Adherence to Long-Term Surveillance Mammography Among Women With Ductal Carcinoma In Situ Treated With Breast-Conserving Surgery

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A B S T R A C T

Purpose

Breast-conserving surgery (BCS) is an effective treatment for ductal carcinoma in situ (DCIS) but women who undergo BCS remain at risk for recurrences. Whether mammographic surveillance after BCS occurs and by whom is not known.

Methods

We reviewed medical records of women diagnosed with DCIS between 1990 and 2001 and treated with BCS. Using descriptive statistics, generalized estimating, and logistic regression modeling, we examined the rates and predictors of surveillance mammography over a 10-year period after BCS.

Results

The cohort included 3,037 women observed for a median of 4.8 years (range, 0.5 to 15.7). Of the 2,676 women observed for at least 1 year after BCS, most (79%) had at least one surveillance mammogram during the first year of follow-up; 69% in year 5 and 61% in year 10. Among those observed for 5 years, surveillance mammograms were more likely among women age 60 to 69 years (odds ratio [OR], 1.72; 95% CI, 1.26 to 2.34), users of menopausal hormone therapy at diagnosis (OR, 1.26; 95% CI, 1.01 to 1.57) as well as those treated with adjuvant radiation (OR, 1.28; 95% CI, 1.08 to 1.53) and adjuvant radiation with tamoxifen (OR, 1.61; 95% CI, 1.13 to 2.30). Surveillance mammograms were less likely among obese women (OR, 0.70; 95% CI, 0.56 to 0.86). The findings were similar among women observed for 10 years. Only 34% and 15% of women observed for 5 and 10 years, respectively, had a surveillance mammogram during each year of follow-up.

Conclusion

Surveillance mammography after BCS among insured women with DCIS often did not occur yearly and declined over time after treatment. Patients and providers must remain vigilant about surveillance after BCS.

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INTRODUCTION

The rates of diagnosis of ductal carcinoma in situ (DCIS), a localized precursor to invasive breast cancer, have been increasing over the past several decades. In 2007, more than 60,000 new cases of DCIS were estimated in the United States—accounting for approximately 25% of all breast cancer diagnoses.¹ The dilemma facing patients with DCIS and their clinicians is that the natural history and appropriate treatment for DCIS remain unclear.² Before the 1980s, virtually all women with breast cancer, in situ as well as invasive, were treated with mastectomy. In the 1990s, trials demonstrated that breast-conserving surgery (BCS) is an appropriate treatment strategy for most women with DCIS.³⁻⁵

Although there are still some geographic variations, BCS has become the most common treatment for women with DCIS.⁶

Unlike women with DCIS treated with mastectomy, those treated with BCS must remain vigilant about surveillance for ipsilateral recurrences of DCIS and newly diagnosed invasive breast cancer; up to 20% of women with DCIS will have a recurrence within 5 years and approximately 50% of recurrences will be invasive breast cancer.³⁻⁵ Further, women with DCIS are at a two to four-fold higher risk of developing cancer in the contralateral breast than women without prior DCIS.^{7,8} Because recurrences after DCIS most commonly occur in the ipsilateral breast, mammographic surveillance for recurrences is important. While optimal

surveillance of women with DCIS treated with BCS remains uncertain,² annual mammography is generally recommended.^{9,10} However, the extent to which women with DCIS who are treated with BCS undergo surveillance, and whether surveillance varies by patient characteristics and/or adjuvant treatment, are unknown. The goal of our study was to examine the rates and predictors of surveillance mammography among women in the United States with DCIS after treatment with BCS.

METHODS

Setting

The study was conducted under the auspices of the National Cancer Institute–funded Cancer Research Network (CRN), a consortium of 11 (now 13) integrated health care delivery systems with more than 10 million enrollees.¹¹ The overall goal of the CRN is to increase the effectiveness of preventive, curative, and supportive interventions for major cancers through a program of collaborative research, and to determine the effectiveness of cancer control interventions that span the natural history of major cancers among diverse populations and health systems. Three sites contributed patients to this study: Harvard Pilgrim Health Care, Kaiser Permanente Northern California, and Kaiser Permanente Southern California; the institutional review boards from each approved the study.

