aged ≥70 years and observed that the use of RT after BCS significantly decreased from 1992 to 2007 for both groups but especially for patients aged <70 years (Fig. 1, top left). On multivariate analysis, factors that were associated independently with the omission of RT were the same in both groups (data not shown). Because breast radiation for left-sided breast cancer has been associated with cardiac toxicity,[16] we evaluated the use of RT after BCS for

Table 5. Geographic Variation in Treatment

	Percentage of Cases			
Registry	Mastectomy	BCS	BCS[a]	
			RT	No RT
San Francisco-Oakland	38.6	61.4	88.2	11.8
Connecticut	34.3	65.7	69.9	30.1
Metropolitan Detroit	46.8	53..2	80.4	19.6
Hawaii	41.4	58.6	83.3	16.7
Iowa	55.6	44.4	91.8	8.2
New Mexico	46.9	53.1	77.6	22.4
Seattle	41.3	58.7	91.9	8.1
Utah	50,4	49.6	77.7	22.3
Metropolitan Atlanta	43.7	56.3	77.9	22.1
San Jose-Monterey	45.7	54.3	87	13
Los Angeles	42.7	57.3	69.5	30.5
Greater California[b],[c]	43.	57	78.8	21.2
Louisiana[c],[d]	52.2	47.8	75.4	24.6
New Jersey[c]	36.4	63.6	71.7	28.3

Abbreviations: BCS, breast-conserving surgery; RT, radiation therapy.

[a] Among the patients who underwent BCS, the proportions that received RT or no RT are indicated.

[b] Includes all areas of California except for San Francisco-Oakland, Los Angeles, and San Jose-Monterey.

[c] Data were available only for patients who were diagnosed from 2000 through 2005.

[d] Cases from 2005 were excluded because of concerns about follow-up after Hurricane Katrina.

right-sided and left-sided breast cancer, and we did not identify any significant differences (data not shown).

Multivariate models were used to assess the impact of BCS and RT use on breast cancer mortality rates after controlling for prognostic and regional factors (Table 6). In all models, BCS plus RT was associated with significantly improved breast cancer survival rates compared with mastectomy or BCS without RT (Fig. 2). Because most patients with ER-positive breast cancer receive endocrine treatment, we evaluated breast cancer mortality rates with RT based on ER status. The magnitude of the benefit was similar for women with ER-positive breast cancer (hazard ratio [HR], 0.693), ER-negative breast cancer (HR, 0.765), and breast cancer with unknown ER status (HR, 0.733). The association between treatment and mortality was maintained when women with tumors >5 cm were removed from the analysis, because such large tumors are a contraindication for BCS.

When the analysis was controlled for treatment, mortality was significantly higher for women with large tumors, ER-negative breast cancer, lymph node

