Breast Cancer in the Elderly

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KEYWORDS

• Screening • Axillary staging • Endocrine therapy • Radiation therapy
• Chemotherapy • Surgical outcomes • Ethics

KEY POINTS

- The incidence of breast cancer in the elderly is high; with increasing life expectancy, screening and treatment methods are evolving for this population.
- Functional status, comorbidities, and treatment side effects are becoming the determining factor in deciding screening and treatment options.
- Additional research in elderly patients with breast cancer needs to determine screening recommendations, ethical considerations, and best practice treatment options.

INTRODUCTION

In 2016, the incidence of breast cancer in women older than 65 years was 436.9 per 100,000 per year.[1,2] More than 50% of breast cancers are diagnosed in patients older than 60 years (**Fig. 1**).[3] The World Health Organization and Medicare define the elderly as individuals older than 65 years.[4,5] Although the average life expectancy of women older than 65 years is 86.6 years, 1 out of 4 will live to more than 90 years of age and 1 out of 10 will live to more than 95 years of age.[2,6] This article attempts to summarize current topics pertaining to breast cancer in the elderly.

PRESENTATION

Presentation varies among the elderly population. Some elderly women are more likely to present later with breast cancer because of their lack of awareness.[7] Yet, some studies show the elderly can present at earlier stages.[8] Many patients older than 85 years self-refer because screening is not provided to them.[9] In general, the older the patients, the more likely their initial presentation of breast cancer will be a palpable mass and less likely to be screen detected.[10]

Some studies show the elderly present with a more favorable characteristic malignancy than their younger counterparts.[11] Other studies show patients with earlier-stage cancer had more poorly differentiated cancer with a higher tumor grade and Ki67 similar to their younger counterparts.[8] Recent studies show estrogen receptor

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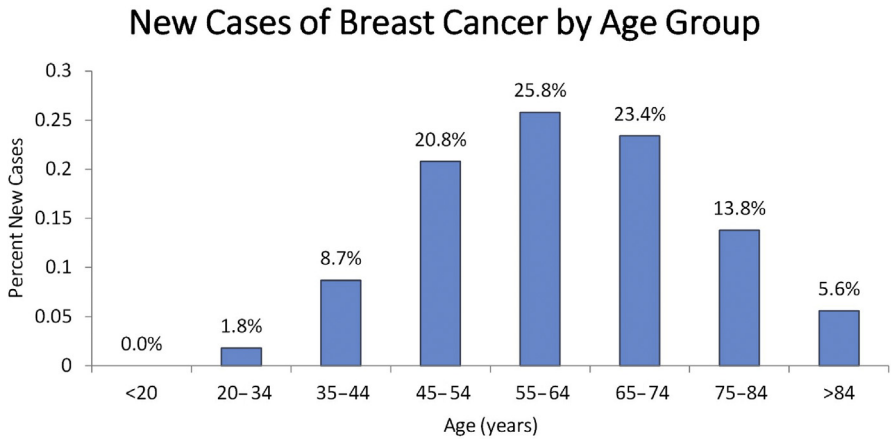

Fig. 1. Surveillance, Epidemiology, and End Results' percent of new cases of breast cancer by age. (*Data from* National Cancer Institute. SEER 18 2010–2014. Available at: https://seer.cancer.gov/statfacts/html/breast.html. Accessed October 9, 2017.)

tumors increase in occurrence with age and human epidermal growth factor receptor 2 (Her2) status decreases with age.[12,13]

Invasive ductal cancer (76%) makes up most breast cancers in the elderly. Invasive lobular carcinoma makes up 5.6%, and ductal carcinoma in situ alone was 10.0% of elderly breast pathology.[14] Overall, the most common presentation for elderly patients is higher-grade, hormone receptor–positive invasive ductal cancer.[11]

SCREENING

Among national organizations, mammography is the imaging modality of choice for screening.[15] Many randomized and case-controlled trials have evaluated the costs and benefits of screening. The Health Insurance Plan trial of New York in 1963 revealed mammographic screening reduced breast cancer mortality by 30%. Recent meta-analysis has shown a 15% to 20% relative risk reduction in mortality with breast cancer screening.[16] Yet, with about 11 trials evaluating screening, the US Preventative Services Task Force, the American Cancer Society, the American Geriatric Society, the American College of Obstetrics and Gynecology, and other organizations have not converged on a single recommendation for screening guidelines in the elderly.[17] Many of these trials did not include patients who were older than 60 years.

Critics of overscreening the elderly cite higher incidence of breast cancer in the elderly, increased risk of death from other disease, and the slow growth of most tumors.[18] The United Kingdom conducted an independent review to evaluate the benefits and harms of screening and concluded that there is an 11% to 19% overdiagnosis.[16] A Cochrane review of 7 randomized trials concluded there is a 15% reduction of breast cancer risk with screening mammogram but a 30% overdiagnosis and overtreatment. Only 6 of the 11 trials included women older than 60 years, and only the Swedish Kopparberg trial included patients older than 65 years.[19] This Swedish trial concluded that reduction in mortality was 34% in women aged 50 years and older with 0.66 odds ratio breast cancer mortality and, therefore, a greater benefit (**Table 1**).[19]

Currently, routine screening for breast cancer in patients older than 74 years is controversial. Some advocate continued clinical breast examinations over mammography in this age group.[20] The National Cancer Institute (NCI) has deferred recommendations

Table 1
Eleven trials evaluating mammography and its correlation to the odds ratio for breast cancer and overall mortality

