

Late and Long-Term Sequelae of Breast Cancer Treatment

How to recognize and help patients manage these often debilitating complications.

ABSTRACT: More than 12% of women will be diagnosed with breast cancer at some point in their lives, and 78% of them can be expected to survive for at least 15 years. More than 2.8 million breast cancer survivors currently reside in the United States. After breast cancer treatment, as many as 90% of survivors report physical problems that can reduce functional ability, produce or exacerbate emotional problems, negatively affect body image, and diminish quality of life. Many survivors will seek care for late and long-term effects of treatment, which will not necessarily be recognized as such by health care providers and appropriately treated. In this article, the authors discuss the underlying causes of late and long-term sequelae of breast cancer treatment and describe effective assessment and management strategies. They focus specifically on the most common and potentially debilitating upper body effects of breast cancer surgery and external radiation therapy: lymphedema, axillary web syndrome, postmastectomy pain syndrome, rotator cuff syndrome, adhesive capsulitis, arthralgias, cervical radiculopathy, and brachial plexopathy.

Keywords: breast cancer, cancer survivorship, late effects of treatment, lymphedema

When 71-year-old Carol Jackson arrives at her internist's office to have her right shoulder pain evaluated, she tells the nurse that she feels a "constant aching pain," which she rates as a 6 on a 10-point pain scale, though it increases to an 8 with adduction, elevation, and internal rotation of the shoulder. (This case is a composite based on our clinical experience.) Ms. Jackson says her pain is worse when she lies down and following repetitive movements. She has tried both topical salicylate creams and acetaminophen during the day and to help her sleep, but the pain persists and is disrupting her quality of life.

On examination, her right arm demonstrates limited range of motion due to pain. She reports pain on palpation of the right subdeltoid bursa and

acromioclavicular joint area. She feels no pain with palpation of the right forearm or bicipital tendon area and reports no numbness, tingling, neck pain, or other symptoms.

In a woman of Ms. Jackson's age, such pain might initially be attributed to osteoarthritis. Ms. Jackson, however, was treated for stage III breast cancer 15 years ago (see *Breast Cancer Staging*^{1,2}). Treatment of stage III breast cancer focuses primarily on surgical excision of the malignancy, which may be preceded or followed by adjuvant therapies that can include a combination of chemotherapy, external radiation therapy, targeted agents, and hormonal agents. Today's breast cancer treatments inflict considerably less morbidity on patients than those used in the late 19th century (see *The History of Breast*



Two potential complications of breast cancer treatment: lymphedema of the left arm and hand (above left) and axillary web syndrome, or cording, which is visible when the shoulder is abducted. Lymphedema photo © Alchemy Health / Illawarra Lymphoedema Service; cording photo © Springer Science + Business Media LLC.

*Cancer Treatment*³⁻⁵). Nonetheless, each component of today's regimens has the potential to produce long-term sequelae that affect health and quality of life, including the type of upper body pain and shoulder dysfunction Ms. Jackson reports (see Table 1).

Ms. Jackson's treatment regimen, for example, included right breast conservation surgery with axillary node dissection. She received four cycles of adjuvant chemotherapy with doxorubicin and cyclophosphamide followed by an additional four cycles of paclitaxel. Her right breast, as well as supraclavicular and axillary fossa, were treated with adjuvant radiation therapy. For the next five years, she received adjuvant tamoxifen therapy, which was followed for an additional five years by aromatase inhibitor therapy. She completed treatment about six years ago, but wears a compression sleeve during the day and at night to relieve the right upper extremity lymphedema she developed in the year following her surgery, and she sees a lymphedema occupational specialist as needed.

After reviewing the patient history and nurse's assessment notes, the internist refers Ms. Jackson to a rehabilitation medicine service, where a physiatrist performs impingement maneuvers with positive results. Ms. Jackson is diagnosed with right rotator cuff syndrome related to her prior breast cancer treatment. She is prescribed physical therapy two times a week for six to 12 weeks and given a subacromial steroid injection, which may be repeated up to three times. Over the course of treatment, her symptoms improve by 80% to 90% and she no longer needs physical therapy. At home, she continues practicing the exercises and stretching techniques she learned in physical

therapy, and she no longer requires any pain medications for sleep.

