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Individualizing Surveillance Mammography in Older Patients After Treatment for Early-Stage Breast Cancer - Multidisciplinary Expert Panel and International Society of Geriatric Oncology Consensus Statement

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Abstract

Importance: There is limited guidance on how to approach surveillance mammography in older breast cancer survivors, particularly when life expectancy is limited.

Objective: To develop expert consensus guidelines that facilitate tailored decision-making for routine surveillance mammography in breast cancer survivors aged ≥75 years.

Evidence: After a literature review of the ipsilateral and contralateral breast cancer event risk in breast cancer survivors and the harms/benefits of mammography, we convened a multidisciplinary expert panel to develop consensus guidelines on surveillance mammography for breast cancer survivors aged ≥75 years. Using an iterative consensus-based approach, input from clinician focus groups, and critical review by the International Society for Geriatric Oncology (SIOG), the guidelines were refined and finalized.

Findings: The literature review established a low risk for ipsilateral and contralateral breast cancer events in most older breast cancer survivors and summarized the benefits/harms of mammography. Draft mammography guidelines were iteratively evaluated by the expert panel and clinician focus groups, emphasizing a patient's risk for in-breast cancer events, age, life expectancy, and personal preferences. The final consensus guidelines recommend discontinuation of routine mammography in all breast cancer survivors when life expectancy is <5 years, including those with a history of high risk cancers, consideration to discontinue mammography when life expectancy is 5-10 years, and continuation of mammography when life expectancy >10

years. Individualized shared decision-making is encouraged to optimally tailor recommendations, after weighing benefit/harms of surveillance mammography and patient preferences. The panel also recommends ongoing clinical breast examinations and diagnostic mammography to evaluate clinical findings and symptoms, with reassurance for patients that these practices will continue.

Conclusions and Relevance: We anticipate that these expert guidelines will enhance clinical practice by providing a framework for individualized discussions, facilitating shared decision-making regarding surveillance mammography for older breast cancer survivors.

INTRODUCTION

It is widely recognized that the benefits of screening mammography wane with increasing age and are diminished when life expectancy is short, with individualized decision-making encouraged.[1,2] Although current U.S. guidelines recommend individualizing continuation and discontinuation of screening mammography based on life expectancy,[3,4] breast cancer survivorship guidelines unvaryingly recommend annual *surveillance* mammography for all survivors with intact breasts.[5] Current survivorship recommendations lack guidance on how to tailor surveillance breast imaging for older breast cancer survivors with regard to chronological and physiological age, life expectancy, risk for in-breast cancers, anticipated benefits and harms of testing, or patient preferences. As a result, the use of routine mammography in older breast cancer survivors is highly variable[6–8] and frequent, even among those with limited life expectancy.[8] With an anticipated increase in the number of older women who will be newly diagnosed with breast cancer in the coming years[9] and the many older breast cancer survivors,[10,11] identifying strategies to individualize approaches to surveillance care is highly relevant.

Recognizing the guideline and clinical practice gaps for older breast cancer survivors, we used a multi-pronged approach to inform decision-making for this population including a literature review on the risks of ipsilateral and contralateral breast cancer events and the benefits/harms of mammography, an expert panel to draft recommendations for surveillance mammography for women age ≥75, focus groups of multidisciplinary clinicians to elicit feedback, and critical review of the proposed guidelines by the International Society of Geriatric Oncology (SIOG). The age ≥75 threshold was selected given the average life expectancy for U.S. women[12] and because it is at this age where there is insufficient evidence in the screening literature to recommend mammography. Herein, we present our final consensus statement on surveillance mammography for older breast cancer survivors and offer strategies for integrating these recommendations into clinical practice. For the purposes of these guidelines, ‘diagnostic’ mammography refers to mammography to evaluate breast symptoms or clinical exam findings. ‘Surveillance’ mammography refers to routine mammography in the *absence* of symptoms or exam findings, including mammograms in the post-treatment setting ordered as ‘diagnostic’ because of institutional practice patterns.

Methods

Step 1: Literature Review

No prospective clinical trials have evaluated the benefits and harms of mammography in breast cancer survivors. Therefore, to indirectly quantify potential benefits, we reviewed the literature for publications addressing the risk of ipsilateral and contralateral breast cancer events among older breast cancer survivors and the harms of mammography.

