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GERIATRIC ONCOLOGY (AR MACKENZIE, SECTION EDITOR)

Surgery in the Older Patient with Breast Cancer

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Abstract

Purpose of Review Breast cancer incidence and mortality increase with age. Older patients (≥ 70) are often excluded from studies. Due to multiple factors, it is unclear whether this population is best-treated using standard guidelines. Here, we review surgical management in older women with breast cancer.

Recent Findings Geriatric assessments can guide treatment recommendations and aid in predicting survival and quality of life. Surgery remains a principal component of breast cancer treatment in older patients, though differences exist compared with younger women, including higher mastectomy rates and evidence-based support of omission of post-lumpectomy radiation or axillary dissection in subsets of patients. In those forgoing surgical management, there is increased use of endocrine therapy. Hospice is also a valuable element of end-of-life care.

Summary Physicians should utilize geriatric assessment to make treatment recommendations for older breast cancer patients, including omission of radiation therapy, alterations to standard surgeries, or enrollment in hospice care.

Keywords Breast cancer · Older patients · Geriatric oncology · Surgery · Lumpectomy · Geriatric assessment

Introduction

Breast cancer is the most commonly diagnosed cancer in women and is the second leading cause of cancer-related mortality in the USA. The risk of breast cancer increases with age, as women aged ≥ 70 account for 53% of new diagnoses and 47% of breast cancer deaths [1]. This finding will likely rise with an aging population. Despite the rising incidence, breast cancer research is more often focused on younger populations, leading to a paucity of data and recommendations regarding breast cancer treatment in older patients.

Differences in diagnostic methods, tumor characteristics, and therapies exist between younger and older patients due to a multitude of factors. Compared with their younger counterparts, older women are more likely to be diagnosed on physical exam than with imaging and typically present with larger tumors. However, their tumors are more likely to be low grade and hormone sensitive [2, 3]. These differences in tumor characteristics, as well as patient comorbidities, are taken into account when planning treatment. Ultimately, these factors may account for alterations in treatment patterns in older women compared with the general population. Lower rates of surgery, radiation therapy, and chemotherapy are reported in older versus younger women [4, 5]. Due to lack of enrollment of older adults in clinical trials [6], it is difficult to conclude whether less aggressive treatment in older women is warranted, and whether differences in treatment patterns correlate with survival outcomes in this population.

With an aging population and rising incidence of breast cancer, it is important to understand the optimal treatment for older breast cancer patients. Here, we outline the considerations in determining surgical treatment for breast cancer in older patients including assessment of functional status, considerations in providing surgical therapy, and options for non-surgical treatment.

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Assessing Functional Status

While decisions regarding treatment of breast cancer are typically based upon clinical characteristics, treatments in older women may be impacted by comorbidities, end-of-life care, and patient wishes. Because of the potential for over- or undertreating patients if treatments are based upon age alone, the Society of Geriatric Oncology has supported the use of geriatric assessment in the workup and care of geriatric oncology patients [7, 8]. A multitude of geriatric-specific and preoperative assessments can be used to evaluate the functional status of patients prior to choosing treatments. Here, we discuss three commonly used strategies applicable to older cancer patients.

Comprehensive Geriatric Assessment

The comprehensive geriatric assessment (CGA) is a multidimensional process for fully evaluating an older patient's health, utilizing the expertise of several specialists in a team-based setting and using validated tools from multiple modalities to create a comprehensive picture of the patient's status, including physical and mental health, functional status, and social environment [9–12]. This assessment contrasts with the routine assessment of an older patient by an individual physician using history and physical exam to assess general health status [7]. CGA programs exist primarily in hospital settings, as resources and specialist availability limit their expansion to lower resource settings [7]. Core components of CGA include functional status, psychosocial information, cognitive function, nutrition, and medications [11], but approaches used for assessment may differ by program. CGA elements used in studies discussed in this review are summarized in Table 1, although there are many other approaches to CGA dependent on the program. CGA is a valuable approach for understanding the potential for treatment toxicity and estimation of survival and quality of life, which can assist in selecting the best treatment plan for individual patients. Poor results in multiple geriatric assessment measures are associated with worse outcomes in older breast cancer patients, independent of disease characteristics and patient age [13].

CGA has been validated for applications in many specialties, including oncology [7]. In one study, breast cancer patients ≥ 70 were evaluated after diagnosis and surgical planning using CGA. Completion of CGA identified factors including comorbidities, polypharmacy, and decline in mobility that were more often present in patients who did not receive surgery for their breast cancer [14]. Another retrospective study of women ≥ 70 with invasive breast cancer used eight assessment tools in line with the CGA, including measures of performance status, activities of daily living, comorbidities, and cognitive status, and qualified patients as "fit" if they had a normal result for seven of the eight tools. More "fit" than "unfit" patients received breast surgery, axillary surgery, and chemotherapy, again demonstrating that CGA identifies factors important to establish surgical candidacy and qualification for other treatments [15•]. The valuable information obtained with a CGA and ease of application in the breast oncology setting demonstrates the value in using this strategy in treatment planning for individual patients.

Preoperative Assessment of Cancer in the Elderly

The preoperative assessment of cancer in the elderly (PACE) provides an oncology-specific application of CGA with additional elements, including American Society of Anesthesiologists (ASA) grade, measure of performance status (Eastern Cooperative Oncology Group Performance Status—ECOG-PS), and assessment of fatigue (Brief Fatigue Inventory—BFI) to accurately assess candidacy for surgery specifically in the older population [16, 17] (complete list in Table 1). The measures included in PACE have been shown to correlate with increased length of stay and mortality and are valuable for a targeted assessment of health prior to cancer treatment [16, 17]. In the setting of evaluating surgical candidacy in older breast cancer patients, PACE proves an effective use of resources to predict tolerance of surgery.