The American Cancer Society estimates that roughly 246,660 women and 2,600 men in the United States will be diagnosed with breast cancer this year, accounting for nearly 15% of all new cancer cases nationwide.⁶ Although breast cancer is rare in men, more than 12% of women will be diagnosed with breast cancer at some point in their lives,⁷ and 78% of them can be expected to survive for at least 15 years.⁶ Today, there are more than 3.1 million

Breast Cancer Staging

Cancer stage at diagnosis, which is based on tumor size and spread, determines treatment options and greatly influences projected survival (a Breast Cancer Staging poster from the American Joint Committee on Cancer is available at <https://cancerstaging.org/references-tools/quickreferences/Documents/BreastMedium.pdf>). The earlier breast cancer is identified, the better the patient's prognosis. About 61% of patients are diagnosed at the local stage (stage I) and have a five-year survival rate of 98.6%.¹ Another 32% of patients are diagnosed with regional spread to nearby lymph nodes, and 84.9% survive longer than five years.¹ Patients with local disease and those with regional spread to lymph nodes undergo surgery to remove the cancer and are then considered for adjuvant therapy to prevent cancer recurrence. Metastatic or stage IV breast cancer is incurable, but 25.9% of those diagnosed with metastatic breast cancer survive for at least five years,¹ and one large study found that 10-year survival in this group was greater than 6%.²

female breast cancer survivors in the United States.⁷ Although each woman's experience is unique, up to 90% of breast cancer survivors report physical problems after cancer treatment that can reduce functional ability, produce or exacerbate emotional problems, negatively affect body image, and diminish quality of life.⁸⁻¹⁰ Many will seek care for late and long-term effects of breast cancer treatment, which will not necessarily be recognized as such by health care providers and appropriately treated. This article seeks to familiarize nurses with the underlying causes of such treatment sequelae and to describe effective assessment and management strategies. The specific focus will be on the most common, painful, and debilitating effects that can result from the combination of surgery and external radiation therapy: upper extremity lymphatic disorders, such as lymphedema and axillary web syndrome, and the musculoskeletal and neuromuscular disorders that can cause upper body symptoms and shoulder dysfunction.

LYMPHEDEMA

Although cancer evaluation and treatment have advanced—consider sentinel node biopsy and

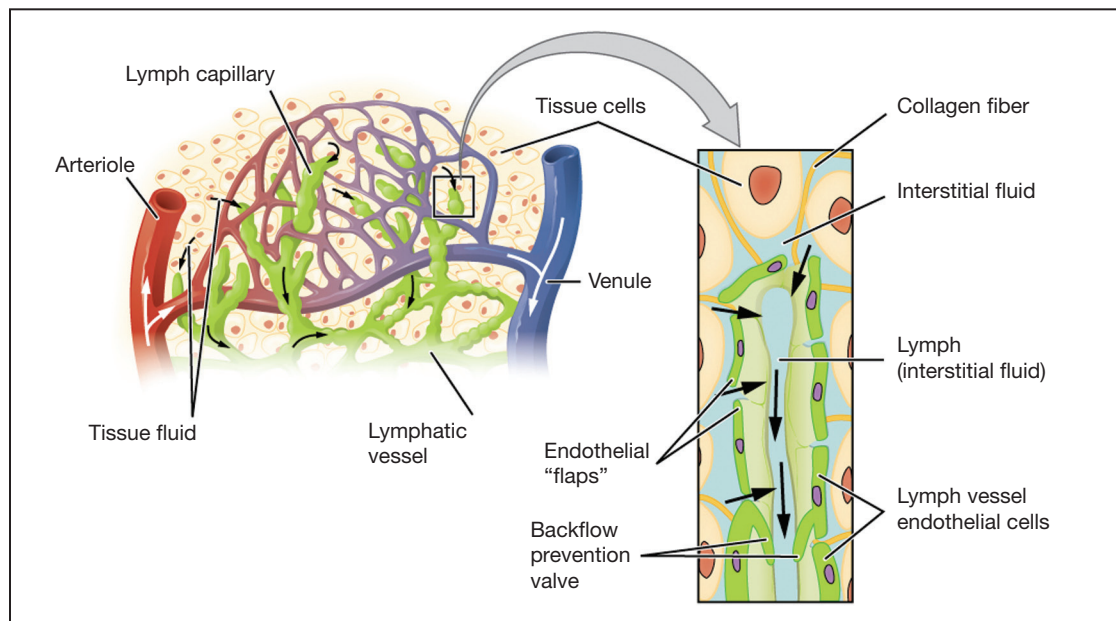
focused radiation therapy, for example—lymphedema continues to be one of the most dreaded complications of breast cancer therapy.¹¹ Upper extremity lymphedema is caused by injury to the axillary lymphatic system, which may occur with lymph node biopsy or radiation, allowing lymphatic fluid to accumulate in the interstitial spaces (see Figure 1 for the normal flow of lymphatic fluid). In breast cancer survivors, the fluid commonly accumulates in the hand, arm, or breast on the side that received axillary radiation therapy or from which lymph nodes were surgically removed. Lymphedema is usually progressive, though symptoms can be controlled if detected and treated before significant tissue damage occurs.¹²