Reference	Year	Age Group (y)	Intervention	Control	Methodologic Quality[a]	OR for Breast Cancer Mortality	OR for Overall Mortality
HIP	1963	40–64	Mammography + CE (n = 31,000)	Nothing (n = 31,000)	Less robust	0.65 (0.49–0.86)	0.95 (0.87–1.04)
Malmö 1	1976	>44	Mammography (n = 21,088)	Nothing (n = 21,195)	Sound	0.96 (0.68–1.35)	0.99 (0.93–1.05)
Kopparberg	1977	40–74	Mammography (n = 39,051)	Nothing (n = 18,846)	Less robust	0.66 (0.46–0.94)	1.03 (0.96–1.10)
Östergötland	1978	>40	Mammography (n = 39,034)	Nothing (n = 37,936)	Less robust	0.77 (0.54–1.10)	0.99 (0.94–1.05)
Malmö 2	1978	45–50	Mammography (n = 9581)	Nothing (n = 8212)	Less robust	0.75 (0.46–1.24)	1.15 (0.99–1.33)
TEDBC Edinburgh	1979	45–64	Mammography + CE (n = 22,926)	SE (n = 21,342)	Biased	0.83 (0.54–1.27)	Reduced
NBSS1	1980	40–49	Mammography + CE + SE (n = 25,214)	Initial CE + SE (n = 25,216)	Sound	1.36 (0.83–2.21)	1.02 (0.82–1.27)
NBSS2	1980	50–59	Mammography + CE + SE (n = 19,711)	CE + SE (n = 19,694)	Sound	0.97 (0.62–1.52)	1.01 (0.85–1.20)
Stockholm	1981	40–64	Mammography (n = 38,525)	Nothing (n = 20,651)	Less robust	0.71 (0.47–1.07)	0.91 (0.85–0.99)
Göteborg	1982	39–59	Mammography (n = 10,821/9903)	Nothing (n = 13,101/15,708)	Less robust	0.73/0.90 (0.26–2.00/ 0.53–1.54)	1.17/0.93 (0.95–1.43/ 0.82–1.06)
UKCCR	1991	39–41	Mammography (n = 53,884)	Nothing (n = 106,956)	Sound	0.83 (0.66–1.04)	0.97 (0.89–1.04)

Abbreviation: OR, odds ratio.

From Paesmans M, Ameye L, Moreau M, et al. Breast cancer screening in the older woman: an effective way to reduce mortality? Maturitas 2010;66(3):264; with permission.

for screening to other organizations but does state the cumulative false-positive rate of mammography with clinical breast examination after 10 years of annual screening to be 50%.[21,22]

A new trial, the Wisdom trial, which looks into personalized screening of patients based on individual risks factors (breast density, family history, age, race/ethnicity, comorbidities, genomic profiling), promises to deliver the answer for how to best screen for breast cancer.[23] Patients and physicians have tools available, such as ePrognosis from the University of California San Francisco (eprognosis.ucsf.edu), which take into account patient demographics and risk factors to determine if screening is harmful or beneficial.[24] With personalized medicine in the forefront, uniformity for best practice screening methods will not only be based on age but also on risk factors and life expectancy.

SURVIVAL

By examining the NCI's Surveillance, Epidemiology, and End Results (SEER) database, the 5-year survival for breast cancer from 1975 to 2013 increased from 74.9% to 91.1%. Among patients older than 65 years, the most recent data show an 89.5% 5-year overall survival. Specifically, those between 65 and 74 years of age have a rate of 91.4% for 5-year survival. These survival rates are comparable with those from individuals aged younger than 45 years (88.1%), 45 to 54 years (90.6%), and 55 to 64 years (90.1%). When looking at survival based on the stage of breast cancer, individuals older than 50 years, stage for stage, have similar survival except for stage 4 distant disease. In this population, the survival is 24.1% for those aged 50 years and older compared with 37.1% in those aged 50 years and younger (**Fig. 2**).[25] These differences may be because, studies show, elderly patients tend to be undertreated for even early stage breast cancer compared with younger patients, which increases their breast cancer recurrence and decreases their survival. Albeit the most common reason for decreased survival may be that the elderly have more comorbidities compared with with their younger counterparts, which prohibits them from tolerating the same treatments.[26]

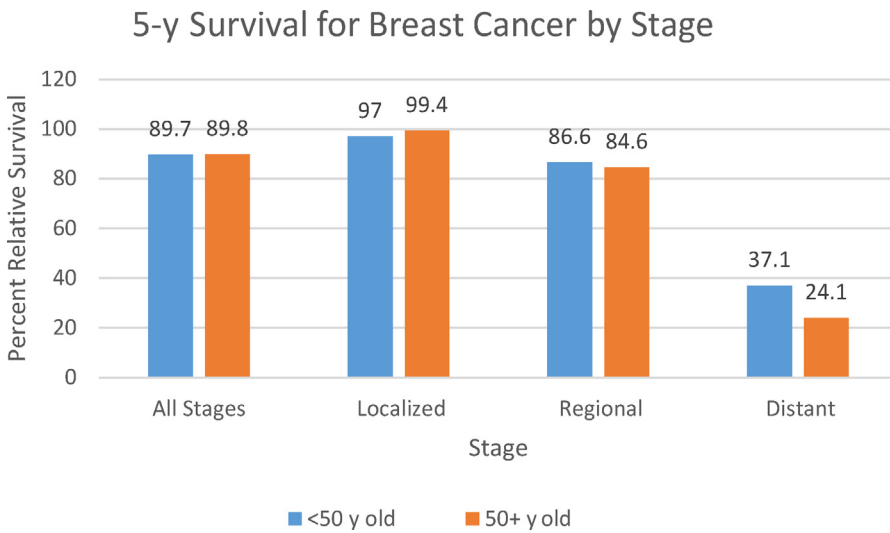

Fig. 2. SEER's 5-year relative survival for breast cancer by stage and age. (*Data from* National Cancer Institute. SEER cancer statistics: breast cancer. Available at: https://seer.cancer.gov/csr/1975_2014/results_merged/sect_04_breast.pdf. Accessed October 9, 2017.)