Frailty Assessment

Frailty, whose definition includes elements of weight loss, exhaustion, weakness, and declines in physical activity, increases with age. There is a higher risk of mortality in those who are classified as frail compared with those who are not [18]. In a cohort of women ≥ 65 with stage I–III invasive breast cancer, a significant difference was found in overall mortality in patients categorized as "frail" compared with "robust." This study compared the breast cancer-specific mortality associated with frailty as similar to mortality associated with node-positive cancer [19]. Current research is being conducted regarding the measurement of frailty biomarkers to better define these categorizations [20, 21]. The impact of frailty is significant, and properly identifying frail patients prior to treatment planning is valuable in reducing morbidity and mortality.

Use of geriatric assessment tools is imperative in evaluating a patient's functional status when undergoing preoperative workup with older patients. Understanding variables impacting a patient's functional status and overall health are important to predicting surgical candidacy and potential treatment toxicity. Complete assessment of factors impacting survival and quality of life is important when making decisions regarding surgical interventions.

Surgical Procedures

Surgical management remains a routine element of breast cancer care as it is a potentially curative treatment strategy. Studies

Table 1 Elements of geriatric assessments in studies discussed

Comprehensive geriatric assessment (CGA)			
CGA elements	Clough-Gorr et al. [13]	Parks et al. [14]	Okonji et al. [15]
Socioeconomic	-Race, education, marital status, analysis of finances	-Education, marital status, who lives at home, employment status, age, ethnicity	–
Clinical/functional status	-Self-rated health status by interview -Physician rated health status -BMI -10-item physical function index of the MOS Short Form-36	-ADL -IADL -Karnofsky self-reported performance rating scale -Number of falls in last 6 months -Total number of medications -Unintentional weight loss in last 6 months -Medical characteristics (cancer type/stage, chemotherapy regimen) -TUG -BMI	-ECOG-PS -ADL -IADL -VES-13 -ASA grade
Comorbidity	-CCI	-Physical health section—subset of the OARS	-G8 Score -CCI -Clinical information from patient's general practitioner
Cognitive status	–	-BOMC	-6-CIT
Psychosocial	-MHI5 -MOS-SSS	-HADS -MOS Social Activity Limitations Measure -MOS-SSS	
Preoperative assessment of cancer in the elderly (PACE)			
PACE elements	Pope et al. [16]	Audisio et al. [17]	
	-SIC -MMS -ADL -IADL -GDS -BFI -ECOG-PS -ASA grade	-SIC -MMS -ADL -IADL -GDS -BFI -ECOG-PS -ASA grade	

Abbreviations: *6-CIT* 6-Cognitive Impairment Test, *ADL* Activities of Daily Living, *ASA* American Society of Anesthesiologists, *BMI* body mass index, *BFI* brief fatigue inventory, *BOMC* Blessed Orientation Memory-Concentration test, *CCI* Charlson Comorbidity Index, *ECOG-PS* Eastern Cooperative Oncology Group Performance Status, *GDS* geriatric depression scale, *HADS* hospital anxiety and depression scale, *IADL* instrumental activities of daily living, *MHI5* 5-item mental health index, from Medical Outcomes Survey short form, *MMS* Mini-mental state inventory, *MOS* Medical Outcomes Study, *MOS-SSS* Medical Outcomes Study Social Support Scale, *OARS* Older American Resources and Services, SIC Satariano's index of comorbidities, *TUG* Timed "up and go," *VES-13* Vulnerable Elders Survey

have revealed lower rates of surgical therapy in older women [22•], despite the validation of surgery's utility in this population [23–25]. The International Society of Geriatric Oncology (SIOG) recommends offering the same surgery to older patients as younger patients [8]. However, it has been shown that the risk of complication increases with age, peaking at age 85 [26]. Here, we explore the changing trends in surgical procedures for older women with breast cancer.

Lumpectomy

It has been reported that older women have been less likely to receive lumpectomy compared with mastectomy or non-operative treatment [4]. However, other studies have shown rates of lumpectomy to be similar to those in younger populations [27, 28••]. One study using Surveillance, Epidemiology, and End Results (SEER)-Medicare data from 1998 to 2009 found that 66.5% of women ≥ 70 with early stage cancer received breast-conserving surgery, and these patients demonstrated an improved cancer-specific survival compared with those who received mastectomy [28••].

While the landmark NASBP B-06 trial established lumpectomy with irradiation an equivalent therapy to mastectomy [29], more recent studies have shown adjuvant therapies may be excluded in older women with no impact on survival. In 2004, the Cancer and Leukemia Group B (CALGB) 9343 randomized study was published, which examined the use of whole breast radiation in women ≥ 70 with clinical stage I, estrogen receptor-positive, clinically node-negative breast cancer. Patients received lumpectomy and tamoxifen and were randomized to omission or receipt of adjuvant whole breast radiation therapy. While radiation improved local control, it

had no impact on overall survival, even after 10 years of follow-up [30, 31]. The PRIME II study examined women ≥ 65 with early stage breast cancer (hormone receptor-positive, axillary node-negative, tumors ≤ 3 cm) who received lumpectomy and adjuvant endocrine therapy. Women were randomized to receive or omit whole breast radiation, and again, there was a local control benefit, but no survival benefit, to providing radiation therapy after lumpectomy [32]. Both studies found that in long-term follow-up, most deaths were due to comorbidities other than breast cancer, supporting the omission of radiotherapy in an attempt to reduce treatment burden in some older women, with minimal survival impact.