Sample Selection and Follow-Up

We identified all women diagnosed with a first unilateral DCIS between 1990 and 2001 and treated with BCS. Women were eligible if they were younger than 85 years of age at diagnosis and had no prior breast cancer or invasive cancer at another site. Women were excluded if the index breast cancer diagnosis was bilateral at the time of diagnosis, if the majority of medical care for their DCIS was obtained from providers outside one of the three sites, or if they had fewer than 6 months of follow-up after initial DCIS diagnosis.

For this analysis of surveillance after BCS, we began follow-up 12 months after DCIS diagnosis which allows ample time for peridiagnostic evaluations and/or re-excisions to be completed and routine surveillance to begin. The follow-up ended at the time of diagnosis of new or recurrent ipsilateral DCIS and/or invasive breast cancer, new contralateral DCIS and/or invasive breast cancer, last follow-up date recorded in the medical record, date of death, or the end of the study period (February 24, 2006), whichever occurred first.

Data Sources

Cancer registries were used to identify women diagnosed with DCIS at the Kaiser Permanente sites. These registries are part of or feed into the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) program of registries and provide information on birth date, race/ethnicity, laterality of the index DCIS, surgical treatment, and treatment with radiotherapy. The registries were also used to exclude women with prior cancer diagnoses. At Harvard Pilgrim Health Care, women with incident DCIS treated with BCS were identified using claims and electronic outpatient medical records. Specifically, in order to avoid missing any women with DCIS, this site used claims data to identify all women with DCIS (including those with invasive components and lobular carcinoma in situ) treated with BCS, and then searched through the electronic medical records to confirm incident DCIS cases without invasion.

Medical records of potentially eligible patients were reviewed at all sites to confirm the initial diagnosis, laterality, and treatment of the index DCIS, and to obtain information on subsequent breast cancer events. Data were collected on patient and clinical factors at the time of index DCIS (eg, height, weight, menopausal status, hormone replacement therapy, family history of breast cancer, and history of diabetes). Information was collected on all mammograms including the dates, indications and results. The indications were coded as 0 = previous assessment incomplete, 1 = follow-up after DCIS, asymptomatic, 2 = patient had symptoms, 3 = new abnormal breast exam or mammogram (unrelated to initial DCIS), and 9 = unknown. The results were coded as 0 = assessment incomplete, 1 = normal (negative), routine follow-up recom-

mended, 2 = benign findings (eg, cyst); routine follow-up recommended, 3 = probably benign; short-term follow-up (< 1 year, usually 6 months), 4 = suspicious of malignancy; order biopsy, 5 = highly suspicious of malignancy; order biopsy, and 9 = unknown.

Operational Definition of Surveillance Mammograms

Surveillance mammograms were defined as those mammograms coded by the medical record abstractors as having an indication of follow-up after DCIS, asymptomatic. We excluded mammograms that occurred within 60 days from a prior mammogram that was coded as incomplete, normal, or benign as these were likely follow-up mammograms and not surveillance; mammograms that occurred within 180 days after a prior mammogram that was coded as short-term follow-up, suspicious or highly suspicious as these were likely diagnostic; and mammograms that occurred within 180 days from a prior mammogram for which the indication was coded as unknown. To allow for possibly different surveillance protocols used by clinicians over the span of this study, mammograms done within 120 to 180 days after a prior mammogram coded as normal or benign were considered surveillance and were included in this analysis.

Statistical Analyses

First, we described the characteristics of the cohort and calculated the percentage of women who had at least one surveillance mammogram per each 12-month period of follow-up (starting 1 year after DCIS diagnosis up to 10 years of follow-up). Analysis for each interval was restricted to women who were in follow-up for that entire 12-month period. We calculated the average number of surveillance mammograms per woman during each year of follow-up.