SURGICAL OUTCOMES

Surgery plays a central role in the treatment of breast cancer. In the elderly population, morbidity and mortality associated with surgery are increased. Even in treating early stage disease (stage 0–II) in octogenarians and nonagenarians, increased age is a significant risk factor for death.[27] Studies show surgical treatment of stage III in those 80 years old or more produces a 5-year survival of 48.5%, which is worse compared with younger patients of the same stage.[28] A multisite Breast Cancer Surgical Outcomes (BRCASO) database exists to monitor morbidity and mortality in patients with breast cancer after surgical intervention.[29] Although the study done by Pettke and colleagues[30] showed overall perioperative mortality is low, patients older than 80 years have increased mortality and systemic morbidity like cardiac arrests and pneumonias. Yet, their wound complications were equal to their younger counterparts. Certain procedures like mastectomy with immediate breast reconstruction have also increased in the elderly from 6.7% in 2004 to 18.1% in 2012, and the trend continues to increase especially in patients with larger tumors.[26,31] The main complication in this demographic is a 34% increase in 30-day readmissions even when the elderly have no comorbidities. More studies need to be conducted to evaluate surgical outcomes in the elderly so appropriate counseling can aid their decision-making for treatment.[26]

Optimal surgical treatment of breast cancer in an older patient population is not clearly defined. Difficulties in determining the optimal treatment include comorbidities, concerns about treatment effects on quality of life, shorter life expectancy, decreased mental and physical capacity, patient preference, and slower progression of disease.

ROLE OF SENTINEL LYMPH NODE BIOPSY AND AXILLARY LYMPH NODE DISSECTION

Surgical treatment of breast cancer initially included an axillary lymph node dissection regardless of lymph node status because of Halsted's theory of clearing axillary disease to prevent distant spread. Findings from National Surgical Adjuvant Breast and Bowel Project (NSABP) showed leaving positive axillary lymph nodes in the group that underwent mastectomy alone did not have an increased rate of distant recurrence or breast cancer–related mortality.[32] These findings led to the theory that axillary lymph node involvement is more likely an indicator of disease spread and that axillary clearance does not prevent distant spread. The information provided by an axillary lymph node dissection, thus, became an important part of staging to help guide adjuvant treatment recommendations. In the elderly, the role of an axillary dissection has been unclear given the morbidity associated with the procedure and shorter life expectancy. A retrospective study that included only patients older than 70 years with operable, clinically node-negative breast cancer compared patients who underwent axillary dissection with patients who did not undergo axillary dissection. Tamoxifen was prescribed for at least 2 years in this study. At a median follow-up of 15 years, there was no difference in breast cancer mortality between the two groups.[33] A meta-analysis composed of 2 randomized controlled studies with a total of 692 patients found no difference in in-breast recurrence or distant recurrence between axillary staging and no axillary staging. They also found no differences in overall survival or breast cancer–specific survival between the two groups.[34] One of the studies included in the meta-analysis looked at quality of life after an axillary lymph node dissection. The study found a significant difference in physician-reported adverse effects in the first postoperative period in terms of restriction of arm movement and arm pain among patients undergoing axillary surgery compared with the group that did not have axillary surgery.[35] Two studies by Martelli and colleagues[33,36] report the incidence of axillary disease in the groups that did not receive an axillary lymph node dissection and found only about a 6% incidence at

15 years. In patients whereby the staging information acquired from an axillary lymph node dissection is unlikely to affect the adjuvant treatment decisions, the data suggest that omission of an axillary lymph node dissection will not affect survival and results in a low rate of axillary recurrence.

The morbidities associated with an axillary lymph node dissection eventually led to the development and use of the sentinel lymph node biopsy for staging in patients with clinically node-negative disease. NSABP-32 showed that omission of the axillary lymph node dissection in patients with clinically node-negative disease had no impact on overall survival, disease-free survival, and regional control.[37] Findings in several other studies showing no survival benefit from an axillary lymph node dissection eventually led to the Society of Surgical Oncology to recommend, in 2016 as part of the Choosing Wisely campaign, that surgeons "do not routinely use sentinel lymph node biopsy in clinically node negative women older than 70 years of age with hormone receptor positive invasive breast cancer."[33,38] This recommendation raises questions about whether or not a sentinel lymph node biopsy should be eliminated for all women older than of 70 years because nodal status can affect adjuvant treatment recommendations. In a study looking at patients older than 70 years from the National Cancer Database, only 15% of the patients studied who underwent nodal evaluation had a positive lymph node. The median number of positive lymph nodes was one. The same group also did a parallel analysis using the SEER database and found that 26% of patients had a positive lymph node. Both analyses showed better overall survival in the group undergoing lymph node evaluation, but the difference was likely due to patient selection factors. The investigators concluded that following the Choosing Wisely guideline would unlikely significantly change survival in the patients who would have otherwise done well based on tumor biology or the patients who already have limited life expectancy. In a group of more high-risk patients who are healthy, lymph node evaluation may provide important information for determining their adjuvant therapy options.[39] Welsh and colleagues[40] developed a model to predict nodal positivity in women older than 70 years with hormone receptor–positive disease to help determine which group of patients has a higher risk of node positivity. They found a low-risk group of patients, those with grade 1 tumors less than 2 cm or those with grade 2 tumors less than 1 cm, had a node positivity rate of 7.8%. Patients not in the low-risk group, all grade 3 tumors, clinically T2 tumors, or grade 2 T1c tumors, were found to have a node positivity rate of 22.3%. The investigators concluded that patients identified to be in the low-risk group were ideal candidates for omission of a sentinel lymph node biopsy. Therefore, the use of sentinel lymph node biopsies in patients older than 70 years should be decided based on individual patient-specific characteristics, such as comorbidities, life expectancy, and surgical risk, as well as likelihood of having a positive node.