Despite changes in treatment guidelines reflecting these results [33, 34], debate exists regarding whether these changes have been implemented in clinical practice. Multiple database studies have shown only a mild reduction in radiotherapy use after the publication of CALGB 9343. A SEER analysis in the years surrounding CALGB 9343 publication (2001–2007) demonstrated a minor but non-significant decrease in radiotherapy administration in the years following publication [35]. A recent single-institution study reported two-thirds women who would qualify for the omission of radiation were treated with radiotherapy despite these changes in clinical guidelines [36••]. A population-based study of cancer centers in British Columbia found no significant change in adjuvant radiotherapy rates following the publication of CALGB 9343 [37]. There is a speculation that these results may be difficult to integrate into clinical practice, as it is more challenging to omit treatment in accordance with new data rather than add to a treatment plan [38]. Alternatively, some older women may opt for radiotherapy for the local control benefit despite no evidence for improved survival, in accordance with CALGB 9343 [30, 31] and PRIME II [32] results. Further study of the integration of CALGB 9343 and PRIME II results into clinical practice is necessary. It will also be important to examine long-term survival and quality of life issues in the context of these studies.

Mastectomy

Mastectomy may be a preferred operation in the setting of multicentric disease, increased tumor size, advanced cancer, or due to patient preference [39]. Some studies have found as women age, they are more often treated with mastectomy compared with other therapies [3, 39, 40], regardless of tumor size [39], and despite increased risk of post-operative complications [26]. In a survey of surgical, medical, and radiation oncologists regarding treatment choices, oncologists were more likely to recommend mastectomy for a woman aged 84 compared with a 76-year-old woman with the same disease characteristics [41]. A study of SEER-Medicare data on patients aged 70 and over found mastectomy was more often performed in patients with larger tumor size, higher stage disease, and clinically positive lymph nodes. There was no difference in comorbidities or functional status noted in those who received breast-conserving surgery compared with mastectomy [28••], suggesting the choice to pursue mastectomy is often based upon disease-specific factors. The finding that those with more aggressive tumors and more advanced disease are more likely to receive mastectomy may explain potential survival discrepancies between those who receive breast-conserving surgery compared with mastectomy [28••]. In the same study, when controlled for factors including comorbidities and functional status, there was no survival difference between breast-conserving surgery and mastectomy groups [28••], indicating any preference for mastectomy cannot be fully explained by the patient's health and is more likely due to disease-specific factors and/or patient preference. A survey of women of various ages who underwent mastectomy for breast cancer demonstrated women aged 50 and over identified the same reasons for mastectomy preference compared with women under 50, including perceptions of reduced recurrence, improved survival, and avoidance of radiation with mastectomy compared with lumpectomy [42]. While patient preference is an important element of shared decision-making, these results identify a potential lack of education in patients regarding evidence-based surgical management. There may also be an element of surgeon bias toward mastectomy, as the patient will usually not require adjuvant radiation. However, the addition of radiation with a lumpectomy in certain older populations does not improve survival and as previously discussed, may be omitted [30–32].

Included in patient preference regarding surgical management is a woman's desire for breast reconstruction following mastectomy. Reconstruction after mastectomy is often overlooked in older patients, and age alone has been shown to be a factor in decreased use of immediate breast reconstruction [43–45]. A SEER-Medicare study found a 6% overall rate of breast reconstruction in patients ≥ 65, identifying disparities based upon age and institution. Hospitals with higher rates of reconstruction were more likely to serve younger, healthier patients, and the likelihood of receiving reconstruction after mastectomy decreased with age [44]. An analysis of the National Cancer Database (NCDB) data found 11% of patients ≥ 65 who received mastectomy had immediate reconstruction and increasing rates of reconstruction in this population each year of the study period (2004–2012) [46•]. Lower rates of reconstruction were found with increasing patient age, more comorbidities, and among those who received treatment at community cancer centers [46•]. These studies reveal a disparity in reconstruction options for older women, especially those treated at smaller hospitals. These findings highlight the importance of education for surgeons regarding the surgical management of older patients, as well as informed discussion and decision-making between surgeons and patients for surgical planning.

While overall mastectomy rates are decreasing for early stage breast cancer in favor of breast conservation therapy [47], further exploration into trends specifically among older patients is necessary. Considerations including patient functional status, disease characteristics, and life expectancy are necessary when making surgical decisions. Anticipated cosmetic results and patient preferences after proper education should hold equal weight when discussing options with patients and choosing appropriate therapies.

Axilla

An essential component of the surgical treatment of breast cancer is assessment of the axilla, including sentinel node biopsy and axillary dissection, for both staging and treatment. For several years, omission of axillary surgery in older women has been explored as a strategy to decrease surgical morbidity in this population. A clinical trial of Italian patients ≥ 70 with clinically node-negative invasive breast cancer who received lumpectomy randomized women to no axillary surgery or completion axillary dissection. This study found no survival advantage to axillary dissection, with up to 15 years follow-up [48]. Subsequently, the Society of Surgical Oncology Choosing Wisely guidelines were published in 2016 to include omission of axillary staging in patients ≥ 70 with early stage hormone receptor-positive cancer who are clinically node negative [33]. The validity of this guideline and the findings of prior studies have been supported in multiple subsequent investigations [49, 50]. These studies have demonstrated the integration of these recommendations into clinical practice, revealing increased likelihood of omission of axillary surgery with increasing age in older women [51].