Second, to determine the association between patient characteristics and the likelihood of yearly surveillance mammograms over the 5- and 10-year periods of follow-up, we used logistic regression modeling for longitudinal data with estimation via generalized estimating equations.¹² We assumed an unstructured working covariance matrix correlation covariance approach based on the examination of the correlation matrix. The generalized estimating equations method accounts for correlations in repeated measures of yearly surveillance mammograms (yes/no) within persons nested in site and uses all available data points. Specifically, the analysis accounted for the fact that women who have yearly mammograms are more likely to continue regular surveillance than those who do not (whether due to their own behaviors, or the practices of their providers and/or clinical sites). In the regression models, we adjusted for clinically significant patient covariates noted in Table 1, year of follow-up and clinical site. In the main analyses presented, we used a definition of annual mammograms as those occurring every 12 months. To give credit to women who had mammograms just before or after a 12-month period, we conducted sensitivity analyses allowing for an interval of 9 to 15 months as an acceptable measure of yearly mammography. These results were similar to those in the main analysis and are not presented.

Finally, we determined the prevalence of annual surveillance over the 5-year and 10-year follow-up by calculating the percentage of women who had surveillance mammograms every year for all 5 years of follow-up and for all 10 years of follow-up. We then used the ordinary logistic regression to model the predictors of annual surveillance, (outcome = having five mammograms over 5 years; 0 = no and 1 = yes), adjusting for the patient covariates, year of diagnosis, and site. Due to small sample sizes, we did not model the predictors of annual surveillance in the cohort of women observed for 10 years.

RESULTS

Of the 3,668 potentially eligible DCIS patients identified by the cancer registries or electronic medical records, 82 were excluded due to incomplete or unavailable medical records. Of the remaining 3,586 women, 520 were ineligible for one or more of the following reasons: miscoded as having DCIS in the tumor registry ($n = 97$), synchronous cancer in the uninvolved or contralateral breast ($n = 29$), prior breast cancer ($n = 91$), prior invasive cancer at another site ($n = 125$),

Table 1. Patient Demographics and Clinical Characteristics of the Women in the DCIS Cohort

Characteristic	No.	%
Total	3,037	100.0
Age at diagnosis, years		
< 50	776	25.6
50-59	865	28.5
60-69	814	26.8
≥ 70	582	19.2
Race		
Asian	362	11.9
Black	292	9.6
Hispanic	263	8.7
Other	8	0.3
White	2,075	68.3
Unknown	37	1.2
Body mass index at diagnosis		
< 25	1,139	37.5
25-29	923	30.4
≥ 30	672	22.1
Unknown	303	10.0
Menopausal status at diagnosis		
Pre/perimenopausal	875	28.8
Postmenopausal	2,095	69.0
Unknown	67	2.2
Family history of breast cancer at diagnosis		
Yes	539	17.8
No	2,427	79.9
Unknown	71	2.3
Diabetes at diagnosis		
Yes	220	7.2
No	2,810	92.5
Unknown	7	0.2
Menopausal hormone therapy use at diagnosis		
Former	1,265	41.7
Current	648	21.3
Never	870	28.6
Unknown	254	8.4
Diagnosis year		
1990-1991	257	8.5
1992-1993	357	11.8
1994-1995	449	14.8
1996-1997	564	18.6
1998-1999	677	22.3
2000-2001	733	24.1
Treatment of DCIS		
BCS alone	1,298	42.7
BCS/radiation	1,268	41.8
BCS/tamoxifen	132	4.3
BCS/radiation/tamoxifen	339	11.2

Abbreviations: DCIS, ductal carcinoma in situ; BCS, breast-conserving surgery.

For this analysis, we excluded 361 women who did not meet the follow-up criteria, leaving a sample size of 2,676 women.

Rates of Surveillance Mammograms Over Time

Over 10 years of follow-up, 9,679 surveillance mammograms were obtained by 2,676 women. During the first year of follow-up, 2,115 (79%) of 2,676 women had at least one surveillance mammogram. By year 5, annual surveillance decreased to 746 (69%) of 1,077 women observed and by year 10, to only 175 of the remaining 287 women observed (61%; Fig 1). This trend was statistically significant in adjusted regression models ($P < .0001$). On average, women had fewer than one surveillance mammogram per year although 11% had more than one surveillance mammogram within the first year of follow-up (Table 2). The average number of mammograms obtained per woman was 0.91 in the first year of follow-up but declined to 0.61 mammograms per woman by 10 years of follow-up.