ROLE OF ENDOCRINE THERAPY ALONE

Surgery plays a role in standard treatment of breast cancer; but in the elderly population, multiple studies have been conducted to look at treatment with endocrine alone in patients who are not ideal surgical candidates. A retrospective study in the Netherlands looked at women older than 75 years who received primary endocrine therapy (PET) and compared those patients with patients who underwent surgical treatment. They found that women who had PET had their survival significantly compromised compared with the women who were treated with surgery. Women receiving PET had a 5-year overall survival of 27.0% compared with 62.3% for women undergoing surgery. Age and prevalence of comorbidities did differ significantly

between the two groups, with the women receiving PET being older and having more comorbidities.[41] Twenty-year follow-up on a study done in Nottingham, conversely, showed no difference in overall survival or in time to distant metastases between the patients who received primary tamoxifen compared with patients who underwent a wedge mastectomy. They did find a significant difference in time to local recurrence between the two groups.[42] A Cochrane review of 7 randomized controlled trials comparing surgery versus endocrine therapy (tamoxifen) alone also showed no significant difference in overall survival but a significant difference in progression-free survival.[43] These conflicting data suggest that patient selection remains an important determinant in deciding whether or not to offer PET to elderly patients. Consideration for a breast surgery without an axillary procedure could be offered to patients who have a reasonable life expectancy and can safely undergo a surgical procedure.

ROLE OF RADIATION THERAPY

Surgical options of early stage breast cancer consist of a mastectomy or a partial mastectomy with adjuvant radiation therapy as a result of the findings from NSABP-B6. This study found breast-conserving surgery compared with mastectomy did not lead to a difference in disease-free survival, distant disease-free survival, or overall survival. The study found, however, radiation after partial mastectomy led to a decrease in in-breast recurrence.[32] Since the publication of NSABP-B6, several newer studies have looked specifically at the use of radiation therapy after breast-conserving surgery in older patients. They showed that in an older patient population, omission of radiation therapy after breast-conserving surgery also results in similar overall survival rates but with differences in local recurrence rates. Both studies randomized patients undergoing lumpectomy and endocrine therapy to either radiation or no radiation (**Table 2**). These studies found a significant difference in local regional recurrence at 5 years but no significant difference in 5-year overall survival.[38,44] However, in a study looking at radiation therapy utilization and outcomes in elderly patients, Haque and

Table 2
Trials evaluating lumpectomy, radiation and tamoxifen treatments in the elderly

	Number of Patients	Age (y)	Inclusion Criteria	Treatment Arms	Local Recurrence	5-y Survival
CALGB 9343	636	70+	T1N0 ER positive	Lumpectomy + tamoxifen + radiation vs lumpectomy + tamoxifen	1% vs 4% (P<.001)	87% vs 86% (P = .94)
PRIME II	1326	65+	Up to 3 cm clear margins, node-negative ER positive, grade 3 or lymphovascular invasion but not both	Lumpectomy + endocrine therapy, lumpectomy + endocrine therapy + whole-breast radiation	4.1% vs 1.3% (P = .0002)	Both groups 93.9% (P = .34)

Data from Hughes KS, Schnaper LA, Berry D, et al. Lumpectomy plus tamoxifen with or without irradiation in women 70 years of age or older with early breast cancer. N Engl J Med 2004;351:971–7; and Kunkler IH, Williams LJ, Jack WJL, et al. Breast-conserving surgery with or without irradiation in women aged 65 years or older with early breast cancer (PRIME II): a randomized controlled trial. Lancet Oncol 2015;16(3):266–73.

colleagues[45,46] found a survival benefit in patients with estrogen receptor (ER)–positive/Her2-negative disease using SEER data. They note in their study that they had a higher proportion of patients with grade 3 disease than the PRIME II patient cohort, which may account for the differences in findings. They also raised concerns about endocrine therapy use and compliance because SEER data are not able to provide this type of information in accounting for the possible difference in their findings compared with CALGB (Cancer and Leukemia Group B) and PRIME II patient cohorts. These studies provide definitive data to support the omission of radiation therapy in the elderly patient population.

ROLE OF ENDOCRINE THERAPY

For ER-positive breast cancers, adjuvant systemic therapy should include endocrine therapy with either tamoxifen or an aromatase inhibitor. NSABP-B14 showed the use of tamoxifen for 5 years in the adjuvant setting for ER-positive breast cancers to have a significant advantage in disease-free survival, distant disease-free survival, and overall survival at the 10-year follow-up. The study also found no advantage to more than 5 years of tamoxifen and a significant reduction in the incidence of contralateral breast cancer.[47] The development of aromatase inhibitors (AIs) led to multiple trials comparing AIs with tamoxifen. The results of a meta-analysis of these trials found a significant reduction in early recurrence with use of an AI.[48] The Breast International Group (BIG) 1-98 study at 8.1 years of median follow-up, treatment with 5 years of letrozole in postmenopausal women with estrogen-positive breast cancers results in significant improvements in disease-free survival, overall survival, distant recurrence-free interval, and breast cancer–free interval compared with tamoxifen.[49] Tamoxifen has been associated with both thromboembolic events and uterine cancer. AI use has been found to increase the odds of developing cardiovascular disease and bone fractures but decreased odds of venous thrombosis and endometrial carcinoma when compared with tamoxifen.[50] Hot flashes, arthralgia, myalgia, and alopecia are also known common side effects of treatment with an AI but seem to be tolerated by women older than 70 years. A study found no difference in toxicity or quality of life in patients treated with letrozole versus placebo-treated patients older than 70 years.[51] The role of endocrine therapy in the adjuvant setting for ER-positive breast cancers either with tamoxifen or an AI has its benefits and should be considered for patients who have a reasonable life expectancy and do not have comorbidities that preclude them from taking endocrine therapy.