One argument for the omission of axillary surgery is that the results of axillary investigation in early stage, clinically node-negative cancer are unlikely to change further management in older women. However, a study using NCDB data found higher rates of adjuvant treatment for those who had received nodal surgery, as well as an overall survival advantage for those who received nodal surgery [52]. This finding suggests the importance of offering axillary surgery in cases where axillary staging may influence further treatment. For example, if a patient refuses to receive chemotherapy regardless of axillary nodal status, then there is no benefit to axillary surgery for this patient. While omission of axillary staging may improve morbidity, debate continues to exist whether omission of nodal surgery may lead to undertreatment and subsequent decreases in survival in the older population. However, it remains clear in those with positive nodes on clinical evaluation; adequate axillary surgery to prevent disease progression remains the standard of care [8].

The relatively recent updates to classical patterns of surgical therapy for breast cancer in older women have opened doors to alternative treatment strategies in this population. Assessment of functional status and surgical candidacy, as well as predicted life expectancy and analysis of comorbidities, is important when making decisions for surgery to provide the best outcomes.

Nonsurgical Treatment

While rates of primary surgical therapy remain high in this population [53•], options remain for those who may choose to forgo surgical management or who are not surgical candidates. The use of primary nonsurgical therapy, including endocrine therapy and forgoing treatment altogether, is increasing [53•]. Non-operative therapy is more likely to be chosen in those with significant comorbidities or higher stage disease, who are likely not surgical candidates [53•]. A single-institution study of breast cancer patients age 80 and over found a higher mean age (90) in patients who did not receive surgery compared with those who did (84), and lower age was the only predictor of treatment with surgery. Tumor stage and grade were similar in both groups, but 100% of tumors in the nonsurgical group were hormone sensitive [54•]. Patients may choose to forgo surgery due to perceptions of decreased morbidity or life expectancy. However, in a study of breast cancer patients ≥ 70, no difference in quality of life was found between those who received surgery for their cancer and those who did not, both 6 weeks and 6 months after diagnosis [14], indicating informed decisions regarding treatment modality are important for maintaining quality of life. Here, we discuss primary endocrine therapy in place of surgical management, as well as hospice for those who have no desire or qualification for treatment.

Endocrine Therapy

The International Society of Geriatric Oncology (SIOG) and European Society of Breast Cancer Specialists (EUSOMA) updated recommendations in 2012 to endorse the use of primary endocrine therapy, tamoxifen or an aromatase inhibitor (AI), for patients with hormone receptor-positive tumors who have short life expectancy or who are unfit for or refusing surgery [8]. In patients with strongly receptor-positive disease, endocrine therapy can significantly reduce tumor burden, albeit at a slower pace than with chemotherapy. These recommendations were modeled after results from a 2007 Cochrane review identifying surgery to be superior to endocrine therapy in local control, with no impact in overall survival in patients who received primary endocrine therapy compared with surgical management [55]. These recommendations have been reflected in clinical practice, as a German study found older women with hormone receptor-positive tumors are more likely to receive endocrine therapy only compared with younger counterparts, and this finding was more common in the

palliative care setting [56]. An NCDB analysis found that in octogenarians who did not undergo primary surgical management, 50% received endocrine therapy only [53•]. This analysis documented increasing rates of primary endocrine management from 2004 to 2012 [53•], indicating this treatment strategy is rising in popularity as a therapeutic option for older patients. A study of women ≥ 75 who received hormone therapy without surgery, despite being surgical candidates, identified reasons for primary endocrine therapy to include age, higher comorbidities, and patient choice [57].

In situations where endocrine therapy is used as the only treatment for a patient's cancer, adherence must be ensured to guarantee proper disease management. A Taiwanese study of adherence to adjuvant endocrine therapy in patients ≥ 70 found while 56.7% of patients were willing to initiate endocrine therapy, only 49.4% of patients completed their treatment and noted improved adherence rates in those who switched from tamoxifen to an aromatase inhibitor [58]. A systematic review of breast cancer studies on general treatment non-adherence found factors associated with non-adherence to include age, therapy-related side effects, socio-economic factors, and health system-related factors [59], indicating the difficulty in identifying specific reasons for patient non-compliance. In general, endocrine therapy has been found to have lower rates of non-adherence compared with chemotherapy, likely due to less intense side effects. However, because of a lack of data on the use of primary or palliative endocrine therapy in older women, it is not clear how applicable these findings are to this population.

Aromatase inhibitors are the preferred treatment over tamoxifen in postmenopausal women [60]. The 2005 ATAC (Arimidex, Tamoxifen, Alone or in Combination) trial demonstrated improved disease-free survival with Arimidex (anastrozole) compared with tamoxifen as adjuvant treatment in postmenopausal women [61], and the BIG 1-98 trial in 2008 found improved disease-free survival with letrozole compared with tamoxifen in older women [62]. A study of 488 women from the UK with ER-positive early stage breast cancer undergoing primary endocrine therapy, 96% of whom received an aromatase inhibitor, concluded primary endocrine therapy is best-suited for older women with high comorbidities. They noted that those with longer life expectancy are more likely to experience treatment failure and subsequent disease progression leading to death, metastatic disease, or further action to control advanced disease [63•]. The lack of data regarding this treatment strategy continues to be a limiting factor. When making decisions regarding endocrine therapy, older women are often placed in the same category as postmenopausal women, which encompasses a much wider age range including women of significantly differing functional status, comorbidity profile, life expectancy, and treatment preferences.