Initially, lymphedema may present as a feeling of heaviness, numbness, or tingling. At this subclinical stage (stage 0), there are no visible changes.¹² Mild swelling that resolves with elevation (stage 1) is believed to result from an obstruction of lymphatic outflow caused by inflammation of surrounding tissues.¹³ Acute lymphedema (stages 0 and 1) usually occurs within the first 18 months following surgery or radiation therapy and is reversible with treatment, as there is no tissue damage. Chronic lymphedema,

Table 1. Potential Sequelae of Breast Cancer Treatment

Radiation Therapy	Chemotherapy	Endocrine Therapy	General Psychosocial Effects
Early		Tamoxifen	Early or late
<ul style="list-style-type: none"> • Redness in breast or affected area • Fatigue 	<ul style="list-style-type: none"> • Nausea and vomiting • Hair loss • Fatigue • Infections • Mouth and throat sores • Weight gain • Nail weakness 	<ul style="list-style-type: none"> • Early hot flashes and night sweats • Vaginal discharge or dryness and itching • Irregular periods or spotting (uterine bleeding) • Blood clots • Cancer of the uterus • Cataracts • Mood swings and depression • Decreased libido 	<ul style="list-style-type: none"> • Emotional distress and depression • Worry, anxiety • Fear of cancer recurrence • Sexuality and intimacy problems • Infertility • Insomnia • Challenges with body image and self-image • Relationship and other social role difficulties • Return-to-work concerns and financial challenges
Late		Aromatase inhibitors	
<ul style="list-style-type: none"> • Lymphedema • Changes in the look and feel of the breast 	<ul style="list-style-type: none"> • Memory problems • Peripheral neuropathy • Sexuality and intimacy problems • Fatigue • Sleep disturbance • Infertility • Early menopause • Hot flashes • Vaginal symptoms • Sexual dysfunction 	<ul style="list-style-type: none"> • Arthralgia and myalgia • Hot flashes and night sweats • Loss of bone mineral density • Vaginal dryness or itching • Carpal tunnel syndrome • Hair thinning • Mood swings and depression • Decreased libido 	

Figure 1. Normal Flow of Lymphatic Fluid



Interstitial fluid flows into lymphatic capillaries, where it is filtered and eventually returned to the venous circulation. When lymph nodes and vessels are removed or damaged during cancer treatment, lymph flow can back up into the surrounding tissues, resulting in lymphedema. Illustration from Anatomy and Physiology, Connexions Web site. Download for free at <http://cnx.org/contents/FPtK1Zmh@6.27:xEZkXdm8@4/Anatomy-of-the-Lymphatic-and-I>.

by contrast, is insidious, often producing symptoms many years after surgery and tending to have a progressive, irreversible course.

Chronic lymphedema (stages 2 and 3) is believed to be caused by fibrosis and obstruction of lymphatic outflow channels due to scarring from surgery or radiation, immobility, or tumor growth. When swelling increases, fails to resolve with elevation, and causes tightness or discomfort with restricted range of motion, such tissue damage has likely occurred. Although stage 2 lymphedema is no longer reversible, it may be managed with treatment if promptly identified.¹² In its most advanced stage (stage 3), chronic lymphedema can be painful and disfiguring, causing functional impairment, altered body image, emotional distress, and infection requiring hospitalization. Based on insurance claims, two-year medical costs for female breast cancer survivors with diagnosed lymphedema are estimated to be \$14,877 to \$23,167 higher than costs for those without lymphedema.¹⁴

Diagnosing lymphedema. When patients develop upper extremity swelling after breast cancer surgery, the differential diagnosis should include deep vein thrombosis, congestive heart failure, superior vena cava syndrome, and breast cancer recurrence. Upon initial presentation with swelling, an upper extremity ultrasound is frequently performed to rule out deep vein thrombosis. A disease workup including

radiologic scans—positron emission tomography-computed tomography and magnetic resonance imaging (MRI), for example—may be considered to rule out recurrent breast cancer.