CHEMOTHERAPY

Elderly patients with breast cancer are less likely to obtain chemotherapy than their younger counterparts based on reasons including comorbidities, life expectancy, and concern for chemotoxicity in the frail. Large studies are lacking that focus solely on chemotherapy in older patients in the neoadjuvant, adjuvant, and palliative settings.[52] Some studies have looked at the role of adjuvant chemotherapy in Her2-positive disease. For older women with small Her2-positive node-negative malignancy, a retrospective study from Memorial Sloan Kettering Cancer Center shows the addition of trastuzumab with adjuvant chemotherapy not only produced low cardiac events (3.2%) in patients but also had a 4-year overall survival of 99% and distant relapse-free survival of 99%.[53] Comparing the toxicity of paclitaxel (Taxol)-based treatment with doxorubicin-based treatments reveals similar rates of adverse events and 5-year breast cancer–specific survival (92% doxorubicin-based treatment vs 96% Taxol-based treatment).[54] In patients older than 65 years with triple-negative

disease, adjuvant chemotherapy decreased mortality by 15% with the greatest advantage for those who had regional disease.[55]

Chemotherapeutic agents like anthracyclines are dose dependent on their cardiac and hematologic toxicity. Studies have shown increased hematoxicity in patients who are frailer, diabetic, and needing assistance at home.[56] The NCI has recommended treatment modification for high-grade toxicities, but newer studies are looking at the impact of the toxicity to activities of daily living in order to determine if modification is necessary.[57] Online Web sites like PREDICT (http://www.predict.nhs.uk/predict.html) aid in deciding chemotherapeutic regimens based on risk modeling.[58] With more trials evaluating the chemotoxicity on geriatric functionality and physiology, a better understanding of the tolerance of chemotherapy on the elderly will be assessed, so recommendations in the neoadjuvant, adjuvant, and even palliative settings may be forthcoming.

ONCOTYPE AND MAMMAPRINT

Decisions on how to best treat an aging population have in the past been reliant on multiple patient factors: comorbidities, expected life expectancy, and patient preferences. Molecular tools and genetic expression profiles can also now be incorporated into the decision-making process because these tools allow for assessment of risk. The 21-gene oncotype recurrence score has been validated in estrogen-positive, node-negative, and node-positive breast cancer in predicting the risk for both local regional recurrence and distant recurrence as well as the benefit from chemotherapy. Patients with high recurrence scores show a significant benefit from chemotherapy compared with endocrine therapy alone.[59] In patients with a low recurrence score, the findings from the TAILORx study (Trial Assigning Individualized Options for Treatment) support the use of endocrine therapy alone.[60] For patients who are candidates for chemotherapy, this recurrence score can be used to predict a benefit from chemotherapy, especially when taking into consideration the effects that chemotherapy has on the elderly population.[60]

The 70-gene Mammaprint assay has been validated to predict which patients may be at risk for recurrence. More recently, an ultralow risk threshold of the Mammaprint assay has been identified. The patients in this study who had ultralow-risk tumors had a significantly lower risk of breast specific death compared with the low-risk and high-risk tumor groups. These findings lead the authors to conclude that the ultralow risk threshold can be used to identify patients who can be safely treated with surgery alone.[61] In the elderly population, this assay could be used as another tool to risk stratify patients during the discussion of which treatments to pursue.

ETHICS AND DISPARITY

With 12% of the US population older than 70 years and increasing at a rate of 2.5% per year, the ethics of treating these patients with multiple comorbidities becomes challenging. Concerns about ageism and rationing care arise when making decisions for breast cancer treatment.[62] The average life expectancy of a 70-year-old person is 12.5 years from their initial presentation.[63] So when deciding treatment, some organizations focus on resource allocation or quality of life to decide which treatment may be fraught with discriminatory bias.[62] Some have advocated using the Comprehensive Geriatric Assessment tool to risk stratify patients in order to aid in treatment of elderly patients with breast cancer.[13,64] Ethical dilemmas for screening and treating patients with dementia have arisen with recommendations to evaluate risks and benefits, including life expectancy and quality of life of patients, to help make those complex decisions (**Fig. 3**).[65,66] The Age Gap Cohort Study in the United Kingdom is currently