Factors Associated With Yearly Surveillance Mammograms

In adjusted regression analyses, we found that yearly mammograms were more likely among women diagnosed with DCIS at 60 to 69 years of age than those diagnosed before age 50 (OR, 1.72; 95% CI, 1.26 to 2.34); menopausal hormone therapy users at diagnosis than never users (OR, 1.26; 95% CI, 1.01 to 1.57); and women treated with either adjuvant radiation (OR, 1.28; 95% CI, 1.08 to 1.53) or adjuvant radiation plus tamoxifen (OR, 1.61; 95% CI, 1.13 to 2.30) than women treated with BCS alone (Table 3). Yearly mammograms were less likely among obese women than those of normal body mass index (OR, 0.70; 95% CI, 0.56 to 0.86). The regression analyses findings were similar for women followed for 10 years (Table 3) although Hispanic women appeared to have a higher likelihood of surveillance than non-Hispanic women. The results did not change significantly in our sensitivity analyses when the interval between annual screenings was defined as every 9 months to every 15 months (data not shown).

Rates and Predictors of Annual Surveillance

Among women observed for at least 5 years, we found that only 34% had mammograms every year for all 5 years (361 of 1,077), and only 15% of women observed for at least 10 years had mammograms every year for all 10 years (43 of 287). In adjusted logistic regression models, women were less likely to have mammograms every year for 5 years if they were obese versus normal weight at diagnosis (OR, 0.53; 95% CI, 0.36 to 0.79) or Hispanic versus non-Hispanic white (OR, 0.50; 95% CI, 0.28 to 0.88; data not shown). Women who were diagnosed in the early 1990s were more likely to have mammograms every year for 5 years of follow-up than women diagnosed in the later 1990s.

DISCUSSION

DCIS is a precursor to invasive breast cancer and while the diagnosis itself does not increase the risk of death, women with DCIS are at an increased risk for subsequent ipsilateral and contralateral DCIS and invasive breast cancer.^{3-5,7,8} Therefore, vigilant surveillance in this population is needed. Our observational cohort study found that among insured health plan members, most women with DCIS treated with BCS had a surveillance mammogram within 1 year of

mastectomy within 6 months of diagnosis ($n = 96$), 85 years of age or older at diagnosis ($n = 15$), and not treated or observed for their breast cancer within the participating site ($n = 101$). An additional 29 women with unknown treatment were excluded. The overall DCIS cohort included 3,037 women (Table 1). The women had a mean age of 58.3 years (standard deviation, 11.4 years) and a median follow-up of 4.8 years (range, 0.5 to 15.7 years). Approximately 43% ($n = 1,298$) were treated with BCS alone, 42% ($n = 1,268$) with adjuvant radiation, 11% ($n = 339$) with both adjuvant radiation and tamoxifen, and 4% ($n = 132$) with tamoxifen alone.

Fig 1. Percentage of women with ductal carcinoma in situ (DCIS) who had at least one surveillance mammogram by year of follow-up after breast-conserving surgery.

follow-up; however, subsequent use of surveillance mammography declined by year of follow-up. Surveillance dropped to rates seen for screening mammography among women without breast cancer¹³ even though the risk of both recurrences and contralateral breast cancer is higher among women with DCIS than among those without prior DCIS. Only 34% and 15% of women observed for 5 and 10 years, respectively, had surveillance mammograms in each of the years of follow-up.

Our findings are consistent with prior studies that examined surveillance mammography among women with invasive breast cancer. Doubeni et al¹⁴ reviewed the charts of 797 women with BCS after being diagnosed with mostly invasive breast cancer. The results were almost identical to ours in that the rates of surveillance mammography decreased over time, from 80% within the first year after treatment to 63% by 5 years after treatment. The study included 131 women with in situ breast cancers who had a similar surveillance pattern. Other studies among women with invasive breast cancer in HMO settings,¹⁵ enrolled in controlled trials,¹⁶ SEER registries,^{17,18} the Breast Cancer Consortium^{19,20} and other community settings^{21,22}

found that surveillance mammography after treatment does not occur yearly for a large proportion of women.

