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How Beneficial Is Follow-up Mammography in Elderly Breast Cancer Survivors?

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Abstract

Background—To determine the rate of non-palpable cancer detection and benign biopsy rates for follow-up mammograms in elderly breast cancer survivors.

Methods—Women 80 years of age and older who underwent operation for ductal carcinoma in situ or invasive breast cancer from 2005–2010 and who had at least 6 months of follow-up were identified from a single-institution, prospectively maintained, HIPAA-compliant database. Patients with mammographic, other imaging, or palpable abnormalities were identified, and the results of their imaging studies and biopsies were reviewed. Number of locoregional recurrences, contralateral cancers, and benign biopsies were determined. Follow-up and survival data were recorded.

Results—429 women with a mean age of 83.4 years were included. Mean follow-up was 50.0 months (range 6–113). Patients had a median of 4 follow-up mammograms (range 0–11). The 1466 mammograms detected 17 biopsy-proven cancers and generated 18 benign biopsies. In the 305 women who had had breast-conserving surgery, 18 (5.9%) experienced local recurrence, 9 detected by mammography alone (mean size 1.2cm), and 9 palpable (mean size 2.0cm). Contralateral cancer developed in 4 (0.9%) of the 429 patients, all detected on screening mammogram alone.

Conclusion—Overall, 13 non-palpable breast cancers were detected in 1466 mammograms (0.9%). While these results are acceptable for screening programs in healthy populations, further study of the need for routine follow-up imaging in the elderly, and the appropriate interval, is needed to maximize resource utilization.

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Background

There are currently more than 3.1 million breast cancer survivors in the United States, and approximately 45% are 70 years of age or older.¹ Current guidelines recommend that women of any age who complete therapy for breast cancer undergo surveillance mammography every 6–12 months.^{2, 3} The goal of follow-up mammography in breast cancer survivors is to detect local recurrence and contralateral breast cancer with the expectation that early detection will improve survival.⁴⁻⁶ Long-term results of large, randomized controlled trials and population-based registries indicate that rates of both local recurrence and contralateral breast cancer are declining among breast cancer survivors.⁷⁻¹⁰ However, elderly patients are largely excluded from randomized controlled trials, so it is uncertain whether these declines have occurred among older breast cancer survivors, and there is a paucity of contemporary literature specifically addressing the benefits and harms of surveillance mammography in older breast cancer survivors.

The use of follow-up mammography among elderly breast cancer survivors has been suggested to be associated with improved survival.¹¹ However, it is unclear whether the improvement in survival is attributable to early detection of recurrent or new breast cancer, or rather, to an increase in health-care access and compliance among women undergoing mammography.¹² The risk of death from other causes is high in elderly breast cancer survivors, raising questions about the benefit of routine mammography in this population.¹³⁻¹⁵ Additionally, the breasts of elderly women are often atrophic and easy to examine, and detection of ductal carcinoma in situ is not a major concern in this population with a more limited life span. The decision as to whether to continue imaging surveillance for recurrent or new breast cancer among breast cancer survivors of advanced age is difficult for physicians to address.¹⁶ In order to better inform this physician-patient discussion, we sought to determine the rate of non-palpable cancer detection and benign biopsy rates for follow-up mammograms in women 80 years of age or older at the original diagnosis of breast cancer.

Methods

Patient Cohort and Study Variables

Cases were obtained by querying our single-institution, prospectively maintained, HIPAA-compliant database. All patients ≥ 80 years of age who underwent surgery for ductal carcinoma in situ or invasive breast cancer at Memorial Sloan Kettering Cancer Center between January 2005 and December 2010 were included. Patients with stage IV disease at presentation, those undergoing bilateral mastectomies, and those with less than 6 months of follow-up information were excluded. A total of 429 patients were eligible for analysis. Clinical information, including age, operation, estrogen receptor (ER) status, HER2/neu status, and pathology results were obtained from the database. Patient charts were reviewed to gather information regarding follow-up mammograms, biopsies, stage (or size) of any newly diagnosed cancer, status at last follow-up, survival and use of chemotherapy, hormonal therapy, and radiation therapy. Patients were staged according to the 7th Edition of the American Joint Committee on Cancer staging system.¹⁷ Charlson Comorbidity Index

score was assigned for each patient based upon chart review.¹⁸ No comorbidity points were assigned for advanced age.