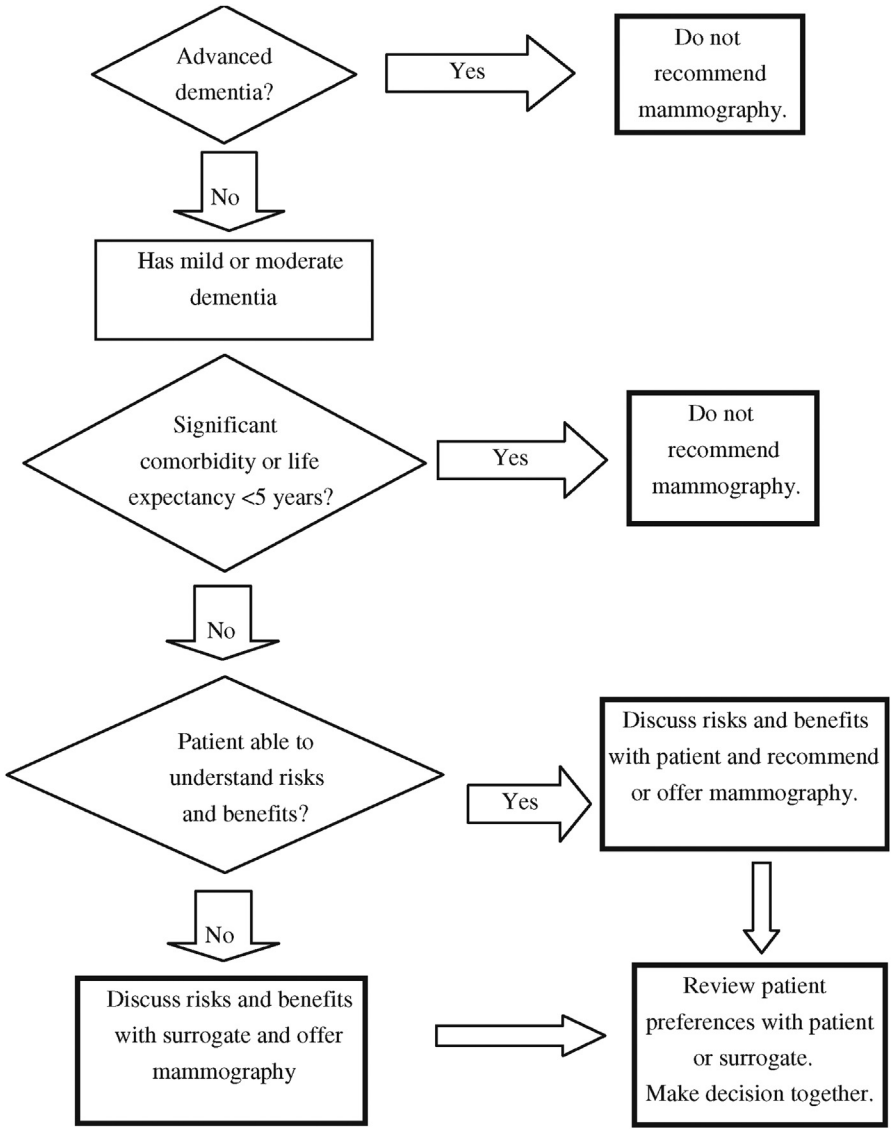

Fig. 3. Decision-making model screening mammography in cognitively impaired women. (*From* Raik BL, Miller FG, Fins JJ. Screening and cognitive impairment: ethics of forgoing mammography in older women. J Am Geriatr Soc 2004;52(3):443; with permission.)

looking into the treatment decision-making process in the elderly with breast cancer with the aim of best practice recommendations.[67]

Studies are also looking into the disparity in care of the elderly. Those with early stage breast cancer tend to die of other comorbidities; but mortality from breast cancer, nevertheless, increases with age. Still, undertreatment of the disease in the elderly is common. The discrepancy lies in adjusting the management of the cancer with the increased comorbidities of the elderly.[13] Most trials have excluded this age group in

their analysis of breast cancer prevention, diagnosis, and treatment.[68] Future trials will need to investigate the best plan of action to minimize the disparity in care.

SUMMARY

With increasing life expectancy and growth of the elderly US population, it becomes paramount that breast cancer research focuses more on the prevention, screening, and treatment of these patients. Age no longer is a cutoff for managing breast cancer in the elderly. Studies have shown the current undertreatment of cancer undermines survival, but the tide is turning to provide evidence-based medicine for the elderly. More often, clinicians and surgeons look not only at tumor-specific characteristics of breast cancer but also the functionality, tolerance, comorbidities, and life expectancy of patients to determine the best treatment. The geriatric population in the twenty-first century needs appropriate assessment before managing breast cancer so individuals obtain the best practice medicine available.

REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA Cancer J Clin 2016; 66(1):7–30.
2. Cancer of the breast (female) - Cancer stat facts. Available at: https://seer.cancer.gov/statfacts/html/breast.html. Accessed October 8, 2017.
3. Inwald EC, Ortmann O, Koller M, et al. Screening-relevant age threshold of 70 years and older is a stronger determinant for the choice of adjuvant treatment in breast cancer patients than tumor biology. Breast Cancer Res Treat 2017;163(1):119–30.
4. Lohr KN, editor. Medicare: A strategy for quality assurance: Volume 1. Chapter 3, The elderly population. Washington, DC: National Academies Press (US); 1990. p. 69–95. Available at: https://www.ncbi.nlm.nih.gov/books/NBK235450/. Accessed October 8, 2017.
5. WHO | Proposed working definition of an older person in Africa for the MDS Project. WHO. Available at: http://www.who.int/healthinfo/survey/ageingdefnolder/en/. Accessed October 8, 2017.
6. Calculators: life expectancy. Available at: https://www-ssa-gov.ucsf.idm.oclc.org/planners/lifeexpectancy.html. Accessed October 9, 2017.
7. Forster AS, Forbes LJL, Abraham C, et al. Promoting early presentation of breast cancer: a preliminary evaluation of a written intervention. Chronic Illn 2014;10(1): 18–30.
8. Montroni I, Rocchi M, Santini D, et al. Has breast cancer in the elderly remained the same over recent decades? A comparison of two groups of patients 70 years or older treated for breast cancer twenty years apart. J Geriatr Oncol 2014;5(3): 260–5.
9. Richards P, Ward S, Morgan J, et al. The use of surgery in the treatment of ER+ early stage breast cancer in England: variation by time, age and patient characteristics. Eur J Surg Oncol 2016;42(4):489–96.
10. Mustacchi G, Cazzaniga ME, Pronzato P, et al. Breast cancer in elderly women: a different reality? Results from the NORA study. Ann Oncol 2007;18(6):991–6.
11. Sierink JC, de Castro SMM, Russell NS, et al. Treatment strategies in elderly breast cancer patients: is there a need for surgery? Breast 2014;23(6):793–8.
12. Dimitrakopoulos F-ID, Kottorou A, Antonacopoulou AG, et al. Early-stage breast cancer in the elderly: confronting an old clinical problem. J Breast Cancer 2015;18(3):207–17.