The appropriate surveillance of women with DCIS treated with BCS remains uncertain.² The National Comprehensive Cancer Center guidelines recommend mammography every 12 months for women with in situ disease.⁹ The American Society for Clinical Oncology recommends that women with breast cancer treated with BCS undergo a post-treatment mammogram 1 year after the initial mammogram and at least 6 months after completion of radiation therapy.¹⁰ In our study, we found that the majority of women had a surveillance mammogram within 1 year of treatment completion, and that some women had more than one mammogram per year in the first few years of follow-up, but then surveillance decreased over time with only approximately 60% of women having a mammogram in the 10th year of follow-up.

We found that age, treatment, obesity, use of menopausal hormone therapy at diagnosis, and year of DCIS diagnosis were associated with the likelihood of receiving yearly surveillance mammograms. Women diagnosed in their 60s were more likely than younger or older

Table 2. Use of Surveillance Mammograms Among Women With Ductal Carcinoma in Situ Observed for Up to 10 Years After Breast-Conserving Surgery

Year of Follow-Up	Total No. of Women	Women With at Least One Surveillance Mammogram		Total No. of Surveillance Mammograms	Average No. of Surveillance Mammograms per Woman	% of Women With Surveillance Mammograms By Year of Follow-Up		
		No.	%			None	1	2-3
1	2,676	2,115	79	2,434	0.91	21.0	67.5	11.5
2	2,390	1,804	75	1,913	0.80	24.5	70.9	4.6
3	1,893	1,432	76	1,515	0.80	24.4	71.3	4.4
4	1,410	1,011	72	1,063	0.75	28.3	68.1	3.6
5	1,077	746	69	769	0.71	30.7	67.1	2.1
6	904	608	67	624	0.69	32.7	65.5	1.8
7	766	518	68	533	0.70	32.4	65.7	2.0
8	581	378	65	391	0.67	34.9	62.8	2.2
9	412	257	62	261	0.63	37.6	61.4	1.0
10	287	175	61	176	0.61	39.0	60.6	0.3

Table 3. Adjusted Relative Odds of Yearly Surveillance Mammography Among Women With DCIS Observed for 5 and 10 Years

Characteristic	Women With at Least 5 Years of Follow-Up (n = 1,077)			Women With at Least 10 Years of Follow-Up (n = 287)		
	OR	95% CI	P	OR	95% CI	P
Age at diagnosis, years			.0002			.02
< 50	1.00	Ref		1.00	Ref	
50-59	1.26	0.98 to 1.64		1.00	0.69 to 1.46	
60-69	1.72	1.26 to 2.34		0.93	0.59 to 1.48	
70+	1.08	0.77 to 1.52		0.52	0.31 to 0.85	
Diagnosis year			.01			.58
1990-1991	1.00	Ref		1.00	Ref	
1992-1993	0.85	0.63 to 1.14		0.88	0.67 to 1.16	
1994-1995	0.66	0.50 to 0.87		0.84	0.58 to 1.21	
1996-1997	0.66	0.50 to 0.87		—	—	
1998-1999	0.81	0.48 to 1.35		—	—	
Race*			.02			.16
White	1.00	Ref		1.00	Ref	
Asian	1.02	0.76 to 1.37		0.97	0.62 to 1.50	
Black	0.79	0.61 to 1.02		1.06	0.67 to 1.69	
Hispanic	0.85	0.64 to 1.12		1.79	1.03 to 3.10	
Other/unknown	5.42	1.93 to 15.20		8.24	2.72 to 24.94	
Body mass index at diagnosis			.004			.12
< 25 (normal)	1.00	Ref		1.00	Ref	
25-29 (overweight)	0.99	0.81 to 1.21		0.79	0.59 to 1.06	
≥ 30 (obese)	0.70	0.56 to 0.86		0.82	0.59 to 1.14	
Menopausal status at diagnosis			.20			.34
Postmenopausal	1.00	Ref		1.00	Ref	
Pre/perimenopausal	1.13	0.86 to 1.47		0.90	0.60 to 1.35	
Diabetes at diagnosis			.31			.27
No	1.00	Ref		1.00	Ref	
Yes	0.87	0.65 to 1.16		0.69	0.46 to 1.03	
Family history of breast cancer at diagnosis			.99			.15
No	1.00	Ref		1.00	Ref	
Yes	1.01	0.82 to 1.24		1.38	1.00 to 1.92	
Menopausal hormone therapy use at diagnosis			.21			.08
None	1.00	Ref		1.00	Ref	
Former use	1.14	0.93 to 1.40		1.49	1.08 to 2.07	
Current use	1.26	1.01 to 1.57		1.43	1.05 to 1.95	
Treatment of DCIS			.003			.17
BCS alone	1.00	Ref		1.00	Ref	
BCS/tamoxifen	0.69	0.37 to 1.28		1.88	1.27 to 2.79	
BCS/radiation	1.28	1.08 to 1.53		1.21	0.93 to 1.57	
BCS/radiation/tamoxifen	1.61	1.13 to 2.30		1.36	0.74 to 2.47	