The risk factors for developing lymphedema include the following^{13, 15}:

- axillary surgery
- positive lymph nodes
- postoperative axillary nodal radiation
- postoperative axillary hematoma, seroma, or infection
- obesity
- poor shoulder mobility

For lymphedema to be diagnosed in a timely manner, it is imperative that nurses take a thorough patient history, identifying the patient's tumor stage and pathology at the time of diagnosis, the specific treatment received (the type of breast cancer surgery performed and any radiation therapy delivered, for example), any postoperative complications, and the time of onset of any new symptoms.

Treating lymphedema. One of the simplest ways to reduce the swelling of lymphedema is to elevate the affected extremity above the level of the heart. Patients can also be fitted with compression garments (elastic sleeves, gloves, or vests) to support the affected limb and promote fluid movement.¹⁶ The National Comprehensive Cancer Network (NCCN) recommends

The History of Breast Cancer Treatment

In 1882, American surgeon William Halsted performed the first radical mastectomy, which became the gold standard for treatment of breast cancer for nearly a century.^{3,4} The procedure he developed removed the breast, axillary nodes, and chest muscles in a single surgery to prevent the spread of cancer. Although the procedure allowed women with breast cancer to survive longer, it left them disfigured, with deformed chest walls, lymphedema, and pain.⁴ Early in the 20th century, this aggressive surgery came under fire for associated morbidity. Women undergoing the procedure lost full range of motion of the upper extremities, rendering them unable to engage in activities of daily living. In the 1930s and 1940s, radical mastectomies and modified radical mastectomies, which spared the pectoralis muscles, were shown to have similar rates of local recurrence and long-term survival; thus, modified radical mastectomy soon became the new standard of care.⁴

In 1976, Fisher and colleagues initiated a study that ultimately concluded that lumpectomy (removal of only the abnormal breast tissue) followed by breast irradiation was as effective as total mastectomy for the treatment of breast cancer.⁵ At present, this procedure is the general recommendation for women diagnosed with stage I or stage II breast cancer.

that patients with lymphedema wear compression garments when engaging in exercise; they should take additional precautions, however, such as not starting strength training if they have an active limb infection.¹⁷ For more considerations for patients with lymphedema from the NCCN, see *Physical Activity Considerations for Patients with Lymphedema*.¹⁷ Breast cancer survivors with lymphedema should be informed that, when appropriately supervised, upper body resistance training can improve symptoms and aid in the long-term management and treatment of lymphedema.^{17, 18}

Occupational and physical therapists specifically trained in lymphedema therapy often use a hands-on technique called manual lymphatic drainage massage. This is not a deep massage but rather uses slow rhythmic movements and gentle pressure to promote the flow of lymphatic fluid from the affected area toward healthy vessels and nodes. Although such massage-based therapy is often recommended and even endorsed by the NCCN,¹⁷ randomized controlled trials have not yet demonstrated that massage therapy produces significant improvement when compared with compression garments.¹⁹

Over the past few years, lymph node transfer has gained prominence as a surgical option for breast cancer survivors with lymphedema. For this procedure, lymph nodes from the patient's groin are harvested and transferred to the affected arm in hopes of restoring lymphatic drainage. In clinical trials,

lymph node transfer has significantly improved post-mastectomy upper extremity lymphedema, with limited morbidity.²⁰ A recent review of this surgical treatment for lymphedema shows further promise, though clinical trial sample sizes have been small.²¹ Further investigation is needed.

AXILLARY WEB SYNDROME

Axillary web syndrome (AWS), or cording, is characterized by palpable, cordlike subcutaneous tissue extending from the axilla into the arm. It is visible and painful when the shoulder is in abduction. AWS occurs on the side of the axillary surgery, and generally develops within eight weeks of surgery, but may emerge more than three months later.²² The precise etiology, typical course, and most effective treatment for AWS have not yet been defined, but lymphovenous damage, hypercoagulation, superficial venous stasis, lymphatic stasis, and tissue injury secondary to lymphatic disruption during surgery are believed to contribute to its development.