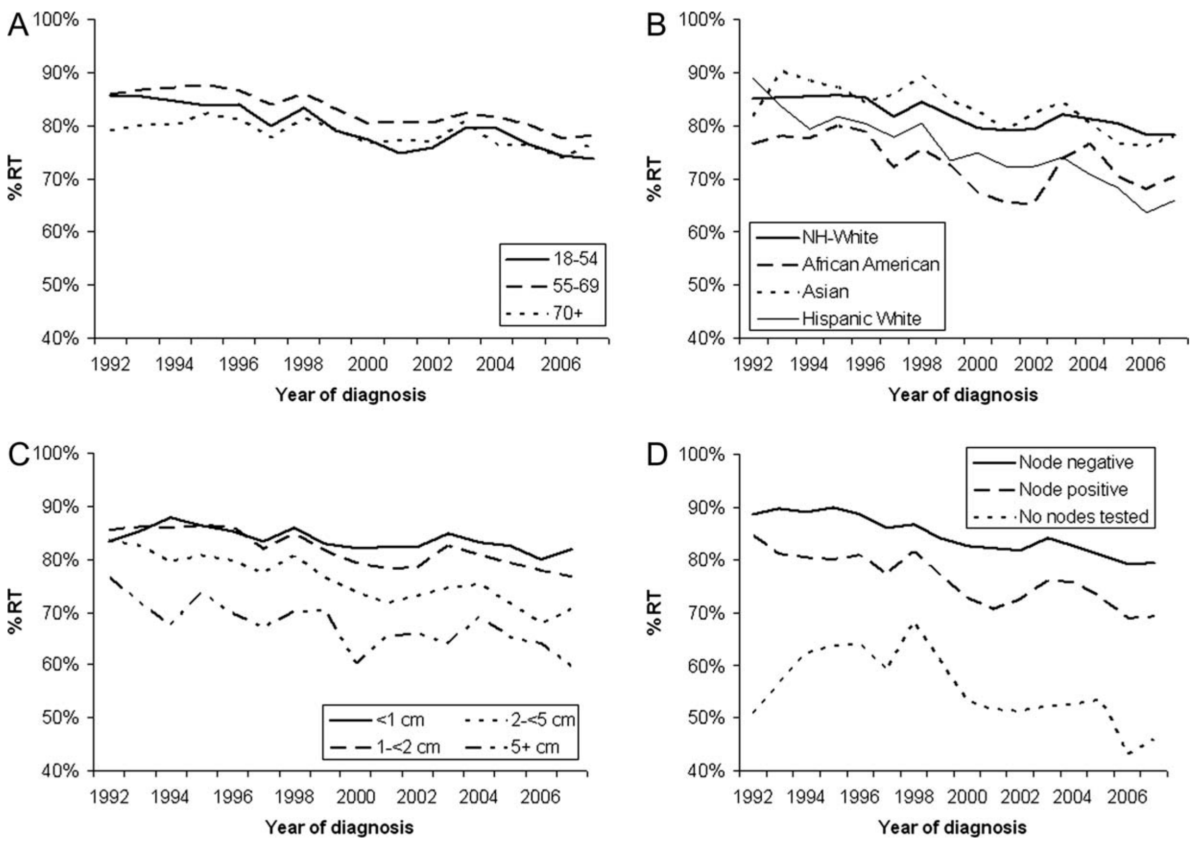


Figure 1. Trends in the receipt of radiation therapy (RT) after breast-conserving surgery (BCS) are illustrated according to (*Top Left*) patient age, (*Top Right*) patient race, (*Bottom Left*) tumor size, and (*Bottom Right*) lymph node status. $P < .0001$ for all groups (Cochran-Armitage test for trend). NH indicates non-Hispanic.

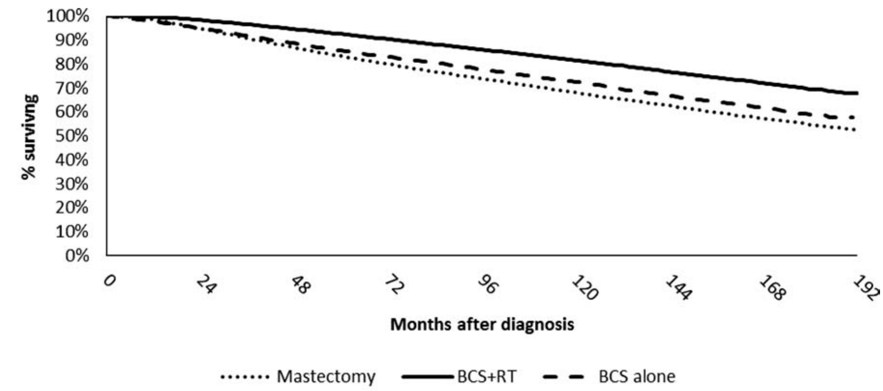
Table 6. Hazard of Mortality[a]