Hospice

In the final stages of life, patients may elect to forgo further treatment and enroll in hospice care for comfort and support. Hospice should be a logical step for those with advanced disease and significant comorbidities contributing to limited life expectancy [56]. However, an under-utilization of hospice has been found, particularly in older cancer patients, and this has been demonstrated in geriatric oncology. In a Swedish study, hospice under-utilization was connected to a lower quality of life in older cancer patients, likely explained by poor communication regarding imminent death due to multiple comorbidities and confounding factors contributing to end of life [64]. A single-institution study of patients with metastatic breast cancer found a higher proportion of patients over 65 with death due to breast cancer treated without hospice compared with those who did receive hospice [65]. Additionally, late enrollment in hospice care has also been reported. A SEER analysis of patients who died of breast, lung, prostate, or colorectal cancer over a 5-year period found advanced age was associated with increased hospice use, although there was lower likelihood to pursue hospice care for breast cancer patients compared with other cancers. Approximately 51% of breast cancer patients received hospice care in their last year of life, and for 17%, this was only in the last 3 days of life [66]. Late enrollment in hospice care has been found in other analyses, including a SEER-Medicare analysis of patients ≥ 65 who died with metastatic breast cancer demonstrating 69% of patients enrolled in hospice, but 11% of those were in the last 3 days of life [67]. Aggressive end-of-life care has been identified in these settings as well. In the same study, 35% of those receiving hospice received care in the emergency department or intensive care unit or were hospitalized in the last 30 days of life [67]. Another SEER analysis of women ≥ 66 who died from metastatic breast cancer identified approximately 60% of patients received aggressive end-of-life care, and those who were treated aggressively were less likely to be enrolled in hospice [68]. It is clear that appropriate timing of hospice enrollment is important in preventing unnecessary treatment in end-of-life care, and further efforts in education and family communication are necessary in providing this valuable element of care.

Conclusions

Breast cancer is a disease of older women, and proper understanding of treatment patterns and outcomes in older women is necessary for their appropriate management. Of greatest importance is consideration of treatment options based on assessment of functional status rather than age alone, which may be accomplished with a full comprehensive geriatric assessment (CGA) or a focused assessment using elements of a

CGA for a streamlined and surgical-focused evaluation. Though studies have shown older women are less likely to receive standard care compared with younger women, treatment patterns and recommendations for breast surgery remain in line with general recommendations. Specifics of breast-conserving surgery and approach to the axilla differ, as recent studies have supported the omission of axillary surgery and post-lumpectomy radiation in subsets of older women. Further work may expand the populations eligible for omission of treatments with no impact on survival. This may also include analysis of primary endocrine therapy in older women who may not benefit from surgical treatment. In those for whom surgery is not an option, proper understanding of hospice candidacy is important in preventing excessive medical care at the end of life. Ongoing study of management and treatment patterns in older women is necessary to optimize outcomes in this population.

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Compliance with Ethical Standards

Conflict of Interest The authors declare they have no conflict of interest.

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References

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1. DeSantis CE, Ma J, Goding Sauer A, Newman LA, Jemal A. Breast cancer statistics, 2017, racial disparity in mortality by state. CA Cancer J Clin. 2017;67(6):439–48. https://doi.org/10.3322/caac.21412.
2. Lodi M, Scheer L, Reix N, Heitz D, Carin AJ, Thiebaut N, et al. Breast cancer in elderly women and altered clinico-pathological characteristics: a systematic review. Breast Cancer Res Treat. 2017;166(3):657–68. https://doi.org/10.1007/s10549-017-4448-5.
