



Review article

Breast cancer treatment in women over the age of 80: A tailored approach

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ABSTRACT

Breast cancer treatment in women over the age of 80 remains a complex issue due to pre-existing comorbidities, therapy-related toxicities, and the lack of evidence-based data in this population, leading to both overtreatment and under treatment. The average life expectancy of an 80-year-old woman is 9.7 years and chronologic age alone should not be a factor in withholding therapy.

Women over age 80 should be treated on an individual basis, taking into account their overall health and life expectancy, their risk of dying from breast cancer versus other causes, and the benefits versus toxicities of therapies for their tumor. Invaluable online tools are readily available to easily assess life expectancy (ePrognosis), as well as the absolute survival benefits for every tumor type and stage in individual patients (PREDICT, Ajuvant!). This information should be presented to the patient so that they are able to make an informed decision based on their goals, wishes and quality of life. Vulnerable patients should not be bullied or scared into taking unwanted or unnecessary treatments.

1. Introduction

Breast cancer is the most common cancer in women, increasing with age until 80 years. It is estimated that in 2017 in the US over 30,000 new breast cancer cases will be diagnosed in women over 80, accounting for 12% of all cases [1]. Management of breast cancer in this population remains controversial, as there is a lack of evidenced-based data to guide therapies. Women over 80 are often omitted or under-represented in clinical trials and treatment recommendations are often extrapolated from results in younger patients. Subgroup analyses of 'elderly' patients most often use age 65 or 70 as the lower age limit, and results might not be valid in women over 80 years of age. This lack of evidence often results in either overtreatment or under treatment. Treatment of the extreme elderly is further complicated by a wide variation in physical and mental comorbidities, which need to be addressed on an individual basis.

The purpose of this study was to examine existing data in women over age 80 on breast cancer screening, diagnosis, treatment and prognosis. Online tools are discussed, which can aid physicians in the clinical care of these complex patients in whom life expectancy and quality of life are major concerns.

2. Methods

A literature search was performed (Google Scholar, PubMed, Cochrane) using terms including breast cancer, DCIS and/or, screening, treatment, endocrine therapy, surgery, radiation therapy, chemotherapy, prognosis and elderly, octogenarian, age over 80, oldest. Further articles were obtained and evaluated from citations in relevant articles. Over 200 articles/abstracts were screened and over 155 articles were reviewed extensively by the co-authors. Articles were selected for octogenarians or age over age 80. Relevant articles were considered if subgroup analyses of included women over age 65, 70 or 75 y.

3. Results

3.1. Comorbidity and life expectancy

The average life expectancy of an 80-year old female is 9.7 years [2]. There are many healthy octogenarians who will tolerate conventional therapy and have a life expectancy of 10–15 years. Age alone should not be a factor in withholding treatment. Significant comorbidities affect life expectancy and alter the benefit/risk ratio from surgical and adjuvant therapies, and in particular, tolerance of chemotherapy. A comprehensive geriatric assessment is a useful tool to

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Table 1
Online tools with links.

Tool	Link
ePrognosis (Life expectancy) calculator	http://eprognosis.ucsf.edu/calculators/index.php/
ePrognosis Breast cancer screening calculator	http://cancerscreening.eprognosis.org/screening/BreastCancerScreening.html
PREDICT – Adjuvant therapy	http://predict.nhs.uk/
Adjuvant! – Adjuvant therapy	http://www.newadjuvant.com/login.aspx

determine functional capacity, nutritional status, cognition, psychological status and social support, which can estimate life expectancy and guide therapy [3]. A weighted index of comorbidities (e.g., Charlson comorbidity index) takes into account the number and seriousness of comorbid conditions, and their effect on mortality [4]. Validated tools like the online ePrognosis calculator can quickly and accurately estimate the life expectancy of an individual patient, which can help with clinical decision-making (Table 1).

- The ePrognosis calculator is an invaluable tool in determining life expectancy in women over 80 years of age, which is critical in decision-making in this population.

3.2. Screening mammography

The incidence of breast cancer in women over 80 years of age is nearly 400 cases per 100,000 women in the US [1]. No one disputes that mammograms save lives through early diagnosis, with a reduction in breast cancer mortality of at least 15% in women over 50 years of age. However, screening mammograms also have ‘harms’, which must be conveyed to the patient. Although the American Cancer Society recommends continuing screening mammography in healthy women with a life expectancy of 10 years or longer [5], the U.S. Preventive Services Task Force concluded that there is insufficient evidence to assess the balance of benefits and harms in women aged 75 and older [6]. A controversial 2013 Cochrane review concluded that although there was an absolute risk reduction in mortality of 0.05%, screening led to 30% over diagnosis and over treatment (absolute risk of 0.5%). This translates to 1 life saved for 2000 women screened over 10 years, while 10 healthy women will be over diagnosed and treated unnecessarily. Furthermore, 200 women will experience psychological distress because of false positive findings [7]. If a healthy octogenarian or patient at increased risk for breast cancer is considering screening mammography, the physician should educate the patient on the actual benefits and harms so that an informed decision can be made.