Data Analysis

Descriptive analyses of the collected variables were performed. Time to local recurrence or contralateral breast cancer was calculated from the date of operation for the index breast cancer. Survival was measured from the time of operation to the time of death. Patients were classified as having received endocrine therapy if they had any record of such therapy. Patients classified as having completed radiation therapy had a documented course of external beam or intraoperative radiation therapy.

Results

Patient Characteristics and Treatment

429 women met our inclusion criteria. Average age at operation was 83.4 years (range 80–94). Mean follow-up was 50.0 months (range 6–113). The average Charlson Comorbidity Index score for the cohort was 0.8. 369 (86.0%) cancers were invasive: 59.9% stage I, 31.4% stage II, 8.7% stage III. Table 1 shows clinicopathologic data for the cohort. The majority of patients had invasive ductal histology (66.2%), and the majority of tumors were node negative (70.6%). 83.7% of the invasive cancers were ER positive (ER+). Table 2 displays surgical therapy by age. 71% of women underwent breast-conserving surgery and 79% had some form of axillary surgery; 58.7% sentinel lymph node biopsy and 20.3% axillary dissection. The majority of women (56.7%) who underwent breast-conserving surgery did not receive radiation therapy. Table 3 shows the percentage of women who completed radiation therapy after breast-conserving surgery by age. Most women (79.1%) with ER+ tumors received endocrine therapy, with little variation based on age. Endocrine therapy was prescribed for 80% of those 80–84 years of age, 75% of those 85–89 years of age, and 80% of those 90 years of age and older with ER+ tumors.

Results of Follow-up Mammography

Patients had a median of 4 follow-up mammograms (range 0–11). The 1466 follow-up mammograms detected 17 biopsy-proven cancers and generated 18 benign biopsies, 2 of which led to surgical excision. There were 18 (5.9%) local recurrences in the 305 women who had breast-conserving surgery, 6 in the 121 (4.9%) patients who received RT, and 12 in the 173 (6.9%) patients treated with excision alone. Local recurrence occurred in 4 of 61 (6.6%) patients with an ER negative tumor, 11 of 309 (3.6%) with an ER positive tumor, and 3 with DCIS and unknown receptor status. Nine local recurrences were detected by mammography alone, and 9 were palpable. Mammographically detected vs. palpable local recurrences were a mean 1.2 cm vs. 2.0 cm in size, respectively. The majority of local recurrences (15/18) were invasive. Of the 18 patients with isolated local recurrence, 3 underwent completion mastectomy, 8 had repeat lumpectomy, 5 had no additional surgical treatment (mainly due to patient refusal), and 2 were lost to follow-up.

Among 429 patients, 4 (0.9%) developed a contralateral breast cancer. All contralateral breast cancers were detected on screening mammogram alone. In total, 13 non-palpable

cancers were detected in 1466 mammograms (0.9%), and 1.2% of mammograms led to benign biopsies.

Patient Survival

120 (27.9%) women died during the follow-up period, 19 (4.4%) of breast cancer, 14 (3.3%) from other cancers, 3 (0.7%) from cardiovascular disease, and 83 (19.3%) from unknown causes. The 83 who died of unknown causes were without evidence of recurrent breast cancer at the time of last follow-up. The 3 patients who developed contralateral breast cancers were alive at last follow-up.

Discussion

Our study of 1466 mammograms in 429 elderly women with breast cancer demonstrated a low rate of locoregional recurrence and new primary breast cancers. The 5.9% local recurrence at a mean follow-up of 50 months is within the expected range for a population of elderly breast cancer survivors, more than half of whom did not receive post lumpectomy radiotherapy. In a randomized controlled trial of women older than 70 years of age with ER+, early-stage breast cancer undergoing lumpectomy, the local recurrence rate was 2% in patients receiving tamoxifen and radiation therapy vs. 10% in patients receiving tamoxifen alone at a median follow-up of 10 years.¹⁹ In a population-based cohort of 1446 breast cancer survivors 75 years of age and older from The Netherlands, of whom 22% had breast-conserving surgery (71% with radiation therapy, 49% with endocrine therapy), the 5-year rate of locoregional recurrence was 3.7%.²⁰ The finding of 0.9% contralateral breast cancer incidence is also what would be anticipated in this population. In women diagnosed with a first breast cancer between 80–84 years of age, the estimated annual contralateral breast cancer incidence rates are 0.26 per 100/year (95% confidence interval [CI] 0.21–0.32) for ER+ first cancers and 0.63 per 100/year (95% CI 0.40–0.86) for ER negative first cancers.²¹ In the Netherlands cohort, the 5-year rate of contralateral cancer was 2.1%, although 51% of patients did not receive endocrine therapy.²⁰ The use of endocrine therapy is well recognized to reduce the rates of both local recurrence and contralateral cancers,^{9, 22} and 79% of patients in this study took endocrine therapy, undoubtedly contributing to the low rates of recurrence and contralateral breast cancer which were observed.