3. Grumpelt AM, Ignatov A, Tchaikovski SN, Burger E, Costa SD, Eggemann H. Tumor characteristics and therapy of elderly patients with breast cancer. J Cancer Res Clin Oncol. 2016;142(5):1109–16. https://doi.org/10.1007/s00432-015-2111-2.
4. Bouchardy C, Rapiti E, Fioretta G, Laissue P, Neyroud-Caspar I, Schafer P, et al. Undertreatment strongly decreases prognosis of breast cancer in elderly women. J Clin Oncol. 2003;21(19):3580–7. https://doi.org/10.1200/JCO.2003.02.046.
5. Litvak DA, Arora R. Treatment of elderly breast cancer patients in a community hospital setting. Arch Surg. 2006;141:985–90; discussion 990.
6. Schonberg MA, Marcantonio ER, Li D, Silliman RA, Ngo L, McCarthy EP. Breast cancer among the oldest old: tumor characteristics, treatment choices, and survival. J Clin Oncol. 2010;28(12):2038–45. https://doi.org/10.1200/JCO.2009.25.9796.
7. Wildiers H, Heeren P, Puts M, Topinkova E, Janssen-Heijnen ML, Extermann M, et al. International Society of Geriatric Oncology consensus on geriatric assessment in older patients with cancer. J Clin Oncol. 2014;32(24):2595–603. https://doi.org/10.1200/JCO.2013.54.8347.
8. Biganzoli L, Wildiers H, Oakman C, Marotti L, Loibl S, Kunkler I, et al. Management of elderly patients with breast cancer: updated recommendations of the Internal Society of Geriatric Oncology (SIOG) and European Society of Breast Cancer Specialists (EUSOMA). Lancet Oncol. 2012;13:e148–60. https://doi.org/10.1016/S1470-2045(11)70383-7.
9. Devons C. Comprehensive geriatric assessment: making the most of the aging years. Curr Opin Clin Nutr Metab Care. 2002;5:19–24.
10. Parker SG, McCue P, Phelps K, McCleod A, Arora S, Nockels K, et al. What is comprehensive geriatric assessment (CGA)? An umbrella review. Age Ageing. 2018;47(1):149–55. https://doi.org/10.1093/ageing/afx166.
11. National Comprehensive Cancer Network. Breast Cancer (Version 1.2019). https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed 8 Jan 2019.
12. Wieland D, Hirth V. Comprehensive geriatric assessment. Cancer Control. 2003;10(6):454–62.
13. Clough-Gorr KM, Stuck AE, Thwin SS, Silliman RA. Older breast cancer survivors: geriatric assessment domains are associated with poor tolerance of treatment adverse effects and predict mortality over 7 years of follow-up. J Clin Oncol. 2010;28(3):380–6. https://doi.org/10.1200/JCO.2009.23.5440.
14. Parks RM, Hall L, Tang SW, Howard P, Lakshmanan R, Winterbottom L, et al. The potential value of comprehensive geriatric assessment in evaluating older women with primary operable breast cancer undergoing surgery or non-operative treatment–a pilot study. J Geriatr Oncol. 2015;6(1):46–51. https://doi.org/10.1016/j.jgo.2014.09.180.
15.• Okonji DO, Sinha R, Phillips I, Fatz D, Ring A. Comprehensive geriatric assessment in 326 older women with early breast cancer. Br J Cancer. 2017;117(7):925–31. https://doi.org/10.1038/bjc.2017.257. **Prospective study examining fitness using comprehensive geriatric assessment (CGA) and treatment strategies in women aged 70 and over with invasive breast cancer, finding all patients in the cohort were deemed "fit" by CGA criteria, but half of these patients did not receive full standard treatment.**
16. Pope D, Ramesh H, Gennari R, Corsini G, Maffezzini M, Hoekstra HJ, et al. Pre-operative assessment of cancer in the elderly (PACE): a comprehensive assessment of underlying characteristics of elderly cancer patients prior to elective surgery. Surg Oncol. 2006;15(4):189–97. https://doi.org/10.1016/j.suronc.2007.04.009.
17. Audisio RA, Pope D, Ramesh HS, Gennari R, van Leeuwen BL, et al. Shall we operate? Preoperative assessment in elderly cancer patients (PACE) can help. A SIOG surgical task force prospective study. Crit Rev Oncol Hematol. 2008;65(2):156–63. https://doi.org/10.1016/j.critrevonc.2007.11.001.
18. Fried LP, CTangen CM, Walston J, Newman AB, Hirsch C, Gottdiener TS, et al. Frailty in older adults: evidence for a phenotype. J Gerontol. 2001:56A.
19. Mandelblatt JS, Cai L, Luta G, Kimmick G, Clapp J, Isaacs C, et al. Frailty and long-term mortality of older breast cancer patients: CALGB 369901 (Alliance). Breast Cancer Res Treat. 2017;164(1):107–17. https://doi.org/10.1007/s10549-017-4222-8.
20. Corona G, Polesel J, Fratino L, Miolo G, Rizzolio F, Crivellari D, et al. Metabolomics biomarkers of frailty in elderly breast cancer