13. Gosain R, Pollock Y, Jain D. Age-related disparity: breast cancer in the elderly. Curr Oncol Rep 2016;18(11):69.
14. Tang S-W, Parker H, Winterbottom L, et al. Early primary breast cancer in the elderly - pattern of presentation and treatment. Surg Oncol 2011;20(1):7–12.
15. Breast cancer screening in older women. Available at: http://www.mdedge.com/clinicianreviews/article/72084/geriatrics/breast-cancer-screening-older-women. Accessed September 25, 2017.
16. Independent UK. Panel on breast cancer screening. The benefits and harms of breast cancer screening: an independent review. Lancet 2012;380(9855):1778–86.
17. p659.pdf. Available at: http://www.aafp.org/afp/2016/0415/p659.pdf. Accessed August 21, 2017.
18. Raffin E, Onega T, Bynum J, et al. Are there regional tendencies toward controversial screening practices? A study of prostate and breast cancer screening in a Medicare population. Cancer Epidemiol 2017;50(Pt A):68–75.
19. Paesmans M, Ameye L, Moreau M, et al. Breast cancer screening in the older woman: an effective way to reduce mortality? Maturitas 2010;66(3):263–7.
20. Jatoi I. Breast cancer screening recommendations. JAMA 2013;310(19):2101–2.
21. Breast cancer screening. National Cancer Institute. Available at: https://www.cancer.gov/types/breast/hp/breast-screening-pdq. Accessed October 5, 2017.
22. Elmore JG, Barton MB, Moceri VM, et al. Ten-year risk of false positive screening mammograms and clinical breast examinations. N Engl J Med 1998;338(16):1089–96.
23. Esserman LJ, WISDOM Study and Athena Investigators. The WISDOM study: breaking the deadlock in the breast cancer screening debate. NPJ Breast Cancer 2017;3:34.
24. ePrognosis. Available at: https://eprognosis.ucsf.edu/. Accessed October 16, 2017.
25. sect_04_breast.pdf. Available at: https://seer.cancer.gov/csr/1975_2014/results_merged/sect_04_breast.pdf. Accessed October 6, 2017.
26. Gibreel WO, Day CN, Hoskin TL, et al. Reconstruction for cancer in the elderly: a national cancer data base study. J Am Coll Surg 2017;224(5):895–905.
27. Merrill AY, Brown DR, Klepin HD, et al. Outcomes after mastectomy and lumpectomy in octogenarians and nonagenarians with early-stage breast cancer. Am Surg 2017;83(8):887–94.
28. Lee CM, Zheng H, Tan VK-M, et al. Surgery for early breast cancer in the extremely elderly leads to improved outcomes – an Asian population study. Breast 2017;36(Supplement C):44–8.
29. Aiello Bowles EJ, Feigelson HS, Barney T, et al. Improving quality of breast cancer surgery through development of a national breast cancer surgical outcomes (BRCASO) research database. BMC Cancer 2012;12:136.
30. Pettke E, Ilonzo N, Ayewah M, et al. Short-term, postoperative breast cancer outcomes in patients with advanced age. Am J Surg 2016;212(4):677–81.
31. Kummerow KL, Du L, Penson DF, et al. Nationwide trends in mastectomy for early-stage breast cancer. JAMA Surg 2015;150(1):9–16.
32. Fisher B, Jeong J-H, Anderson S, et al. Twenty-five-year follow-up of a randomized trial comparing radical mastectomy, total mastectomy, and total mastectomy followed by irradiation. N Engl J Med 2002;347(8):567–75.
33. Martelli G, Miceli R, Daidone MG, et al. Axillary dissection versus no axillary dissection in elderly patients with breast cancer and no palpable axillary nodes: results after 15 years of follow-up. Ann Surg Oncol 2011;18(1):125–33.

34. Liang S, Hallet J, Simpson JS, et al. Omission of axillary staging in elderly patients with early stage breast cancer impacts regional control but not survival: a systematic review and meta-analysis. J Geriatr Oncol 2017;8(2):140–7.
35. International Breast Cancer Study Group, Rudenstam CM, Zahrieh D, Forbes JF, et al. Randomized trial comparing axillary clearance versus no axillary clearance in older patients with breast cancer: first results of International Breast Cancer Study Group Trial 10-93. J Clin Oncol 2006;24(3):337–44.
36. Martelli G, Boracchi P, Orenti A, et al. Axillary dissection versus no axillary dissection in older T1N0 breast cancer patients: 15-year results of trial and out-trial patients. Eur J Surg Oncol 2014;40(7):805–12.
37. Krag DN, Anderson SJ, Julian TB, et al. Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival findings from the NSABP B-32 randomised phase 3 trial. Lancet Oncol 2010;11(10):927–33.
38. Hughes KS, Schnaper LA, Bellon JR, et al. Lumpectomy plus tamoxifen with or without irradiation in women age 70 years or older with early breast cancer: long-term follow-up of CALGB 9343. J Clin Oncol 2013;31(19):2382–7.
39. Chagpar AB, Hatzis C, Pusztai L, et al. Association of LN evaluation with survival in women aged 70 years or older with clinically node-negative hormone receptor positive breast cancer. Ann Surg Oncol 2017;24(10):3073–81.
40. Welsh JL, Hoskin TL, Day CN, et al. Predicting nodal positivity in women 70 years of age and older with hormone receptor-positive breast cancer to aid incorporation of a society of surgical oncology choosing wisely guideline into clinical practice. Ann Surg Oncol 2017;24(10):2881–8.
41. Wink CJ, Woensdregt K, Nieuwenhuijzen GA, et al. Hormone treatment without surgery for patients aged 75 years or older with operable breast cancer. Ann Surg Oncol 2012;19(4):1185–91.
42. Chakrabarti J, Kenny FS, Syed BM, et al. A randomised trial of mastectomy only versus tamoxifen for treating elderly patients with operable primary breast cancer-final results at 20-year follow-up. Crit Rev Oncol Hematol 2011;78(3):260–4.
43. Hind D, Wyld L, Reed MW. Surgery, with or without tamoxifen, vs tamoxifen alone for older women with operable breast cancer: Cochrane review. Br J Cancer 2007;96(7):1025–9.
44. Kunkler IH, Williams LJ, Jack WJL, et al. PRIME II investigators. Breast-conserving surgery with or without irradiation in women aged 65 years or older with early breast cancer (PRIME II): a randomised controlled trial. Lancet Oncol 2015;16(3):266–73.
45. Haque W, Kee Yuan DM, Verma V, et al. Radiation therapy utilization and outcomes for older women with breast cancer: impact of molecular subtype and tumor grade. Breast 2017;35:34–41.
46. Fyles AW, McCready DR, Manchul LA, et al. Tamoxifen with or without breast irradiation in women 50 years of age or older with early breast cancer. N Engl J Med 2004;351(10):963–70.
47. Fisher B, Dignam J, Bryant J, et al. Five versus more than five years of tamoxifen therapy for breast cancer patients with negative lymph nodes and estrogen receptor-positive tumors. J Natl Cancer Inst 1996;88(21):1529–42.
48. Dowsett M, Cuzick J, Ingle J, et al. Meta-analysis of breast cancer outcomes in adjuvant trials of aromatase inhibitors versus tamoxifen. J Clin Oncol 2010;28(3):509–18.

