Care of Breast Cancer Survivors after Treatment

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More than 200,000 women in the United States will be diagnosed with breast cancer in 2014. It is estimated that by 2022, the number of survivors will climb to nearly 4 million. Breast cancer survivors require regular follow-up care, some of which requires the skills of an oncologist and some of which can be provided by a primary care physician. This article looks at common conditions affecting survivors and discusses ways that oncologists and primary care physicians can work together to best serve this population.

Breast cancer is the most common malignancy in women, striking one in eight during their lifetime. It is estimated that more than 200,000 women will be diagnosed in 2014. Because of improvements in detection and treatment, there are nearly 3 million breast cancer survivors in the United States today, accounting for nearly 25% of all cancer survivors in this country. By 2022, it is estimated that the number of breast cancer survivors will climb to nearly 4 million and the number of survivors of all cancers to nearly 18 million. In Minnesota, more than 3,500 invasive breast cancers were diagnosed between 2003 and 2007, with the age-adjusted rate in 2007 being 132.1 new cases per 100,000 women. Among women 50 years of age and older, the age-adjusted rate was 362 new cases per 100,000 in 2009. Most breast cancers are diagnosed at a stage in which the malignancy is localized; thus, with appropriate care, long-term survival is anticipated.

Breast cancer survivors require regular follow-up care, some of which is specialized and some of which can be provided by a primary care physician. Often, having both an oncologist and a generalist involved is optimal.

According to a study commissioned by the American Society of Clinical Oncology (ASCO), by 2020 there will be a shortage of as many as 4,000 oncologists in the United States. This shortage will occur at the same time the population is aging and the number of long-term cancer survivors is growing. Thus, it is clear that the demand for oncology care will be greater than the supply of oncologists needed to provide it. It should be noted that mid-level providers will play an increasingly important role in the care of oncology patients.

Although survivors’ needs related to breast cancer (surveillance, treatment-related concerns) are typically well-managed, their general health care needs often are unwittingly overlooked. In considering how those needs could best be met, one must consider the role primary care physicians can play in the care of breast cancer survivors. In fact, ASCO has suggested involving them in the care of survivors. Their participation will not only ensure that these patients will receive important screenings and care for comorbid conditions; it also will free up oncologists to see newly diagnosed patients. Ideally, a collaborative care model involving oncology specialists and primary care physicians would result in appropriate care without duplication of efforts.

Health Care Needs of Breast Cancer Survivors

Excellent evidence-based guidelines for follow-up care of breast cancer survivors are available from both ASCO (asco.org) and the National Comprehensive Cancer Network (nccn.org). Surveillance should include a health history and physical exam, and regular mammography (except after bilateral mastectomies), with the first happening no sooner than six months after completing radiation therapy. Regular assessment for local/regional and distant recurrence as well as complications secondary to radiation, chemotherapy or endocrine therapy is necessary. (Note: endocrine therapy typically continues for five years.) The health care needs of breast cancer survivors extend beyond those directly related to the malignancy and its treatment, however. Physicians also must address concerns such as diabetes, cardiovascular disease and depression as well as age-appropriate screenings for other cancers and immunizations.

They should also discuss lifestyle. There is an increasing volume of literature related to the impact of diet, alcohol use, physical activity or lack thereof, and excess body weight on breast cancer recurrence. Given the potential positive impact of healthy lifestyle choices, physicians should strongly encourage patients to embrace them and advise them to avoid potentially harmful behaviors.

Intensive surveillance (eg, laboratory serologies, bone scans, abdominal ultrasounds, chest X-rays, CT scans) of asymptomatic breast cancer survivors is not recommended. ASCO and NCCN guidelines clearly advise against intensive surveillance and instead recommend that clinical decisions be based on history and physical examination.

Signs of Possible Recurrence

After completing therapy for breast cancer, survivors should be regularly monitored for recurrence, which may be local/regional (in the skin, chest wall, breast or...
regional nodal basin) or distant. Distant relapse is most likely to occur in the bone, liver or lung, although it can be present in other sites.

Although the first five years after diagnosis and treatment is considered the time of highest risk of relapse, survivors (especially those who had estrogen-receptor positive disease) remain at elevated risk beyond that time period. A primary care physician will likely follow patients for many years after active follow-up by their treating oncologist, so it is essential that they are comfortable assessing patients for potential relapse and referring them to oncology when appropriate.

Symptoms to carefully consider in breast cancer survivors include anorexia or other constitutional symptoms, GI or GU symptoms, neurological changes, abdominal pain, unexplained cough or dyspnea, bone pain or spine pain, and unexplained headaches. Signs of potential relapse include a change found through clinical breast or axillary exam; skin lesions without other explanation in the region of the primary malignancy (may indicate skin recurrence) or contralateral breast/chest wall; abnormal pulmonary, abdominal or pelvic examinations; vertebral or other bone point tenderness; or a fracture with minimal or no trauma.