patients. J Cell Physiol. 2014;229(7):898–902. https://doi.org/10.1002/jcp.24520.

21. Brouwers B, Dalmasso B, Haste S, Laenen A, Kenis C, Swerts E, et al. Biological ageing and frailty markers in breast cancer patients. Aging. 2015;7:319–33.
22.• Ward SE, Richards PD, Morgan JL, Holmes GR, Broggio JW, Collins K, et al. Omission of surgery in older women with early breast cancer has an adverse impact on breast cancer-specific survival. Br J Surg. 2018;105(11):1454–63. https://doi.org/10.1002/bjs.10885. **Database analysis of women over 70 with ER-positive breast cancer in the UK indicating worse breast cancer-specific survival with omission of breast surgery.**
23. Cortadellas T, Cordoba O, Gascon A, Haladjian C, Bernabeu A, Alcalde A, et al. Surgery improves survival in elderly with breast cancer. A study of 465 patients in a single institution. Eur J Surg Oncol. 2015;41(5):635–40. https://doi.org/10.1016/j.ejso.2015.01.027.
24. Lee CM, Zheng H, Tan VK-M, Tan TJ-Y, Kanesvaran R, Wong F-Y, et al. Surgery for early breast cancer in the extremely elderly leads to improved outcomes – an Asian population study. Breast. 2017;36:44–8. https://doi.org/10.1016/j.breast.2017.09.002.
25. Reed MW, Audisio RA, Wyld L. The role of surgery in the treatment of older women with breast cancer. Clin Oncol (R Coll Radiol). 2009;21(2):103–10. https://doi.org/10.1016/j.clon.2008.11.010.
26. de Glas NA, Kiderlen M, Bastiaannet E, de Craen AJ, van de Water W, van de Velde CJ, et al. Postoperative complications and survival of elderly breast cancer patients: a FOCUS study analysis. Breast Cancer Res Treat. 2013;138(2):561–9. https://doi.org/10.1007/s10549-013-2462-9.
27. Cortina CS, Agarwal S, Mulder LL, Poirier J, Rao R, Ansell DA, et al. Are providers and patients following hormonal therapy guidelines for patients over the age of 70? The influence of CALGB 9343. Clin Breast Cancer. 2018;18(6):e1289–e92. https://doi.org/10.1016/j.clbc.2018.07.004.
28.•• Mogal HD, Clark C, Dodson R, Fino NF, Howard-McNatt M. Outcomes after mastectomy and lumpectomy in elderly patients with early-stage breast cancer. Ann Surg Oncol 2017;24(1):100–107. doi:https://doi.org/10.1245/s10434-016-5582-8. **A SEER analysis of patients 70 and over examining tumor characteristics, treatment patterns, and breast cancer-specific survival identifying improved survival with breast conservation compared with mastectomy in older patients.**
29. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med. 2002;347.
30. Hughes KS, Schnaper LA, Berry D, Cirrincione C, McCormick B, Shank B, Wheeler J, Champion LA, Smith TJ, Smith BL, Shapiro C, Muss HB, Winer E, Hudis C, Wood W, Sugarbaker D, Henderson IC, Norton L, Cancer and Leukemia Group B., Radiation Therapy Oncology Group., Eastern Cooperative Oncology Group. Lumpectomy plus tamoxifen with or without irradiation in women 70 years of age or older with elderly breast cancer. N Engl J Med 2004;351, 971, 977.
31. Hughes KS, Schnaper LA, Bellon JR, Cirrincione CT, Berry DA, McCormick B, 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. https://doi.org/10.1200/jco.2012.45.2615.
32. Kunkler IH, Williams LJ, Jack WJL, Cameron DA, Dixon JM. 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. https://doi.org/10.1016/s1470-2045(14)71221-5.
33. Society of Surgical Oncology. Choosing wisely. 2016. http://www.choosingwisely.org/clinician-lists/sso-sentinel-node-biopsy-in-node-negative-women-70-and-over/. Accessed 18 Dec 2018.
34. National Comprehensive Cancer Network. Older adult oncology (Version 1.2019). https://www.nccn.org/professionals/physician_gls/pdf/senior.pdf. Accessed 8 Jan 2019.
35. Soulos PR, Yu JB, Roberts KB, Raldow AC, Herrin J, Long JB, et al. Assessing the impact of a cooperative group trial on breast cancer care in the medicare population. J Clin Oncol. 2012;30(14):1601–7. https://doi.org/10.1200/JCO.2011.39.4890.
36.•• Wallace AS, Keene KS, Williams CP, Jackson BE, Pisu M, Partridge EE, et al. Radiation therapy utilization in medicare beneficiaries with early-stage breast cancer. Cancer. 2018;124(3):475–81. https://doi.org/10.1002/cncr.30989. **Single-institution study identifying delayed compliance with recommendations for omission of radiation therapy following CALGB 9343 results. In this cohort, two-thirds of patients who qualified for omission of radiation therapy received radiation as a component of their treatment.**
37. Nichol AM, Chan EK, Lucas S, Smith SL, Gondara L, Speers C, et al. The use of hormone therapy alone versus hormone therapy and radiation therapy for breast cancer in elderly women: a population-based study. Int J Radiat Oncol. 2017;98(4):829–39. https://doi.org/10.1016/j.ijrobp.2017.02.094.
38. Palta M, Palta P, Bhavsar NA, Horton JK, Blitzblau RC. The use of adjuvant radiotherpay in elderly patients with early-stage breast cancer: changes in practice patterns after publication of cancer and leukemia group B 9343. Cancer. 2015;121:188–93. https://doi.org/10.1002/cncr.28937.
39. Feigelson HS, James TA, Single RM, Onitilo AA, Aiello Bowles EJ, Barney T, et al. Factors associated with the frequency of initial total mastectomy: results of a multi-institutional study. J Am Coll Surg. 2013;216(5):966–75. https://doi.org/10.1016/j.jamcollsurg.2013.01.011.
40. Besic N, Besic H, Peric B, Pilko G, Petric R, Zmuc J, et al. Surgical treatment of breast cancer in patients aged 80 years or older - how much is enough? BMC Cancer. 2014;14(700).
41. Hamelinck VC, Stiggelbout AM, van de Velde CJH, Liefers GJ, Bastiaannet E. Treatment recommendations for older women with breast cancer: a survey among surgical, radiation and medical oncologists. Eur J Surg Oncol. 2017;43(7):1288–96. https://doi.org/10.1016/j.ejso.2017.02.006.
42. Fisher CS, Martin-Dunlap T, Ruppel MB, Gao F, Atkins J, Margenthaler JA. Fear of recurrence and perceived survival benefit are primary motivators for choosing mastectomy over breast-conservation therapy regardless of age. Ann Surg Oncol. 2012;19:3246–50.
43. Weenk M, Wunschel P, Heine E, Strobbe LJ. Factors influencing the decision to pursue immediate breast reconstruction after mastectomy for breast cancer. Gland Surg. 2017;6(1):43–8. https://doi.org/10.21037/gs.2016.11.11.
44. In H, Jiang W, Lipsitz SR, Neville BA, Weeks JC, Greenberg CC. Variation in the utilization of reconstruction following mastectomy in elderly women. Ann Surg Oncol. 2013;20(6):1872–9. https://doi.org/10.1245/s10434-012-2821-5.
45. Jeevan R, Browne JP, Gulliver-Clarke C, Pereira J, Caddy CM, van der Meulen JH, et al. Association between age and access to immediate breast reconstruction in women undergoing mastectomy for breast cancer. Br J Surg. 2017;104(5):555–61. https://doi.org/10.1002/bjs.10453.
46.• Gibreel WO, Day CN, Hoskin TL, Boughey JC, Habermann EB, Hieken TJ. Mastectomy and immediate breast reconstruction for cancer in the elderly: a national cancer data base study. J Am Coll Surg. 2017;224(5):895–905. https://doi.org/10.1016/j.jamcollsurg.2016.12.051. **NCDB analysis examining mastectomy and reconstruction for women under 65 years old compared with**

women age 65 and older, identifying rising rates of immediate breast reconstruction after mastectomy in older women.

