

Primary Care of Breast Cancer Survivors

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With declining mortality rates, the number of breast cancer survivors is increasing. Ongoing care after breast cancer treatment is often provided by primary care physicians. This care includes surveillance for cancer recurrence with a history and physical examination every three to six months for the first three years after treatment, every six to 12 months for two more years, and annually thereafter. Mammography is performed annually. Magnetic resonance imaging of the breast is not indicated unless patients are at high risk of recurrence, such as having a hereditary cancer syndrome. Many breast cancer survivors experience long-term sequelae from the disease or treatment. Premature menopause with hot flashes can occur and is managed with pharmacologic and nonpharmacologic treatments. Vaginal dryness is treated with vaginal lubricants and gels. Because cardiotoxicity from chemotherapy is possible, clinicians should be alert for this complication and perform echocardiography if appropriate. Impaired cognition after chemotherapy is also common; treatment includes cognitive rehabilitation therapy. Patients with treatment-induced menopause develop decreased bone density and should receive dual energy x-ray absorptiometry and pharmacologic and nonpharmacologic therapies. Others experience lymphedema, often best managed with weight loss and complex decongestive therapy. Some women develop chronic pain, which is treated by addressing psychological factors and with appropriate pharmacologic therapy. (*Am Fam Physician*. 2019;99(6):370-375. Copyright © 2019 American Academy of Family Physicians.)

There are approximately 300,000 new cases of breast cancer (in situ or invasive) each year in the United States, with about one in eight women having breast cancer at some point in life.¹ The annual incidence is 129 per 100,000 for non-Hispanic whites, 126 per 100,000 for non-Hispanic blacks, 100 per 100,000 for Native Americans, 92 per 100,000 for Hispanics, and 91 per 100,000 for Asians.¹ Mortality rates have been declining for many years. The current annual mortality rates are 21 per 100,000 for non-Hispanic whites, 30 per 100,000 for non-Hispanic blacks, 14 per 100,000 for Native Americans, 14 per 100,000 for Hispanics, and 11 per 100,000 for Asians.¹

Because of the declining mortality rates, most patients with breast cancer survive and require

ongoing surveillance for recurrence and management of sequelae from the disease or its treatment. Primary care physicians are often involved in the care of these patients.

Screening for Recurrence

Guidelines published by the American Cancer Society/American Society of Clinical Oncology emphasize that primary care physicians should ensure that breast cancer survivors follow the recommendations of the oncology team, as well as receive a history and physical examination every three to six months for the first three years after treatment, every six to 12 months for two more years, then annually thereafter. Patients should also be educated about the signs and symptoms of local recurrence.²

Radiologic surveillance should consist of annual mammography of both breasts or the remaining breast.²⁻⁴ Annual magnetic resonance imaging should be performed only in patients at high risk of recurrence.⁵ Risk factors for recurrence include a calculated lifetime risk of more

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BEST PRACTICES IN ONCOLOGY

Recommendations from the Choosing Wisely Campaign

Recommendation	Sponsoring organization
Do not routinely recommend follow-up mammograms more often than annually for women who have had radiotherapy following breast-conserving surgery.	American Society for Radiation Oncology
Do not perform surveillance testing (biomarkers) or imaging (positron emission tomography, computed tomography, and radionuclide bone scans) for asymptomatic individuals who have been treated for breast cancer with curative intent.	American Society of Clinical Oncology

Source: For more information on the Choosing Wisely Campaign, see <https://www.choosingwisely.org>. For supporting citations and to search Choosing Wisely recommendations relevant to primary care, see <https://www.aafp.org/afp/recommendations/search.htm>.

than 20%, a strong family history of breast or ovarian cancer, and a personal history of Hodgkin disease.⁵

Clinicians should use a validated tool to screen for risk factors for hereditary breast cancer.⁶ These risk factors include developing breast cancer before 50 years of age, triple-negative cancer types (estrogen receptor negative, progesterone receptor negative, and human epidermal growth factor negative), or a strong family history of breast or ovarian cancer. Genetic counseling referral is indicated if there is a hereditary component. Tools for determining risk are available in the U.S. Preventive Services Task Force guideline at <https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/brca-related-cancer-risk-assessment-genetic-counseling-and-genetic-testing>. This guideline is currently being updated.

In addition to breast cancer screening, breast cancer survivors should continue to be screened for cervical, colon, lung, and ovarian cancers according to published guidelines. In the absence of a genetic syndrome, there is no indication for enhanced screening for these other cancers.