NOTE. Analyses adjusted for diagnosis year; age, race, body mass index, menopausal status, diabetes, family history, menopausal hormone therapy use (all at the time of diagnosis), treatment of DCIS, year of follow-up and site.

Abbreviations: OR, odds ratio; DCIS, ductal carcinoma in situ; Ref, reference; BCS, breast-conserving surgery.

*The statistical significance of the race variable appears to be driven by the other/unknown category. When the other/unknown category was removed from the model, the variable was no longer statistically significant.

women with DCIS to undergo yearly mammograms. This is consistent with prior SEER-Medicare and Breast Cancer Surveillance Consortium studies.^{17,19} We also found that women who were treated more aggressively (receiving adjuvant radiation or adjuvant radiation with tamoxifen) were more likely to have annual mammography than women treated with BCS alone. Ironically, those treated with BCS alone are at the highest risk for recurrences³⁻⁵ and are theoretically most likely to benefit from vigilant surveillance. It is possible that women who are treated most aggressively think of DCIS as cancer, while those treated less aggressively may think of DCIS as a precancer and are therefore less vigilant about surveillance.²³

To our knowledge, less frequent surveillance mammography among obese DCIS patients has not been reported previously, but

the association has been shown in a study of mammographic screening in the general population.²⁴ The findings suggesting that women diagnosed in later years were less likely to undergo surveillance mammography is contrary to a prior study by Keating et al¹⁷ which showed that women diagnosed with invasive breast cancer in the later 1990s were more likely to have a surveillance mammogram than women diagnosed in the early 1990s. Whether our observation is due to changing practices or perceptions about the risk of recurrence among women with invasive breast cancer versus DCIS is not clear. It may also be in part a reflection of the recently decreasing rates of mammography utilization in the general population.^{25,26} Race did not have a consistent association with surveillance.

Our study has a number of strengths. The findings are based on one of the largest cohorts of women with DCIS to date and because the study was conducted in integrated health care delivery settings, the women received most, if not all, of their care within their respective settings. Unlike prior studies relying on automated claims data, we conducted a comprehensive review of the medical records and were able to differentiate between surveillance and diagnostic mammograms based on chart review. Our study does have limitations. First, because the women in our settings were insured (and from only three United States delivery sites), these results may not be generalizable to other settings in which post-treatment surveillance mammography may not be a covered benefit. Second, we lacked data and were not able to adjust for the type of provider seen by the women after treatment. Prior studies have suggested that women seen by oncologists were more likely to have surveillance mammograms than women observed primarily by primary care providers.^{17,27} As the women in integrated health care delivery systems are probably more likely to be followed by the primary care providers, surveillance may have been less frequent. Finally, with the exception of diabetes and obesity, we did not collect data on comorbid conditions. However, because our cohort was relatively young, we suspect that comorbidities would not have been highly prevalent and would not have influenced the course of surveillance after diagnosis.

In summary, we found that surveillance mammography after BCS for DCIS among insured women often did not occur yearly and that surveillance declined over time. Because DCIS is considered to be a precursor to invasive breast cancer, it is particularly important for women to receive surveillance for recurrences of DCIS and/or newly

diagnosed invasive breast cancer. Monitoring efforts should be adopted by health care delivery sites to ensure that surveillance occurs after BCS for DCIS.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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