Our finding that 50% of local recurrences were mammographically detected and 50% clinically detected is consistent with previously published studies of surveillance mammography after treatment of primary breast cancer in patients of all ages.²³ The fact that half of the local recurrences in the current study were palpable underscores the importance of clinical breast exam, an inexpensive surveillance method, in patient follow-up. A 2002 review of the impact of method of detection of local recurrence after breast-conserving therapy on survival outcomes showed no association between method of detection and overall or disease-specific survival among women of all ages. This finding is consistent with other observations that the size of a local recurrence is not a prognostic factor.^{24, 25} Of note, 5.7% of the patients who developed local recurrence in our series refused further surgical treatment, emphasizing the importance of conversations with older

women about their desires regarding management of abnormal findings, particularly as they experience changes in overall health status, prior to ordering routine imaging studies.

While the yield of mammographically detected cancers was low in this study, there was relatively little harm from follow-up mammography in our elderly population. The positive predictive value of biopsies performed was high at 50%. We found a benign biopsy rate of 1.2% (18/1466 mammograms) at a median 50 months follow-up. Two patients had surgical excisions for benign disease (0.14% of mammograms). These rates are lower than the 10-year cumulative false-positive rate of 14–27% reported in a recent review of screening mammography in healthy women 75 years of age and older.²⁶ The surveillance mammography literature also suggests increased false-positive rates in elderly women screened yearly vs. biennially.²⁶ Studies of women undergoing screening mammography suggest a negative psychological impact from a false-positive mammographic finding that can last up to 3 years, leading to a decline in patient compliance with follow-up.²⁷ The psychological impact of false-positive follow-up mammograms in elderly women is not known and was not measurable in the current study.

Our study cannot address the question of whether imaging detection of local recurrence translates to improvements in patient survival. In 2007 Lash et al¹¹ performed a matched case-control study to determine the association between surveillance mammography and breast cancer mortality in breast cancer survivors 65 years of age or older. Having one surveillance mammogram was associated with improved survival compared to women having no surveillance mammogram. The authors also reported a 31% decrease in the odds of breast cancer mortality for women having additional surveillance mammograms. This reduction was highest among patients 80 years of age or older, a finding they attributed to lower breast density and consequent improvement in detection. However, because this was a retrospective study, it is difficult to attribute the observed decrease in mortality to mammographic surveillance. Rather, these results may imply that survival is improved among patients who access preventive medical care. Bessen and Karnon²⁸ used data from the South Australia Cancer Registry, and administrative and clinical hospital databases to develop a model considering both health outcomes and costs to inform screening strategies for postmenopausal breast cancer survivors. In this model, screening at 2-year intervals in women 70–79 years of age, similar to general population recommendations in Australia, was felt to be the optimal strategy. However, this model has not been validated in other populations.

A recent paper by van Ravenstyn et al utilized 3 independently developed models to simulate the benefits and harms of mammography in a cohort of American women. They found a continual increase in the overdiagnosis of both invasive breast cancer and DCIS from 74–96 years of age. Also noted was a continual decrease in breast cancer deaths averted and quality adjusted life-years gained, suggesting diminishing returns for screening mammography, particularly after age 90.²⁹ Despite the limited data, there are no randomized trials addressing optimal surveillance after breast cancer in older women, and guidelines do not address the issue of when yearly mammography should be discontinued among breast cancer survivors. Recently updated American Cancer Society recommendations for average-risk women also do not specify the age at which women should discontinue screening

mammography; rather, they recommend biennial screening in women in overall good health if their life expectancy is 10 years or longer.³⁰ The U.S. Preventive Services Task Force concluded in 2009 that evidence was insufficient to assess additional benefits and harms of screening mammography in women 75 years of age and older.³¹ Thus, current evidence-based screening recommendations provide limited guidance on appropriate mammographic follow-up for cancer survivors