Variable	Overall HR	Overall P	ER Status: Positive HR	Positive P	Negative HR	Negative P	Unknown HR	Unknown P
Treatment								
Mastectomy	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref
BCS no RT	0.989	.6762	1.036	.379	0.964	.3798	0.962	.5608
BCS and RT	0.722	<.0001	0.693	<.0001	0.765	<.0001	0.733	<.0001
Stage								
I	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref
II	1.361	<.0001	1.378	<.0001	1.357	<.0001	1.421	<.0001
III	2.342	<.0001	2.353	<.0001	2.349	<.0001	2.434	<.0001
Patient age, y								
18-39	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref
40-54	0.808	<.0001	0.714	<.0001	0.906	.007	0.75	<.0001
55-69	0.927	.0028	0.845	<.0001	1.014	.7253	0.819	.0032
≥70	1.14	<.0001	1.055	.1894	1.254	<.0001	0.923	.2852
ER status								
Positive	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref
Negative	1.926	<.0001	NA	NA	NA	NA	NA	NA
Not tested	1.26	<.0001	NA	NA	NA	NA	NA	NA
Lymph node status								
Positive	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref
Negative	0.434	<.0001	0.444	<.0001	0.442	<.0001	0.43	<.0001
Not tested	1.076	.0305	1.196	.0003	1.05	.3988	0.947	.4961
Grade								
Low-intermediate	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref
High	1.859	<.0001	1.999	<.0001	1.354	<.0001	2.088	<.0001
Tumor size, cm								
<1.0	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref
1-1.9	1.678	<.0001	1.612	<.0001	1.644	<.0001	1.913	<.0001
2.0-4.9	2.824	<.0001	2.922	<.0001	2.455	<.0001	3.182	<.0001
≥5.0	3.404	<.0001	3.552	<.0001	2.85	<.0001	4.235	<.0001
Lobular histology								
No	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref
Yes	0.869	<.0001	0.897	.0003	0.953	.3836	0.785	.0003
Race								
Non-Hispanic white	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref
African	1.512	<.0001	1.513	<.0001	1.415	<.0001	1.657	<.0001
American Indian	1.531	<.0001	1.531	.0037	1.569	.0025	0.969	.9382
Hispanic	1.088	.0019	1.074	.0856	1.098	.0291	1.028	.6731
Asian	0.866	<.0001	0.95	.2703	0.787	<.0001	0.775	.0076
Year diagnosed								
1992-1996	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref
1997-2000	0.817	<.0001	0.786	<.0001	0.876	<.0001	0.816	<.0001
2001-2005	0.742	<.0001	0.691	<.0001	0.836	<.0001	0.711	<.0001

Abbreviations: BCS, breast-conserving surgery; ER, estrogen receptor; HR, hazard ratio; NA, not applicable; Ref, referent category; RT, radiation therapy.
[a] Multivariate analysis included Surveillance, Epidemiology, and End Results registry (results not shown). Patients with unknown RT status were excluded from the analysis.

metastases, and higher grade tumors. Women between ages 40 years and 69 years had lower mortality rates than women who were aged <40 years or >70 years at diagnosis. After controlling for other factors, Asian race was associated with the lowest mortality rate. Mortality decreased in the recent years of our study period. We also evaluated potential measures of quality of care, including failure to assess ER status or to evaluate lymph node status, and both were associated significantly with increased mortality. Within ER categories (positive, negative and

A



Number remaining

	0	24	48	72	96	120	144	168	192
Mastectomy	126558	100515	75075	52439	32369	21191	12688	5569	206
BCS+RT	132342	107579	80715	55687	33136	19946	20433	4404	131
BCS alone	35354	26139	18377	11646	5864	3271	1597	609	19

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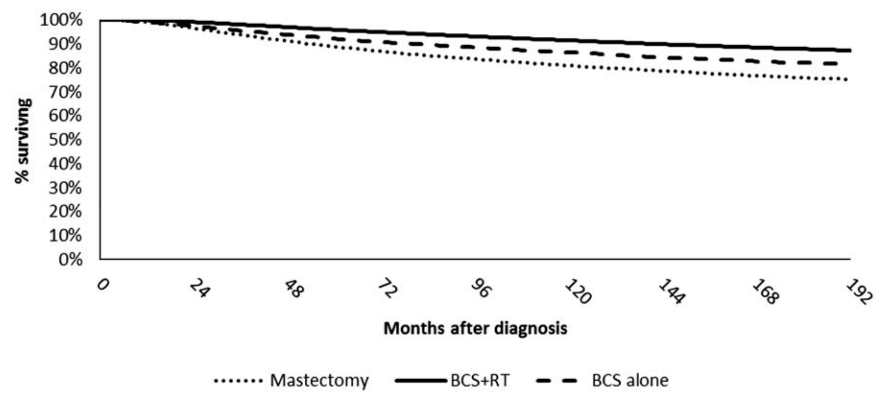

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BCS alone	35354	26139	18377	11646	5864	3271	1597	609	19

Figure 2. These Kaplan-Meier survival curves illustrate (*Top*) overall survival and (*Bottom*) cancer-specific survival according to treatment received ($P > .001$ for both). BCS indicates breast-conserving surgery; RT, radiation therapy.

unknown), similar patterns were observed, suggesting that ER status is an independent factor that does not change the relative influence of other variables in our model.