47. Kummerow KL, Du L, Penson DF, Shyr Y, Hooks MA. Nationwide trends in mastectomy for early-stage breast cancer. JAMA Surg. 2015;150(1):9–16. https://doi.org/10.1001/jamasurg.2014.2895.
48. Martelli G, Miceli R, Daidone MG, Vetrella G, Cerrotta AM, Piromalli D, 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. https://doi.org/10.1245/s10434-010-1217-7.
49. Esposito E, Sollazzo V, Di Micco R, Cervotti M, Luglio G, Benassai G, et al. Can axillary node dissection be safely omitted in the elderly? A retrospective study on axillary management of early breast cancer in older women. Int J Surg. 2016;33(Suppl 1): S114–8. https://doi.org/10.1016/j.ijsu.2016.06.022.
50. Limite G, Di Micco R, Sollazzo V, Esposito E, Cervotti M, Compagna R, et al. Clinically cN0 breast cancer in elderly: what surgery? Int J Surg. 2014;12:S130–S4. https://doi.org/10.1016/j.ijsu.2014.08.364.
51. Sun SX, Hollenbeak CS, Leung AM. Deviation from the standard of care for early breast cancer in the elderly: what are the consequences? Ann Surg Oncol. 2015;22(8):2492–9. https://doi.org/10.1245/s10434-014-4290-5.
52. Tamirisa N, Thomas SM, Fayanju OM, Greenup RA, Rosenberger LH, Hyslop T, et al. Axillary nodal evaluation in elderly breast cancer patients: potential effects on treatment decisions and survival. Ann Surg Oncol. 2018;25(10):2890–8. https://doi.org/10.1245/s10434-018-6595-2.
53.• Kantor O, Pesce C, Liederbach E, Wang C-H, Winchester DJ, Yao K. Surgery and hormone therapy trends in octogenarians with invasive breast cancer. Am J Surg. 2016;211(3):541–5. https://doi.org/10.1016/j.amjsurg.2015.11.005. **NCDB analysis of women aged 80 and over with invasive, estrogen receptor positive breast cancer identifying rising incidence of primary non-operative therapy in this population.**
54.• Ferrigni E, Bergom C, Yin Z, Szabo A, Kong AL. Breast cancer in women aged 80 years or older: an analysis of treatment patterns and disease outcomes. Clin Breast Cancer. 2019. https://doi.org/10.1016/j.clbc.2019.01.007 **Single-institution analysis of breast cancer treatment patterns and outcomes in women aged 80 and over. Highlights the importance of keeping updated on patterns of practice and considering women aged 80 and over.**
55. 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. https://doi.org/10.1038/sj.bjc.6603600.
56. Fietz T, Zahn MO, Kohler A, Engel E, Frank M, Kruggel L, 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. https://doi.org/10.1007/s10549-017-4534-8.
57. Wink CJ, Woensdregt K, Nieuwenhuijzen GA, van der Sangen MJ, Hutschemaekers S, Roukema JA, 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. https://doi.org/10.1245/s10434-011-2070-z.
58. Peng M-T, Chen S-C, Shen W-C, Lin Y-C, Chang H-K. The adherence and tolerance of adjuvant endocrine therapy in geriatric breast cancer patients. J Cancer Res Pract. 2016;3(3):69–72. https://doi.org/10.1016/j.jcrpr.2016.05.002.
59. Puts MT, Tu HA, Tourangeau A, Howell D, Fitch M, Springall E, et al. Factors influencing adherence to cancer treatment in older adults with cancer: a systematic review. Ann Oncol. 2014;25(3):564–77. https://doi.org/10.1093/annonc/mdt433.
60. Fabian CJ. The what, why and how of aromatase inhibitors: hormonal agents for treatment and prevention of breast cancer. Int J Clin Pract. 2007;61(12):2051–63. https://doi.org/10.1111/j.1742-1241.2007.01587.x.
61. Howell A. Results of the ATAC (Arimidex, Tamoxifen, Alone or in Combination) trial after completion of 5 years' adjuvant treatment for breast cancer. Lancet. 2005;365(9453):60–2. https://doi.org/10.1016/s0140-6736(04)17666-6.
62. Crivellari D, Sun Z, Coates AS, Price KN, Thurlimann B, Mouridsen H, et al. Letrozole compared with tamoxifen for elderly patients with endocrine-responsive early breast cancer: the BIG 1-98 trial. J Clin Oncol. 2008;26(12):1972–9. https://doi.org/10.1200/JCO.2007.14.0459.
63.• Thomas R, Rowell R, Crichton S, Cain H. An observational study investigating failure of primary endocrine therapy for operable breast cancer in the elderly. Breast Cancer Res Treat. 2018;167(1):73–80. https://doi.org/10.1007/s10549-017-4494-z. **Retrospective study of failure rates of primary endocrine therapy in older patients, concluding this is most effective in older women with more comorbidities.**
64. Lindskog M, Tavelin B, Lundstrom S. Old age as risk indicator for poor end-of-life care quality - a population-based study of cancer deaths from the Swedish Register of Palliative Care. Eur J Cancer. 2015;51(10):1331–9. https://doi.org/10.1016/j.ejca.2015.04.001.
65. O'Connor TL, Ngamphaiboon N, Groman A, Luczkiewicz DL, Kuszczak SM, Grant PC, et al. Hospice utilization and end-of-life care in metastatic breast cancer patients at a comprehensive cancer center. J Palliat Med. 2015;18(1):50–5. https://doi.org/10.1089/jpm.2014.0238.
66. Dinan MA, Curtis LH, Setoguchi S, Cheung WY. Advanced imaging and hospice use in end-of-life cancer care. Support Care Cancer. 2018;26(10):3619–25. https://doi.org/10.1007/s00520-018-4223-0.
67. Check DK, Rosenstein DL, Dusetzina SB. Early supportive medication use and end-of-life care among Medicare beneficiaries with advanced breast cancer. Support Care Cancer. 2016;24(8):3463–72. https://doi.org/10.1007/s00520-016-3174-6.
68. Accordino MK, Wright JD, Vasan S, Neugut AI, Gross T, Hillyer GC, et al. Association between survival time with metastatic breast cancer and aggressive end-of-life care. Breast Cancer Res Treat. 2017;166(2):549–58. https://doi.org/10.1007/s10549-017-4420-4.