We first quantified in-breast cancer events for breast cancer survivors, accounting for cancer subtype, treatment, and age whenever possible. We re-examined publications from a review on surveillance mammography,[13] which focused on clinical trials, meta-analyses, and registry-, medical record-, and cohort-based studies that reported on in-breast cancer events in survivors with a focus on breast cancer subtype, treatment received, and patients aged ≥65 years (when available). Additionally, we examined all current National Comprehensive Cancer Network (NCCN) guideline[14] citations (clinical trials and meta-analyses) reporting on in-breast cancer events in patients with non-metastatic breast cancer. We did not include neoadjuvant trials focusing on pathologic and surgical outcomes, trials only reporting distant recurrence or death, trials combining distant and local recurrence endpoints, or trials including only mastectomy-treated patients. To synthesize these data, we approximated the risks for in-breast cancer events for older survivors by cancer subtype and treatment over 10 years from diagnosis.

In a second literature review, because the risk for in-breast cancer events in older breast cancer survivors is similar to or marginally higher than the risk in women without a history of breast cancer in most cases,[13,15–17] and because there are no prospective studies on the benefits and harms of *surveillance* mammography specifically, we examined published studies on the benefits and harms of *screening* mammography in older women. We updated a previously published review by Walter and Schonberg[1] that included relevant studies available through 2/1/2014, adapting the same search strategy in PubMed during 2/1/2014-6/29/2020 for articles in English, using the MeSH terms ‘breast neoplasms’, ‘mammography’, and ‘older women’, including any clinical trials, meta-analyses, multicenter studies, reviews, and observational or retrospective registry studies. Articles were included if they specifically addressed the benefits/harms of mammography in women aged ≥65 years.[1]

Step 2: Expert Panel and Consensus Process

We utilized an iterative consensus-based approach which was adapted from a nominal group technique and a modified-Delphi process[18,19] to formulate best practice guidelines for surveillance mammography in older breast cancer survivors. Recommendations were drafted by a subgroup of the expert panel based on clinical expertise and the literature review. We then engaged experts from a breadth of specialties and geographic areas who were identified through academic networks, literature review, and clinical expertise and/or leadership positions. Of the 18 multidisciplinary clinicians and 3 patient/patient advocates invited, 15 clinicians and 2 patient advocates participated in a three-hour, in person panel discussion on June 3, 2019, in Chicago, IL (eTable 1). The expert panel discussed the

literature review and draft guidelines for surveillance mammography. After an open-forum for feedback on guideline content, plans for guideline revisions were agreed upon. Revised versions of the guidelines were shared with the panel in two rounds via email. Following incorporation of feedback, the guidelines were discussed in five clinician focus groups (see below), and revisions were made. Finally, following two additional rounds of critical review by the expert panel via email, the revised guidelines were reviewed by SIOG representatives and approved by the SIOG Publications Committee, after which a final working document was circulated to the expert panel members and SIOG. After reaching >95% consensus by panelists and SIOG members, the guidelines were finalized.

All research conducted as part of this work was approved by the Office of Human Research at Dana-Farber Cancer Institute (DFCI; Boston, MA) and was funded by the National Cancer Institute (NCI; R21CA227615-01A1 to RAF).

Clinician Focus Groups

We held three in-person and two web-based 60-minute clinician focus groups. The in-person focus groups were conducted at Brigham and Women's Hospital with primary care clinicians (n=5) and at DFCI with oncology clinicians (n=21 across two focus groups), including 5 breast surgeons, 9 medical oncologists, 1 radiation oncologist, 1 palliative care physician, and 5 breast oncology advanced practice providers. The two virtual groups involved clinicians from academic and community sites across the U.S., including 6 primary care/women's health clinicians, 1 family practitioner, 2 geriatricians, and 11 oncology and radiology clinicians (2 breast imagers, 2 breast medical oncologists, 5 community medical oncologists, and 2 breast radiation oncologists). All focus group participants were recruited by email.

After verbal consent, the focus groups began with a brief literature review followed by discussion of the draft expert guidelines (with feedback elicited), a discussion on how/if clinicians currently talk with patients about life expectancy, and a review of a draft patient information tool (Supplemental Data contain the clinician focus group guide). All discussions were audio-recorded, and a $50 gift card was provided to each participant. One investigator (RAF) and a project manager (APG) listened to the focus group recordings to identify major themes; example quotes were selected.