DISCUSSION

In this population-based study, we observed important changes in the treatment of nonmetastatic breast cancer in the United States from 1992 to 2007. Although the rates of BCS increased substantially, the receipt of RT after BCS decreased markedly. This trend was not limited to patients who had a low risk of recurrence after BCS. On the contrary, the omission of RT after BCS increased significantly for women who had increased cancer stage, young age, high-grade tumors, large tumors, lymph node-positive or not tested status, African American or Hispanic race, and negative or unknown ER status. Other investigators have reported that the omission of RT after BCS is associated with older age,[17,18] African American race,[17-19] Hispanic race,[19] Medicaid insurance coverage,[19] widowed or never married status,[20] patient comorbidities,[18] inner quadrant tumor location,[21] lymph node metastases,[21] negative or unknown ER status,[22] and larger tumor size.[23]

We observed considerable variation in the use of RT after BCS across geographic areas. Other investigators also have reported significant geographic variation in the use of BCS and RT.[24,25] Nattinger et al reported that women who resided $\geq$40 miles from a hospital with a radiation therapy center were less likely to receive BCS.[25] We did not observe any association between mastectomy rates and omission of RT. Thus, although it is possible that areas with high mastectomy rates offer less comprehensive care for BCS recipients, we were unable to detect this pattern at the SEER registry level.

Declining rates of RT after BCS ultimately may forecast increased local recurrence rates after BCS. Several randomized trials have demonstrated that local recurrence rates are significantly higher if RT is omitted after BCS.[2,4-9] In a recent meta-analysis, the EBCTCG estimated that the absolute 5-year local recurrence risk is 19% lower for women who receive RT after BCS, and the absolute benefit was greater in younger women.[10] In our population-based analysis, we observed that the group of women who are most likely to benefit from RT is the same group that had significantly lower rates of RT. Because of these trends, more women may require mastectomy or additional systemic therapy to treat local recurrences of breast cancer.

Although individual randomized trials have not demonstrated a survival difference between BCS alone and BCS plus RT, the EBCTCG analysis demonstrated a significantly increased risk of death from breast cancer for patients who did not receive RT (BCS plus RT alone, 30.5%; BCS alone, 35.9%).[10] Moreover, other non-randomized studies have demonstrated similar findings.[18,20] The results from our population-based study are consistent with the ECTCG study. Indeed, our study indicated that increased mortality rates with the omission of RT were observed for all patients regardless of ER status. Because of the trends reported here, breast cancer mortality rates may increase in the future.

It is noteworthy that, in contrast to the findings from randomized trials, we observed that the adjusted breast cancer mortality rates for women who received RT after BCS were significantly lower than the rates for women who underwent mastectomy. This pattern was maintained when women with the largest tumors were removed from analysis. Although selection bias partially may explain our results, an alternative hypothesis is that women who receive RT after BCS may receive improved multidisciplinary cancer care. This disparity would be less likely to occur in a controlled randomized trial. For women to receive both RT and BCS, referral to at least 1 oncology specialist is required. In contrast, women who receive BCS alone or who undergo mastectomy alone may not necessarily be evaluated by a medical or radiation oncologist. Consequently, women who are evaluated by breast cancer specialists are more likely to receive endocrine therapy or systemic chemotherapy, which reduces mortality rates for all stages of breast cancer compared with no systemic therapy. Thus, the improved survival rate associated with RT may reflect more comprehensive breast cancer care. In our study, women who received RT after BCS were more likely to have known ER status and lymph nodes evaluated, again consistent with a quality-of-care hypothesis. Unfortunately, SEER does not contain information of evaluation by a medical oncologists or the use of endocrine or systemic chemotherapy to allow direct testing of this hypothesis.

The reasons for the increased omission of RT after BCS, particularly among high-risk patients, are unclear. The daily requirement of RT for about 6 weeks likely contributes to the observed trends. Transportation may be difficult for some patients and particularly for elderly women, employed women, and those who live in rural locations. Also, because of the complex multidisciplinary nature of modern breast cancer treatment, "handoffs" between surgeons, medical oncologists, and radiation oncologists may not occur smoothly, particularly among nonaffiliated physicians and institutions. Finally, some patients may overestimate the frequency and severity of side effects during and after RT.