A Cochrane review studied standard follow-up surveillance (history and physical examinations with annual mammography) conducted by a primary care physician vs. follow-up surveillance conducted by a subspecialist.³ Patients treated by a subspecialist received the same care as those treated by a primary care physician, but some in the subspecialist group also received enhanced radiology and laboratory testing (e.g., chest radiography, bone scans, tumor markers). All patients were survivors of breast cancer stage I, II, or III. There was no difference in overall survival, disease-free survival, or quality of life; however, patient satisfaction was higher among patients treated by a primary care physician. Another study showed that

patients receiving follow-up care from a primary care physician are as likely as those receiving care from a subspecialist to receive recommended surveillance testing.⁷

Treating Sequelae from Breast Cancer or Its Treatment

HOT FLASHES AND VAGINAL DRYNESS

Breast cancer survivors may have a variety of symptoms related to low estrogen levels as a result of chemotherapy-induced ovarian failure or antiestrogen hormonal therapy. Low estrogen can lead to hot flashes, dyspareunia, vaginal dryness, and urogenital atrophy.

The prevalence of hot flashes varies with the type of therapy, but it may be as high as 50% to 70% in premenopausal survivors who are treated with tamoxifen.⁸ Because of the risk of cancer recurrence, the use of oral estrogen to treat hot flashes is contraindicated in breast cancer survivors.⁹ There is also concern about topical estrogen preparations because some have been shown to increase serum estradiol levels.¹⁰ Treatment of hot flashes in breast cancer survivors begins with lifestyle modifications (e.g., dressing in layers, using a fan, sipping cool drinks). For women who want pharmacologic treatment, selective serotonin reuptake inhibitors, the serotonin-norepinephrine reuptake inhibitor venlafaxine, and gabapentin (Neurontin) are preferred medications.^{2,11,12} Physicians should consider each medication's adverse effects when deciding which one is most appropriate for individual patients.

For vaginal dryness and dyspareunia, guidelines suggest the use of vaginal lubricants for sexual intercourse and vaginal moisturizers for general comfort.¹⁰ In addition, there is evidence that pH-balanced vaginal gel is effective for vaginal symptoms and a lidocaine compress applied to the vulvar vestibule is effective for dyspareunia.^{13,14}

CARDIOTOXICITY

Multiple aspects of breast cancer treatment may contribute to a higher risk of cardiovascular disease in survivors.¹⁵ These risk factors include induced menopause, use of hormonal treatments, and use of certain chemotherapies such as anthracycline-type drugs (e.g., doxorubicin [Adriamycin]) and trastuzumab (Herceptin). Current doses and techniques of radiation therapy for breast cancer do not appear to increase cardiovascular toxicity.¹⁶ Breast cancer survivors should continue to receive regular age-appropriate

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	Evidence rating	References
Breast cancer survivors should receive a history and physical examination every three to six months for the first three years after treatment, then every six to 12 months for two more years, then annually thereafter.	C	2
Radiologic surveillance after breast cancer treatment should consist of annual mammography of both breasts or the remaining breast.	A	2-4
Annual magnetic resonance imaging is indicated only in breast cancer survivors at high risk of recurrence (high lifetime risk, strong family history of breast or ovarian cancer, or personal history of Hodgkin disease).	C	9
Nonhormonal treatments should be used to manage hot flashes in breast cancer survivors.	C	2, 9, 12
Primary care physicians should monitor breast cancer survivors for signs and symptoms of cardiotoxicity. Routine echocardiography is not recommended in asymptomatic patients unless they are at high risk of cardiotoxicity.	C	2
For postmenopausal breast cancer survivors without risk factors, dual energy x-ray absorptiometry should be performed at baseline.	C	2
Breast cancer survivors who develop lymphedema should be referred for complex decongestive therapy.	C	2, 4

A = consistent, good-quality patient-oriented evidence; **B** = inconsistent or limited-quality patient-oriented evidence; **C** = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <https://www.aafp.org/afpsort>.

cardiovascular risk screening and risk factor reduction according to the U.S. Preventive Services Task Force and other guidelines. Patients should be encouraged to report potential cardiac symptoms, such as shortness of breath or unexplained fatigue.² If symptoms are present, appropriate workup and cardiology referral should be initiated.¹⁷