RESULTS

Literature Review

Ipsilateral and contralateral breast cancer events—The literature review confirmed the low risk of in-breast cancer events in older breast cancer survivors (eTable 2) and the potential benefits/harms of screening (eTable 3). Rates of in-breast cancer events are particularly low among patients with hormone receptor-positive tumors treated with endocrine therapy. In patients who do not receive systemic therapy for human epidermal growth factor receptor 2 (HER2)-positive or triple negative cancers, the rates for ipsilateral recurrence are estimated to be higher, although some of these patients have substantial competing distant recurrence risk which mammograms do not detect. Based on the literature

review, we determined best estimates of the 10-year risk for in-breast cancer events by treatment and cancer subtype (Table 1[20–31]). These risks range from 1-15% for ipsilateral breast cancers and 1-5% for contralateral cancers. As a frame of reference, in women without a personal history of breast cancer, the five-year risk of developing invasive breast cancer for an average-risk 75-year-old woman is 2.2%,[32] closely mirroring our risk estimations for new in-breast cancers in survivors with prior low-risk breast cancers (Table 1). In addition, our risk estimates are similar to those cited in a large-scale mammography study, where breast cancer survivors ages 70-80 had a 1.1% annual risk of in-breast cancers compared with 0.7-0.9% for women in the same age-group *without* a breast cancer history.[17]

Benefits and Harms of Mammography—The literature review findings are summarized in eTable 3, presented in similar format as Walter and Schonberg's summary for benefits/harms of screening mammography in older women.[1] Although the benefits of mammography for older women are poorly defined, the literature suggests that mammography offers little-to-modest clinical benefit for many older women. The limited benefits are likely due to the >10-year time lag[33] required to realize small improvements in breast cancer mortality and the low rates of life-threatening breast cancer events in older women with[34] and without[1] a history of breast cancer. The primary harms of mammography include false positives, anxiety associated with diagnostic testing, and over-treatment, some of which may be amplified in breast cancer survivors.[17] According to Walter and Schonberg's review,[1] over 10 years of screening 10,000 women in their 70s, 20 breast cancer deaths will be averted, while 2000 false positives will occur, and 130 patients will be over-diagnosed.[1] Our updated literature review (studies 2014-present) did not identify new findings to modify these estimates.

Clinician Focus Group Feedback

In addition to receiving direct feedback in focus groups on the content of the guidelines, several themes were identified through discussions with clinicians, including varying opinions on the appropriate time to discontinue mammography, comfort/discomfort with communicating life expectancy, strategies for approaching discontinuation of mammograms, the value of clinical breast exam, and who should be responsible for mammography discussions/recommendations in older breast cancer survivors.

All clinicians felt that having expert guidelines and talking points to guide discussions would be helpful. However, some oncology clinicians felt that age 75 is often "*too young*" to stop surveillance mammography, and that age 80 may be a more comfortable age to stop routine testing. Most clinicians felt that estimations of life expectancy should inform the timing of this discussion more than age. Although several primary and geriatric care clinicians reported comfort discussing life expectancy with patients, oncology clinicians reported discomfort. They expressed preferences to have life expectancy information available but felt it was easier to communicate findings indirectly, without specifically revealing life expectancy to patients. One oncology clinician, however, felt it would be "*sneaky*" to calculate life expectancy without communicating this to patients, supporting more open discussions. All clinicians acknowledged that framing the conversation around patients' low risk for in-breast cancer events and how mammography will not benefit them was more

appealing than discussing life expectancy. *"If their risk is really equivalent to the general population—that is very powerful."* Non-oncology clinicians felt they could reassure their patients they are *"more like other women (without cancer) than they think."*

All clinicians supported discussing discontinuation a few years before they might recommend doing so, so that patients can "*ease into the idea. It's not just a one-time conversation*." Some reported that they '*focus on the risks'* or frame such discussions by asking: *"if you were to find something on mammogram, would you do anything about it?"* If a patient answered '*no*', clinicians felt this was a signal to stop mammography. Some non-oncology clinicians noted that they defer decisions about mammography to oncology clinicians (*"I reflexively continue to screen most survivors"*).

The potential value of continued clinical breast examination was also raised during discussions. Some primary care physicians questioned whether this was necessary: "*What is the role here?*" However, all oncology clinicians felt strongly that the clinical breast exam should remain a component of follow-up as a key way to show patients they are still being cared for and to identify potentially symptomatic disease. All clinicians supported engaging patients in shared decisions with individualized estimates of benefits/harms that incorporates their patients' values and preferences.