Other symptoms or signs that do not have a logical explanation should be evaluated with clinically indicated laboratory and/or imaging investigations. It should not automatically be assumed that such abnormalities are the result of recurrence; they should be evaluated appropriately to determine etiology. Referral to oncology once recurrence (local/regional or distant) is diagnosed must be prompt.

Potential Sequelae of Breast Cancer Therapy
A number of potential consequences of breast cancer therapy should be considered during follow-up and long-term surveillance. The most potentially concerning ones are pathologies of the cardiovascular and pulmonary systems or secondary malignancies.

Cardiovascular Pathologies
Cardiovascular disease (CVD) is the leading cause of death in women, including breast cancer survivors. Thus, careful attention to risk factors for CVD is essential, as cancer treatment may compound risk for CVD. Improvements in chemotherapy have resulted in significant reductions in cardiovascular damage. However, there is still potential for cardiac toxicity, including from novel biologic (targeted) agents, and physicians must be aware of both early and late effects of treatment. Significant improvements in radiation therapy have also led to dramatically reduced cardiovascular damage. Careful targeting of radiation to limit exposure of cardiovascular structures as well as newer techniques of administering radiation continue to drive down the risk for cardiovascular damage. However, increased risk of ischemic heart disease in breast cancer survivors after radiotherapy remains a concern. It must be noted that radiation-induced CVD is generally related to treatment done in the past. Although the late cardiovascular effects of modern radiotherapy remain unclear, the degree of risk is likely to be significantly lower.

Potential cardiovascular sequelae of breast cancer therapy include cardiomyopathy with eventual heart failure, pericardial disease, valvular disease, coronary artery disease and arrhythmias. Presentation may be early (during or shortly after therapy and almost certainly recognized by the treating oncologist) or late. For that reason, primary care physicians who work with survivors must be cognizant of the potential late effects of therapy.

Pulmonary Pathologies
The chemotherapeutic and targeted agents used to treat breast cancer generally do not have a direct effect on the pulmonary system, although there have been reports of pulmonary toxicity. Modern radiotherapy techniques reduce the risk substantially; but adjuvant radiation therapy may cause pulmonary changes including altered pulmonary function, changes on high-resolution CT and pneumonitis. Toxic pulmonary effects are more likely to be identified in patients treated years ago than in patients who completed treatment more recently; therefore, physicians should be aware of potential late effects.

Secondary Malignancies
Survivors treated with radiation therapy may develop angiosarcoma, a rare but highly aggressive malignancy. Evaluation of any suspicious skin finding in the field of radiation must be undertaken without delay. Other skin abnormalities such as atypical vascular lesions or malignancies such as basal cell carcinoma may also be seen more often after radiation therapy. Secondary leukemia, though uncommon, may develop following chemotherapy. Patients presenting with new or abnormal skin findings or symptoms that could indicate a hematologic abnormality must be promptly evaluated.

Other Health Concerns
Breast cancer patients may face other health concerns related to treatment for which early identification and management can lead to improved outcomes and quality of life. These include:

Lymphedema
Lymphedema (swelling secondary to disrupted lymphatic flow) affecting the upper extremity and/or breast may occur after breast cancer treatment. Arm lymphedema is a well-recognized potential complication of treatment, which can result from axillary nodal surgery and axillary nodal basin irradiation, as well as other factors. Breast lymphedema is less well-recognized; risk factors include breast surgery and axillary nodal surgery. A recent study demonstrated a significantly increased risk regardless of the type of axillary nodal surgery or number of nodes removed.

Lymphedema is a risk factor for cellulitis, pain and decreased upper extremity function. Of note, lymphedema may develop at any time after treatment—both
early and late presentations have been observed. Early recognition of lymphedema and involvement of specialists improves both short- and long-term outcomes.

Musculoskeletal Issues
Breast cancer survivors can experience physical limitations involving the shoulder girdle, arm and chest wall after treatment.\textsuperscript{31,32} Attending to such limitations early is essential to keeping them from progressing and affecting a person’s quality of life. Prescribing physical therapy early on is encouraged. Additionally, there is emerging evidence about the benefits of yoga and Pilates in both reducing and managing musculoskeletal problems in breast cancer survivors.\textsuperscript{33,34}

Bone Health
Breast cancer survivors who develop chemotherapy-induced premature ovarian failure, who are premenopausal and taking tamoxifen, or who were postmenopausal at diagnosis and are taking aromatase inhibitors must pay special attention to bone health. Tamoxifen and the aromatase inhibitors (AIs) are the cornerstones of endocrine therapy for estrogen receptor-positive breast cancer and are known to reduce recurrence and improve survival.\textsuperscript{35,36} Although tamoxifen is known to improve bone density in postmenopausal women, it has been associated with bone-densitprotein loss in premenopausal women.\textsuperscript{37} AIs (exemestane, letrozole and anastrozole) can reduce bone density in postmenopausal women, a population already at risk for osteopenia and osteoporosis.\textsuperscript{38} Therefore, bone-density monitoring at appropriate intervals, weight-bearing exercise, and adequate calcium and vitamin D consumption are strongly recommended. Initiation of a bisphosphonate during endocrine therapy may be appropriate and should be based on estimated fracture risk.