There are no well-established recommendations on screening for cardiotoxicity in breast cancer survivors. However, echocardiography should be considered six to 12 months after breast cancer treatment in asymptomatic patients at high risk of cardiotoxicity (e.g., those who received high-dose anthracycline chemotherapy, trastuzumab or low-dose anthracyclines in combination with cardiac risk factors or radiation therapy with the heart in the treatment field, or high-dose radiation with the heart in the treatment field).¹⁷

may occur as a result of chemotherapy-induced ovarian failure or ovarian suppression from adjuvant therapies such as aromatase inhibitors.²³

Women who have chemotherapy-induced premature menopause, women who are premenopausal and were treated with tamoxifen or a gonadotropin-releasing hormone agonist, and women who were treated with an aromatase inhibitor should receive dual energy x-ray absorptiometry (DEXA) at baseline and then every two years, unless more frequent screening is indicated by DEXA results. For postmenopausal breast cancer survivors without these risk factors, DEXA should be performed at baseline, and then existing guidelines for osteoporosis screening should be followed.²

There are several strategies to limit the bone loss associated with breast cancer treatment, most importantly weight-bearing exercise, limiting alcohol intake, not smoking, and adequate intake of dietary calcium and vitamin D.

COGNITIVE IMPAIRMENT

Cognitive impairment is common during and after breast cancer treatment and may affect the patient's daily functioning.¹⁸ Cognitive impairment, measured by a variety of neuropsychiatric tests, is most pronounced in survivors who received systemic chemotherapy, with 39% of these patients reporting cognitive difficulty up to five years after diagnosis.¹⁹ Verbal memory and psychomotor function are particularly affected.¹⁹

Physicians should ask about cognitive impairment after breast cancer treatment and refer affected patients for neuropsychiatric testing.² There is evidence that cognitive rehabilitation therapy, consisting of exercises to improve verbal and visual memory and speed of processing information, is effective in reversing cognitive deficits in breast cancer survivors.²⁰ Cognitive rehabilitation is effective in group and individual settings.^{20,21} Stimulants, mindfulness-based stress reduction, and cognitive behavior therapy are ineffective.²²

DECREASED BONE DENSITY

Breast cancer survivors, including those who are premenopausal, are at increased risk of osteoporotic fractures. Rapid and profound bone loss

Zoledronic acid (Reclast) or denosumab (Prolia) is recommended for the prevention of bone loss in patients receiving aromatase inhibitor therapy.²⁴ If zoledronic acid is chosen, it should be given for three to five years. The optimal duration of denosumab therapy is unclear, but durations of up to 24 months have been studied.^{24,25} Of note, the use of bisphosphonates may be associated with a lower risk of metastatic disease in patients with early breast cancer.²⁶

Teriparatide (Forteo), a parathyroid hormone agonist, is not recommended for improving bone density in patients with breast cancer because of the risk of bone metastases or radiation-induced osteosarcomas.²⁷ Selective estrogen receptor modulators are contraindicated because of their antiresorptive effects, which mitigate the benefits of aromatase inhibitor therapies.²⁸

LYMPHEDEMA

The reported occurrences of lymphedema after breast cancer treatment vary widely, depending on the type of treatment received and the criteria used to diagnose lymphedema. Rates of lymphedema are as much as double in women who undergo radiotherapy, and they are also increased in women who were obese or who had advanced cancer at the time of diagnosis. There is also a greater incidence of lymphedema in patients receiving axillary lymph node dissection vs. sentinel node biopsy. Of women who undergo axillary node dissection, the cumulative incidence of lymphedema is 41% at 10 years.^{2,29}

New cases of lymphedema may emerge months or years after treatment, with the cumulative incidence rising over five years of follow-up.³⁰ However, not all cases of lymphedema are clinically significant. In one study, the incidence of lymphedema at 60 months posttreatment was 94% when using a criterion of increased arm circumference of 2 cm or more, but only 43% of the same patients had signs and symptoms of limb heaviness or swelling.³⁰

Guidelines advise primary care physicians to counsel patients about weight management as a strategy to prevent or reduce the risk of lymphedema after breast cancer. Patients who develop lymphedema should be referred to a lymphedema therapist. There is ample evidence for the effectiveness of complex decongestive therapy in the management of lymphedema related to breast cancer.^{2,4,31} Complex decongestive therapy consists of therapist-administered drainage massage followed by a maintenance phase of self-administered manual lymphatic drainage, ongoing skin care, and use of compression garments. Complex decongestive therapy has been shown to decrease arm volume and increase quality of life.³² In addition, physical therapy improves range of motion and strength in the affected arm and does not cause or worsen lymphedema.³¹

Women with breast cancer-related lymphedema are twice as likely as age-matched controls to develop cellulitis or lymphangitis.³³ Episodes of cellulitis may further damage lymphatic drainage, worsening lymphedema. It is therefore imperative to promptly diagnose and treat infections.