Guideline Disclaimer

The Expert Guidelines presented herein are provided to assist clinicians and patients with decision-making but are not meant to mandate any specific follow-up care and are not intended to substitute professional judgement. In all cases, the selected course of action should be considered by the treating clinician in the context of shared decision-making with individual patients. The authors assume no responsibility for any injury or damage to persons arising out of or related to use of this information, or for any errors or omissions.

Expert Consensus Guidelines

The final expert consensus guidelines are detailed below and summarized in Table 2 and Supplement 2. The guidelines provide recommendations for surveillance mammography based on a patient's life expectancy,[35–37] age, breast cancer subtype, and treatment. These recommendations are intended to provide a framework for shared decision-making and are meant to be tailored to the individual patient's clinical situation and preferences. Of note, validated measures are readily available to support clinicians in estimations of life expectancy, such as ePrognosis,[35] but the approach to these conversations should be adapted to patient preferences.[38–40] We recognize that conversations about life expectancy may be challenging,[41–43] but with appropriate talking points, guidance, and practice, sharing this information thoughtfully with patients may benefit the many women who want more information about their health.[39,44–47]

Because of the low risk for breast cancer events, the time-lag required to realize the small benefits of mammography, and the persistence of the harms of mammography over time, we recommend discontinuation of routine mammography in all breast cancer survivors, including those with a history of higher-risk tumors (locally advanced triple negative or HER2-positive cancers), at any age once life expectancy is <5 years, consideration to

discontinue mammography when life expectancy is 5-10 years, and continuation of testing with annual or biennial mammography when life expectancy exceeds 10 years. Surveillance mammography every 2 years may be preferred by some women, perhaps easing a transition to discontinuation over time. By age 85, given that life expectancy is <5 years for most women,[12] we recommend cessation of mammography unless a patient is in extraordinary health or has strong preferences to continue testing. However, given the small benefits of mammography even when life expectancy exceeds 10 years, shared decision-making for clinicians and patients is encouraged at all ages to optimally individualize recommendations and incorporate patient preferences.

Despite the possibility of false positive findings and lack of consensus for clinical breast exam in the screening setting,[3] the panel recommends ongoing clinical breast examinations, education for patients on breast self-awareness, diagnostic mammography to evaluate symptoms and clinical findings, and reassurance for patients that these practices will continue. Talking points for clinicians to share with patients when having discussions about possible discontinuation of mammography are also provided in Supplement 2, with a focus on reassuring patients about the low risk of breast cancer events over time and how diagnostic evaluations will continue.

SUMMARY AND FUTURE DIRECTIONS

To directly address gaps in recommended follow-up care of older breast cancer survivors, we used a comprehensive approach to develop expert consensus guidelines for surveillance mammography in older breast cancer survivors through literature review and clinical expertise. We acknowledge that every patient scenario is not represented in our guidelines (e.g. those with genetic susceptibility). Nonetheless, our suggestions are relevant for most older survivors and offer a foundation for decision-making that can then be individualized as appropriate.

It is important to recognize the lack of prospective data to precisely inform the risk of breast cancer events and the benefits/harms of surveillance mammography in older breast cancer survivors. However, given evidence about the low risk of breast cancer events across ages in randomized controlled trials for women with breast cancer, the long-term population-based and site-based studies confirming low risk of breast cancer events, and the extended time required to realize the small benefits in older women undergoing screening mammography,[33] our expert consensus recommendations are pragmatic and applicable to most breast cancer survivors aged ≥75.

The panel understands that reassuring messaging to patients is important, reflected in the talking points in Supplement 2 that address how to approach discussions on mammography discontinuation with patients. We recognize that clinical breast exams are not recommended in screening guidelines and have their own set of harms (e.g. false positive findings leading to diagnostic evaluation and anxiety). Nevertheless, there was universal consensus from oncology clinicians in our focus groups that the physical exam was an important part of survivorship care. Future studies should address the benefits/harms of a clinical breast exam in this context.

Although we anticipate patients may require a series of conversations before discontinuing surveillance mammography becomes comfortable, initiating discussions a few years before discontinuing routine mammography may ease the transition. In addition, as clinicians work to integrate these expert guidelines into practice, they will need to collaborate closely across disciplines so that patients receive uniform messaging from their multi-specialty oncologists, as well as primary care, geriatrics, gynecology, and radiology clinicians.