The true incidence of AWS is unknown because it is not routinely or consistently measured. In a prospective cohort study that included 193 women who had undergone breast cancer surgery, the incidence of AWS was 28%.²³ Clinical trials have evaluated the prevalence of AWS after sentinel lymph node biopsy versus axillary lymph node biopsy and found that the risk of developing AWS was 20% and 72%, respectively, for the two procedures.²⁴

Although AWS almost always resolves spontaneously without treatment, treatment is important to prevent reduced shoulder flexion and myofascial pain syndrome.^{22, 25} It is possible that early postoperative movement restriction, functional deficits, pain, and edema may be associated with development of AWS.

PERSISTENT UPPER BODY SYMPTOMS

The prevalence of upper body symptoms as long-term sequelae of breast cancer treatment remains high. A large, cross-sectional Danish study found that 47% of women treated for breast cancer between 2005 and 2006 reported some type of upper body pain two to three years following treatment, with 13% describing it as severe and 39% describing it as moderate.²⁶ In an Australian study that assessed such upper body symptoms as pain, weakness, poor range of motion, tingling, numbness, stiffness, or swelling in 287 women who had been treated for unilateral breast cancer, nearly half the women reported at least one such symptom six months following surgery, and 51% continued to report symptoms 18 months following surgery.²⁷ Of those reporting symptoms, 57% to 82% characterized them as moderate, the remainder as severe or extreme.

Common underlying causes of persistent upper body symptoms in this population include postmastectomy pain syndrome, musculoskeletal disorders,

and neuromuscular disorders, which can reduce upper body function and have substantial psychosocial ramifications. Accurate diagnosis is essential to effective treatment. For example, a woman reporting upper body pain related to adhesive capsulitis may obtain substantial relief from a comprehensive treatment plan that includes physical therapy, a non-steroidal antiinflammatory drug (NSAID), and subacromial or intraauricular corticosteroid injections.²⁸ If the pain is acute or severe, opioids may also be prescribed. It is important to recognize that pain and other upper body symptoms in these patients may have more than one cause and that coexisting causes as well as resulting dysfunction may evolve over time, further complicating diagnosis and treatment strategies.

POSTMASTECTOMY PAIN SYNDROME

Postmastectomy pain syndrome (PMPS) is defined by the International Association for the Study of Pain as chronic pain affecting the anterior aspect of the thorax, axilla, or upper half of the arm that arises soon after mastectomy or lumpectomy and may endure for years.²⁹ It is believed to result from associated tissue damage from axillary dissection or breast reconstruction and, possibly, from intercostobrachial nerve damage. Prevalence is roughly 44%,^{30,31} and incidence has been found to be as high as 52%.³² PMPS may manifest as a dull, burning, or aching sensation in the chest wall, arm, or axilla that is exacerbated by shoulder movement, or by phantom sensations of breast pain, itching, or numbness. Treatment typically focuses on physical therapy, skin desensitization, and myofascial release, but pain medications may also be necessary.

MUSCULOSKELETAL DISORDERS

Following breast cancer surgery, axillary dissection, and radiation, patients often experience pain that can inhibit their use of the shoulder and arm on the affected side. Postmastectomy pain can be complicated by reconstruction (immediate or delayed) and radiation with scar formation and upper quadrant dysfunction. Both immediate and delayed reconstruction, including with implant, free flap, or pedicle flap, can cause pain and dysfunction.³³ Protective posturing in response to pain may shorten pectoralis major and minor muscles in the chest wall, resulting in forward depression of the shoulder joint, which may be compounded by radiation fibrosis.³⁴ Such misalignment of the shoulder may lead to rotator cuff syndrome and, ultimately, adhesive capsulitis. To help women stretch and strengthen chest wall muscles, hospital-based exercise classes are often incorporated into postoperative care. Patients should be encouraged to continue the stretching exercises routinely after discharge.

Rotator cuff syndrome (also called rotator cuff disease) is, in our experience, a major cause of shoulder

pain in breast cancer survivors, which is not surprising since it is the leading cause of shoulder pain in the general population.^{34,35} Major contributing factors may include surgery, reconstruction, and radiation, as well as the subsequent shortening of the surrounding chest wall muscles and soft tissues, misalignment of tendons, and narrowing of the acromial arch.^{28,34} The presence of lymphedema can contribute to rotator cuff syndrome.³⁶ Advanced age is also a well-established factor in its development.