CHRONIC PAIN

Chronic pain after breast cancer treatment is a well-described phenomenon. The most common subtype, post-mastectomy pain syndrome (PMPS), lasts at least three months. The pain occurs in the arm, axilla, chest wall, scar, or shoulder, or it may present as phantom breast pain.³⁴ This syndrome is thought to be neuropathic in nature. The quality of pain is usually burning, stinging, or like an electric shock.³⁵ The incidence of PMPS is estimated to be 20% to 50% but varies depending on type of surgery and use of chemotherapy or radiation.³⁶

Axillary node dissection leads to a higher rate of persistent pain than sentinel node biopsy alone. The pain is thought to be caused by damage to the intercostobrachial nerve that occurs with node dissection.³⁷ The effect of chemotherapy on the incidence of PMPS is inconsistent and may be confounded by stage of breast cancer or patient age,³⁸ but radiation therapy increases the risk of persistent pain.³⁷ Lower age is another risk factor for persistent pain, possibly because younger women may have more severe disease.³⁹ Pain may also be a result of peripheral neuropathy related to use of chemotherapy in breast cancer treatment.³⁸

There are many other risk factors for the development of chronic pain after breast cancer treatment, such as the presence of preoperative breast pain (from breast cancer itself or prior treatments) or an unrelated preexisting pain syndrome, such as headache or back pain.^{37,40} Aggressive postoperative pain control has been demonstrated to reduce the risk of persistent pain.⁴¹

Psychological factors are also involved in chronic pain after breast cancer treatment. Anxiety, catastrophizing mindset, disturbed sleep patterns, and tendency toward somatization each predict the presence of ongoing pain at three years of follow-up.⁴² Depression is also a predictor of chronic pain in breast cancer survivors. The incidence of chronic pain at nine months was decreased by approximately one-half in patients who were psychologically resilient before breast cancer treatment.⁴³

Primary care physicians should assess patients for persistent pain beyond the expected time of healing and for neuropathy. Preferred treatments include acetaminophen, nonsteroidal anti-inflammatory drugs, physical activity, and occupational therapy as indicated. Duloxetine (Cymbalta) is recommended for neuropathic pain, numbness, or tingling.² Amitriptyline has an established role in treating

neuropathic pain, and there is evidence that it relieves pain in the ipsilateral breast and surgical scar after breast surgery.⁴⁴ However, physicians must consider the anticholinergic adverse effects of amitriptyline and its possible contraindication in older patients. Because neuropathic pain may be resistant to opioid analgesia, there is little or no role for chronic opioid use in patients with PMPS.

Physical and occupational therapies after breast surgery focus on preserving range of motion and strength in the ipsilateral arm and are effective in treating postoperative pain. Early referral for physical or occupational therapy may be more effective than delayed referral.⁴⁵

HEALTH-RELATED QUALITY OF LIFE

Nearly 50% of breast cancer survivors experience anxiety and/or depression in the first year after diagnosis.⁴⁶ In addition, one year after treatment, breast cancer survivors have significantly lower scores than the general population in the domains of emotional state, social functioning, fatigue, insomnia, and body image. They also have ongoing breast cancer-specific symptoms (e.g., arm and breast symptoms).⁴⁷ Another study showed that some quality-of-life difficulties persisted at 10 years, including cognitive issues, social issues, and fatigue.⁴⁸ Body image may be negatively affected by surgeries, weight gain, changes in physical conditioning, and changes in sexual functioning. Younger women are particularly affected by declines in body image.^{49,50}

Patients with breast cancer should be screened for depression and anxiety, and asked about body image and social support.² Group therapy using guided imagery has been shown to lessen concerns about appearance and increase quality of life.⁵¹ Women with body image concerns should be referred for adaptive therapies, such as breast reconstruction, breast prosthesis, or wigs.² A systematic review found that the only interventions that improved body image were those containing an exercise component.⁴⁹

Data Sources: The Cochrane database, PubMed, and National Guideline Clearinghouse were searched using the key words breast cancer, lymphedema, post-mastectomy pain syndrome, chronic pain, hot flashes, dyspareunia, and quality of life. Search dates: June and July 2018.

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