Strengths of this study include a large group of breast cancer survivors in their 80s treated in a contemporary fashion for whom rates of local control are known. Potential weaknesses include physician selection for frequency of mammographic follow-up, which was not annual in all patients, and which could mask both benefits and harms of mammography. However, this reflects real-world practice where it is likely that healthy and compliant older women have more frequent mammography.

Conclusions

Local recurrences and contralateral breast cancers are uncommon in elderly breast cancer survivors, and many are palpable. In this series, the false-positive rate of a yearly mammogram was low, but it remains unclear whether annual imaging is necessary for this group. Our findings emphasize that open discussions are needed between physicians and elderly breast cancer survivors regarding the risks and benefits of annual follow-up mammography, which should not be considered “routine” in this relatively low-risk subset. Further study is needed to determine the most resource-effective follow-up strategy to use among this increasing population of breast cancer survivors.

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Table 1

Clinicopathologic characteristics of study population by age

	80–84 years		85–89 years		90+ years		Total	
	n=310	%	n=92	%	n=27	%	n=429	%
Histology								
Ductal carcinoma in situ	51	16.5	7	7.6	2	7.4	60	14.0
Invasive ductal	196	63.2	69	75.0	20	74.1	285	66.4
Invasive lobular	45	14.5	13	14.1	4	14.8	62	14.5
Invasive mammary	7	2.3	2	2.2	0	0.0	9	2.1
Other	11	3.5	1	1.1	1	3.7	13	3.0
Extent of Disease								
T stage								
T1S	51	16.5	7	7.6	2	7.4	60	14.0
T1	195	62.9	58	63.0	16	59.3	269	62.7
T2	51	16.5	23	25.0	8	29.6	82	19.1
T3/4	11	3.5	4	4.3	1	3.7	16	3.7
T0/Tx	2	0.6	-	-	-	-	2	0.5
Pathologic Nodal Status								
Negative	159	51.3	46	50.0	9	33.3	214	49.9
Positive	90	29.0	28	30.4	7	25.9	125	29.1
No surgical staging	61	19.7	18	19.6	11	40.7	90	21.0
Estrogen Receptor Status*	n=259		n=85		n=25		n=369	
Positive	218	84.2	71	83.5	20	80.0	309	83.7
Negative	39	15.1	14	16.5	5	20.0	58	15.7
Unknown	2	0.8	0	0.0	0	0.0	2	0.5
HER2 Receptor Status*	n=259		n=85		n=25		n=369	
Positive	10	3.9	11	12.9	2	8.0	23	6.2
Negative	240	92.7	67	78.8	23	92.0	330	89.4
Unknown	8	3.1	7	8.2	0	0.0	15	4.1

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	80-84 years		85-89 years		90+ years		Total	
	n	%	n	%	n	%	n	%
Equivocal	1	0.4	0	0	0	0	1	0.3
	310		92		27		429	

* invasive cases only

Table 2
Surgical therapy by patient age

	80-84 years		85-89 years		90+ years		Total	
	n=310	%	n=92	%	n=27	%	n=429	%
Treatment of Primary Tumor								
Mastectomy	88	28.4	28	30.4	8	29.6	124	28.9
Lumpectomy	222	71.6	64	69.6	19	70.4	305	71.1
Axillary Treatment								
Sentinel lymph node biopsy	185	59.7	55	59.8	12	44.4	252	58.7
Axillary lymph node dissection	64	20.6	19	20.7	4	14.8	87	20.3
None	61	19.7	18	19.6	11	40.7	90	21.0

Table 3
Use of adjuvant radiation therapy among patients with breast conservation by patient age

	80–84 years		85–89 years		90+ years		Total	
	n=222	%	n=64	%	n=19	%	n=305	%
Adjuvant Radiation Therapy								
Yes	96	43.2	23	35.9	2	10.5	121	39.7
No	116	52.3	40	62.5	17	89.5	173	56.7
Unknown	10	4.5	1	1.6	0	0.0	11	3.6