To further enhance patient education, comfort level, and decision-making, we developed a companion patient information guide with input from patients and clinicians that is currently undergoing pilot testing to assess feasibility, usability, and acceptability of the guide by patients and their clinicians. Decision aids for patients aged ≥75 years in the screening setting (i.e. for women *without* a history of breast cancer) have been developed[48] and shown in a randomized clinical trial to improve older women's knowledge of the benefits and harms of mammography screening and to decrease the number of women choosing to be screened.[49] With patients' increasing understanding of the benefits and harms of mammography, these recommendations can increase the likelihood that breast cancer survivors receive care that is consistent with their values and preferences. In future work, we will continue to develop talking points to support clinicians in discussing surveillance mammography for this growing population of breast cancer patients and survivors. We anticipate these recommendations will provide a framework for clinicians to use in discussions with older breast cancer survivors and will facilitate an individualized approach to surveillance mammography use and discontinuation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Approximation of ipsilateral and contralateral breast cancer risk for older breast cancer survivors who had breast conservation, based on breast cancer subtype and treatment received[20–31]

Clinical scenario for past diagnosis and treatment received [a]			Estimated cumulative risk of in-breast cancer events over 10 years	
Surgery	**Cancer subtype**	**Adjuvant therapy**	**Ipsilateral Breast**	**Contralateral Breast**
Unilateral mastectomy	All	No endocrine therapy	Not applicable	3-5%
		Endocrine therapy	Not applicable	1-2%
*Breast conserving s*urgery	*Hormone receptor-positive breast cancer* [a]	Endocrine therapy	7-9%	1-2%
		Radiation and endocrine therapy	1-2%	1-2%
		Radiation only	4-6%	3-5%
	Human epidermal growth factor receptor 2-positive (HER2+) [a,b]	Chemotherapy or HER2-directed therapy and radiation	3-4%	3-5%
		Radiation only	10-15%	3-5%
	Triple negative [a,b]	Chemotherapy and radiation	3-5%	3-5%
		Radiation only	10-15%	3-5%

HER2=human epidermal growth factor receptor 2

[a]For all subtypes, the risk will vary based on stage of disease and other tumor factors. In general, if appropriate local and systemic therapy are administered and the tumor is deemed lower risk, there is a lower risk for breast events. If a patient has a history of unilateral mastectomy, only the contralateral breast risk is relevant to mammography decision-making.

[b]If no radiation is given after breast conservation, ipsilateral breast cancer risks will be higher than estimated here, but the contralateral risk estimates are not impacted. The data for patients with HER2+ breast cancers are primarily extrapolated from longer-term results of adjuvant trastuzumab trials[30] (which primarily enrolled younger patients and where the control groups received chemotherapy) and were then further augmented after considerations of longer follow-up and lack of any systemic therapy. Estimations for 'no systemic therapy' in triple negative disease are extrapolated from meta-analysis/overview data.[31]

Table 2.

Summary of Expert Consensus Guidelines for Older Breast Cancer Survivors

Breast Cancer History and Risk Considerations		**Recommendations by Age and Life Expectancy**		
Clinical Scenarios and Definitions	**Cancer Risk**	**Ages 75-79**[a]	**Ages 80-84**[a]	**Age 85+ or life expectancy <5 years at any age**[a]
Engage in shared decision making regardless of life expectancy				
History of lower-risk cancers, such as: -most hormone receptor (HR)+/ HER2- tumors -stage I HER2+ or triple negative tumors[b]	In-breast cancer risks are low but steady over time (for HR+ disease in particular); overall risks are lower than the general population (especially with use of endocrine therapy)	If life expectancy is ≥10 years, continue annual or biennial surveillance mammography If life expectancy is <10 years, consider discontinuation	Consider discontinuation of surveillance mammography unless life expectancy ≥10 years	Discontinue surveillance mammography unless patient is in extraordinary health or has a strong desire to continue
History of higher-risk cancers, such as: -stage II-III triple negative or HER2+ tumors; higher-risk HR+ tumors[b]	Ipsilateral risk may be higher for the first 5 years but then becomes similar to the general population	Continue annual surveillance mammography unless life expectancy <5 years	Consider discontinuation of surveillance mammography unless life expectancy >5 years	

[a]Physiological age as assessed by some form of geriatric assessment[37] or eprognosis[35] will give a better view on global health and life expectancy than chronological age. Average life expectancy in the US is <10 years for those ages ≥80.[12]

[b]Risk for ipsilateral recurrence will depend on tumor biology, stage, and family history and will be lowered by the degree of systemic and local treatment received. Contralateral risk for breast cancer is consistently low for *most* older women and particularly low for those treated with endocrine therapy because of the protective effects of treatmen