Sexual Dysfunction
Both the effects of breast cancer treatment and the emotional and psychological impact of a cancer diagnosis can impair sexual function in women. Mastectomy or breast-conserving therapy that has an unsatisfactory cosmetic result can affect body image. Chemotherapy-induced ovarian suppression and endocrine therapy often result in significant vaginal atrophy, which can lead to dyspareunia. Libido changes may also develop during and after therapy. Over-the-counter vaginal moisturizers and vaginal lubricants are safe and can help relieve some symptoms. Vaginal estrogen may be considered for intractable symptoms. Physicians should do a careful risk-benefit analysis before prescribing vaginal estrogen and should do so in collaboration with an oncologist. Involvement of a specialist in sexual and menopausal health is strongly encouraged for women suffering from these symptoms.

Uterine Health
Breast cancer survivors taking tamoxifen have a small-but-increased risk of uterine dysplasia and malignancy, particularly if they are postmenopausal.\textsuperscript{39} Thus, regular pelvic exams and appropriate evaluation of suspicious symptoms such as vaginal spotting must be promptly evaluated. Additionally, even though premenopausal women treated with tamoxifen may have menstrual irregularity or even amenorrhea, conception is still possible. Despite inconclusive studies in humans, teratogenicity observed in animals has led the FDA to classify tamoxifen as a Pregnancy Category D drug. Caution must be taken to prevent pregnancy using nonhormonal contraceptive methods.

Vasomotor Symptoms
Chemotherapy and endocrine therapy are strongly associated with vasomotor instability, which can significantly impair quality of life. The frequency and severity of symptoms is variable. Wearing loose, light-weight clothing that “breathes” and appropriate dietary choices can be helpful.\textsuperscript{40} Acupuncture has been found to relieve hot flashes and is considered safe.\textsuperscript{41} Studies have been done on the effect of multiple drugs on vasomotor symptoms, including but not limited to selective serotonin reuptake inhibitors. Venlafaxine, in particular, has demonstrated benefit but is not tolerated by all patients. Drugs that use CYP2D6 in the cytochrome P450 pathway (eg, paroxetine) may interfere with tamoxifen metabolism; therefore, it is important to consult with a patient’s oncologist when considering drug therapy to manage vasomotor symptoms.

Depression and Anxiety
Breast cancer survivors frequently struggle with psychological distress.\textsuperscript{42} Undiagnosed depression and/or anxiety may lead to significant morbidity and impaired quality of life. Several well-validated easy-to-use tools can be used to identify patients who may be suffering. They include the Patient Health Questionnaire-9 (PHQ-9), Patient Health Questionnaire-2 (PHQ-2) and Beck Depression Index (BDI) for depression and the Generalized Anxiety Disorder-2 (GAD-2) questionnaire for anxiety. Early involvement of a psychologist and/or psychiatrist is encouraged.

Conclusion
Although it might be natural to assume that an oncologist would be the best person to care for a breast cancer survivor, involving both oncology specialists and primary care physicians will likely lead to the best outcomes for patients. ASCO guidelines specify that transferring a patient’s care to a primary care physician one year after diagnosis and treatment for early stage breast cancer is acceptable with re-referral to oncology as needed. Despite this endorsement, oncologists often still provide both breast cancer-related care and general medical care to survivors, even those who have had early-stage disease.\textsuperscript{43} One could argue that this is not the best use of the oncologist’s time and expertise. Furthermore, such care is within the purview and expertise of the primary care physician. There is an emerging body of literature regarding the role of primary care physicians in the care of cancer survivors.\textsuperscript{44,45} Primary care physicians are best equipped to manage comorbidities (eg, diabetes, hypertension, thyroid disease) during active cancer treatment. Following treatment, they can provide ongoing care for such conditions, screen for emerging health concerns and provide appropriate
preventive care such as immunizations and other age-appropriate cancer screenings (primarily cervical and colon cancer). With the guidance of oncologists, they can also monitor for cancer recurrence and sequelae of cancer therapy and help manage side effects of endocrine therapy. Additionally, primary care physicians can screen for and manage depression and anxiety during and after active treatment.

Coordinated care and diligent communication among physicians and with survivors, along with use of survivorship care plans,47 can result in improved outcomes and quality of life for breast cancer survivors. MM

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REFERENCES