49. Regan MM, Neven P, Giobbie-Hurder A, et al. Assessment of letrozole and tamoxifen alone and in sequence for postmenopausal women with steroid hormone receptor-positive breast cancer: the BIG 1-98 randomised clinical trial at 8·1 years median follow-up. Lancet Oncol 2011;12(12):1101–8.
50. Amir E, Seruga B, Niraula S, et al. Toxicity of adjuvant endocrine therapy in postmenopausal breast cancer patients: a systematic review and meta-analysis. J Natl Cancer Inst 2011;103(17):1299–309.
51. Muss HB, Tu D, Ingle JN, et al. Efficacy, toxicity, and quality of life in older women with early-stage breast cancer treated with letrozole or placebo after 5 years of tamoxifen: NCIC CTG intergroup trial MA.17. J Clin Oncol 2008; 26(12):1956–64.
52. Fietz T, Zahn M-O, Köhler A, et al. Routine treatment and outcome of breast cancer in younger versus elderly patients: results from the SENORA project of the prospective German TMK cohort study. Breast Cancer Res Treat 2018;167(2):567–78.
53. Cadoo KA, Morris PG, Cowell EP, et al. Adjuvant chemotherapy and trastuzumab is safe and effective in older women with small, node-negative, HER2-positive early-stage breast cancer. Clin Breast Cancer 2016;16(6):487–93.
54. Reeder-Hayes KE, Meyer AM, Hinton SP, et al. Comparative toxicity and effectiveness of trastuzumab-based chemotherapy regimens in older women with early-stage breast cancer. J Clin Oncol 2017;35(29):3298–305.
55. Elkin EB, Hurria A, Mitra N, et al. Adjuvant chemotherapy and survival in older women with hormone receptor-negative breast cancer: assessing outcome in a population-based, observational cohort. J Clin Oncol 2006;24(18):2757–64.
56. Sostelly A, Henin E, Chauvenet L, et al. Can we predict chemo-induced hematotoxicity in elderly patients treated with pegylated liposomal doxorubicin? Results of a population-based model derived from the DOGMES phase II trial of the GINECO. J Geriatr Oncol 2013;4(1):48–57.
57. Extermann M, Reich RR, Sehovic M. Chemotoxicity recurrence in older patients: risk factors and effectiveness of preventive strategies-a prospective study. Cancer 2015;121(17):2984–92.
58. Karuturi M, VanderWalde N, Muss H. Approach and management of breast cancer in the elderly. Clin Geriatr Med 2016;32(1):133–53.
59. Albain KS, Barlow WE, Shak S, et al. Prognostic and predictive value of the 21-gene recurrence score assay in postmenopausal women with node-positive, oestrogen-receptor-positive breast cancer on chemotherapy: a retrospective analysis of a randomised trial. Lancet Oncol 2010;11(1):55–65.
60. Sparano JA, Gray RJ, Makower DF, et al. Prospective validation of a 21-gene expression assay in breast cancer. N Engl J Med 2015;373(21):2005–14.
61. Esserman LJ, Yau C, Thompson CK, et al. Use of molecular tools to identify patients with indolent breast cancers with ultralow risk over 2 decades. JAMA Oncol 2017;3(11):1503–10.
62. Kearney N, Miller M. Elderly patients with cancer: an ethical dilemma. Crit Rev Oncol Hematol 2000;33(2):149–54.
63. Capocaccia R, Gatta G, Dal Maso L. Life expectancy of colon, breast, and testicular cancer patients: an analysis of US-SEER population-based data. Ann Oncol 2015;26(6):1263–8.
64. Albrand G, Terret C. Early breast cancer in the elderly: assessment and management considerations. Drugs Aging 2008;25(1):35–45.
65. Yousef GM, Sovani P, Devabhaktuni S, et al. Screening mammograms in Alzheimer's disease patients. W V Med J 2012;108(3):92–5.

66. Raik BL, Miller FG, Fins JJ. Screening and cognitive impairment: ethics of forgoing mammography in older women. J Am Geriatr Soc 2004;52(3):440–4.
67. Collins K, Reed M, Lifford K, et al. Bridging the age gap in breast cancer: evaluation of decision support interventions for older women with operable breast cancer: protocol for a cluster randomised controlled trial. BMJ Open 2017;7(7): e015133.
68. Weijer C, Freedman B, Shapiro S, et al. Assessing the interpretation of criteria for clinical trial eligibility: a survey of oncology investigators. Clin Invest Med 1998; 21(1):17–26.