The independent association between unfavorable tumor characteristics (large tumor size, lymph node metastases) and omission of RT is counterintuitive. Given the lack of data, we can only speculate on this observation. We hypothesize that this effect may be secondary to fumbled handoffs between cancer treatment providers. Patients with favorable tumor characteristics who do not require adjuvant chemotherapy undergo surgery and are referred for RT within a few weeks. Conversely, patients with unfavorable tumor characteristics undergo surgery followed by several months of chemotherapy and are then referred for RT. Perhaps this increased time interval between surgery and RT accounts for this observation among patients who have unfavorable tumor characteristics. Also, patients may confuse the goals of chemotherapy with those of RT ("I just had 4 months of chemotherapy: Why do I need RT too?"). Finally, patients may develop cancer treatment fatigue after surgery and several months of chemotherapy and may decide to forgo RT.

Several strategies have been used to enhance the appropriate delivery of RT after BCS for more patients. The web-based program IBTR! version 2.0 (available at: http://160.109.101.132/ibtr/ [Accessed April 11, 2011]) provides quantitative estimates of the risk of local recurrence with and without RT after BCS.[26] These decision aids may give patients and providers more useful information on the benefits of RT after BCS. Patient navigators can be used to assist patients through the complex maze of multidisciplinary breast cancer, especially for patients with unfavorable tumor characteristics who require several months of adjuvant chemotherapy before initiating RT. Because African American race is associated significantly with the omission of RT, this population should be especially targeted to prevent inadequate treatment. Other innovative strategies have been initiated to reduce the likelihood of fumbled handoffs between different breast cancer specialists in nonaffiliated clinics. Bickell et al recently described a prospective tracking system to ensure multidisciplinary care for more breast cancer patients in New York City.[27] Because we observed significant geographic variation in the rates of radiation therapy after BCS, improved resource allocation and distribution may be necessary.

Several studies currently are evaluating novel fractionation schemes and treatment techniques to allow faster and safer RT delivery. The National Surgical Adjuvant Breast and Bowel Project B39/Radiation Therapy Oncology Group 0413 protocol is a phase 3 randomized trial comparing conventional whole-breast RT with partial breast irradiation (PBI). In that study, PBI includes high-dose-rate, multicatheter brachytherapy; high-dose-rate, single-catheter balloon brachytherapy (MammoSite, Hologic, Inc., Bedford, Mass); or 3-dimensional, conformal, external-beam RT. In a recently published analysis using the SEER registry, Abbott et al reported that the use of balloon catheter brachytherapy increased by 1600% from 2000 to 2007 in the United States.[28] Targeted intraoperative partial-breast RT is another innovative strategy that delivers a single fraction of RT to the tumor site at the time of BCS.[29] Finally, accelerated hypofractionated RT delivered over 3 weeks represents an attractive alternative to whole-breast RT after BCS. In a prospective randomized trial, Whelan et al reported that local recurrence rates at 10 years were not significantly different between accelerated, hypofractionated whole-breast RT and standard RT.[30]

Because our study used cancer registry data from SEER, detailed patient and tumor information that may have influenced treatment were not available. Important factors regarding family history, genetic testing results, human epidermal growth factor receptor (Her2/*neu*) status, patient comorbidities, receipt of systemic chemotherapy, tumor margin status, and mammographic findings were not available to us. In addition, information regarding endocrine treatment is not reported by SEER. Our assessments fit points to variance that were not fully explained by the factors included in our model. Several of these are discussed above, and we expect that, with a richer array of variables, we would be able to more accurately predict the use of BCS and RT. However, we have no reason to worry that our models are unstable or that our results are invalid. Despite the potential limitations of our study, SEER includes large numbers of patients from diverse locations and practices in the United States.

The omission of RT after BCS represents a serious health care concern because of the potential increased risk of local recurrence and breast cancer mortality. Nevertheless, many registries in diverse areas of the United States deliver adequate local breast cancer therapy to a high proportion of women. If the trend of declining use of RT is to be reversed, then strategies must be developed and implemented to correct these deficiencies.

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