Results of the ePrognosis Breast Cancer Screening calculator/tool (Table 1) concur with the results of the Cochrane review. For healthy 80-year old patients in excellent health, 100/1000 patients screened will experience harms in the first year including false positive exams (and subsequent unnecessary workups), false negative exams, over diagnosis, overtreatment, and psychological distress. After 10 years, 1/1000 80-year old women will avoid death from breast cancer due to screening and 200/1000 will die whether or not they got tested for breast cancer.

- There is no data supporting routine screening mammography in women over 80 years of age

3.3. Surgery

Mastectomy or breast conserving surgery remains the standard of care for women of any age, unless they are not surgical candidates, refuse surgery, or have a limited life expectancy (< 2–3 years). Surgery improves breast cancer-specific survival in octogenarians with early stage breast cancer [8,9], and has a low post-operative mortality rate,

i.e., 0.5% [10]. In contrast, in elderly women (70 y plus) with locally advanced disease (Stage III) breast cancer-specific survival was the same in surgical and non-surgical groups [9]. In frail elderly women with hormone receptor positive tumors who are unfit for surgery, or women who refuse surgery, primary endocrine therapy should be offered [11].

Most older women are candidates for breast preservation, and those with smaller, hormone receptor positive tumors and clinically negative axilla (on physical examination and imaging) are unlikely to benefit from sentinel node biopsy, which would not change management. Although there are no studies in women 80 years and older, a study in women over 70 showed that omission of axillary staging did not affect overall or breast cancer specific mortality [12]. Patients with clinically involved axillary nodes should be considered for axillary dissection to control disease [13].

Women over age 80 have a high incidence of ductal carcinoma in situ (DCIS). A study in octogenarians showed that although surgery did not provide an overall survival benefit in DCIS, it did provide a survival benefit for those with ‘high grade’ DCIS and should be considered in fit elderly [14].

- Surgical therapy should be considered in women over age 80 unless comorbidities and limited life expectancy are prohibitive

3.4. Radiation therapy

Though adjuvant radiation therapy after lumpectomy is the standard of care, there is a high rate (64%) of noncompliance in octogenarians [15]. The main benefit of radiation therapy is lowering the risk of local recurrence, which is 1% per year on average. Although no trial has exclusively investigated women over 80 years of age, the CALGB 9343 trial looked at women over age 70 with stage 1, estrogen receptor (ER) positive tumors [16]. At 10.5 years there was a 9% local recurrence with endocrine therapy alone versus 2% with the addition of radiation therapy. Less than 1/100 (0.67) women per year benefited from therapy. Omission of radiation therapy did not affect distant recurrence or overall survival. Morbidity was much higher in the radiation therapy group [16]. The PRIME II trial, which included women over 65 y, reported 4.1% versus 1.3% local recurrence at 5 years [17]. In addition, a 15-year non-randomized trial reported similar findings for stage 1 disease [18]. This study also included tumors up to 5 cm. For 2–5 cm (pT2) tumors, there was a 14.6% incidence of ipsilateral breast tumor recurrence at 15 years in untreated women. However, breast cancer mortality and distant metastasis did not differ significantly [18]. These results may be even more significant for octogenarians.

There are no studies investigating the absolute benefits versus risks of radiation therapy in women over 80 years of age with ER negative tumors and/or with more advanced disease. A fit octogenarian may tolerate radiation therapy and derive a benefit in local and regional control of disease and should not be undertreated. Mastectomy with or without axillary dissection would also be an option for local control of advanced disease. Although there is a lack of data in women over 80 years of age, post mastectomy chest wall radiation may be considered for fit elderly patients with four or more positive nodes or a tumor over 5 cm.

- Radiation therapy may be omitted in octogenarians with early stage, hormone receptor positive disease undergoing breast conservative surgery

3.5. Endocrine therapy

Over 85% of breast cancers in women over 80 years of age are ER positive (versus ER negative), which offers a survival advantage even in women unfit for surgery or chemotherapy [19,20]. Endocrine therapy is well tolerated in octogenarians. However, women in this age group are

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