Rotator cuff syndrome can usually be diagnosed on the basis of clinical symptoms such as shoulder pain, limited range of motion, shoulder weakness, and reduced arm function. Associated pain may be anterior or anterolateral, possibly with radiation to the elbow. Pain may occur when patients reach overhead or behind or sleep on the affected side. Trained providers, such as physiatrists, may assist in diagnosis by performing physical maneuvers that elicit pain, though this is seldom necessary.

Most patients respond well to conservative treatments such as physical therapy and nonopioid pain medications as needed. Radiologic imaging, including X-ray, MRI, and ultrasound, is generally reserved for patients who do not respond to initial therapy or

Physical Activity Considerations for Patients with Lymphedema

- Use compression garments when engaging in exercise.
- Work with a trained exercise professional if considering weight training or resistance training.
- Undergo baseline and periodic evaluation for development or exacerbation of lymphedema.
- Initiate strength training involving affected body parts only if lymphedema is stable:
 - no need for lymphedema therapy within the past three months
 - no recent limb infections requiring antibiotics
 - no change in limb circumference > 10%
 - no change in ability to perform activities of daily living
- For resistance training/weight lifting: gradually increase resistance by the smallest increment possible, with monitoring.
- Stop exercise and contact a lymphedema specialist if exacerbation of lymphedema occurs.
- Continue full use of extremity and range-of-motion exercises to maintain strength and range of motion even in the presence of lymphedema.

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whose symptoms are worsening. Physical therapy, which plays an important role in treating rotator cuff syndrome, focuses on improving the shoulder's range of motion, strengthening shoulder muscles, and restoring anatomic alignment. Physical therapists may use such techniques as myofascial release, transcutaneous electrical nerve stimulation, or neurolysis (nerve blockade). Lymphedema should be managed as well—lymphedema in the chest wall can limit shoulder motion.

NSAIDs may be helpful in reducing mild to moderate pain during therapy. For patients with severe pain, subacromial corticosteroid injection may be necessary but should not be used as monotherapy. Opioids may be prescribed in addition, and surgery may be considered for patients whose symptoms do not improve with physical therapy and for those with rotator cuff tears or severe degenerative osteoarthritis.

those effects. Postsurgical pain from scarring and damage to skin, muscle, fascia, and soft tissues is compounded by radiation fibrosis, as well as by fear of complications and pain, which causes patients to limit shoulder movement, further reducing function and increasing inflammation.

Treatment of adhesive capsulitis focuses on physical therapy geared toward improving soft tissue dysfunction. Physical therapy strategies are similar to those used for rotator cuff syndrome, and as with rotator cuff syndrome, NSAIDs may benefit those who have pain during therapy. It is unclear whether corticosteroid injections are helpful in improving symptoms.

Arthralgias are commonly seen in breast cancer survivors who received neurotoxic chemotherapy or aromatase inhibitors, which are used in the adjuvant setting to prevent disease recurrence. Arthralgias can occur in up to 50% of those treated with aromatase

Evidence on the effect of venipuncture in the affected arm is mixed; for this reason, nurses should continue to use the contralateral arm for routine medical interventions.

Adhesive capsulitis. Breast cancer survivors frequently have restricted range of motion in the arm on the side of the surgery. The loss of both active and passive glenohumeral motion is known as adhesive capsulitis, or “frozen shoulder.” In breast cancer survivors, adhesive capsulitis often results from a cycle of morbidity in which the patient's response to the adverse effects of various treatments exacerbates

inhibitors.³⁷ Pain can be so severe that aromatase inhibitor therapy must be interrupted or discontinued, despite its proven capacity to prevent breast cancer recurrence. In a cross-sectional analysis of 300 postmenopausal breast cancer survivors treated with aromatase inhibitors, 139 (47%) attributed their arthralgias to aromatase inhibitors.³⁸ The most common sites of joint pain in those women were the wrist or hand, knee, back, ankle or foot, and hip.

Arthralgia treatment includes patient education, antiinflammatory drugs, opioids, and the antidepressant duloxetine (Cymbalta), a serotonin and norepinephrine reuptake inhibitor that has been shown to significantly reduce pain associated with aromatase inhibitors and improve physical functioning.^{39, 40}

Other antidepressants and anticonvulsants are often used in the treatment of chronic pain disorders, but their use has not been evaluated in arthralgias associated with aromatase inhibitor therapy. Treatment strategies also include aerobic exercise, nerve stabilizers, and switching from one aromatase inhibitor that is poorly tolerated to another, but there is not yet strong support for any of these.

NEUROMUSCULAR DISORDERS

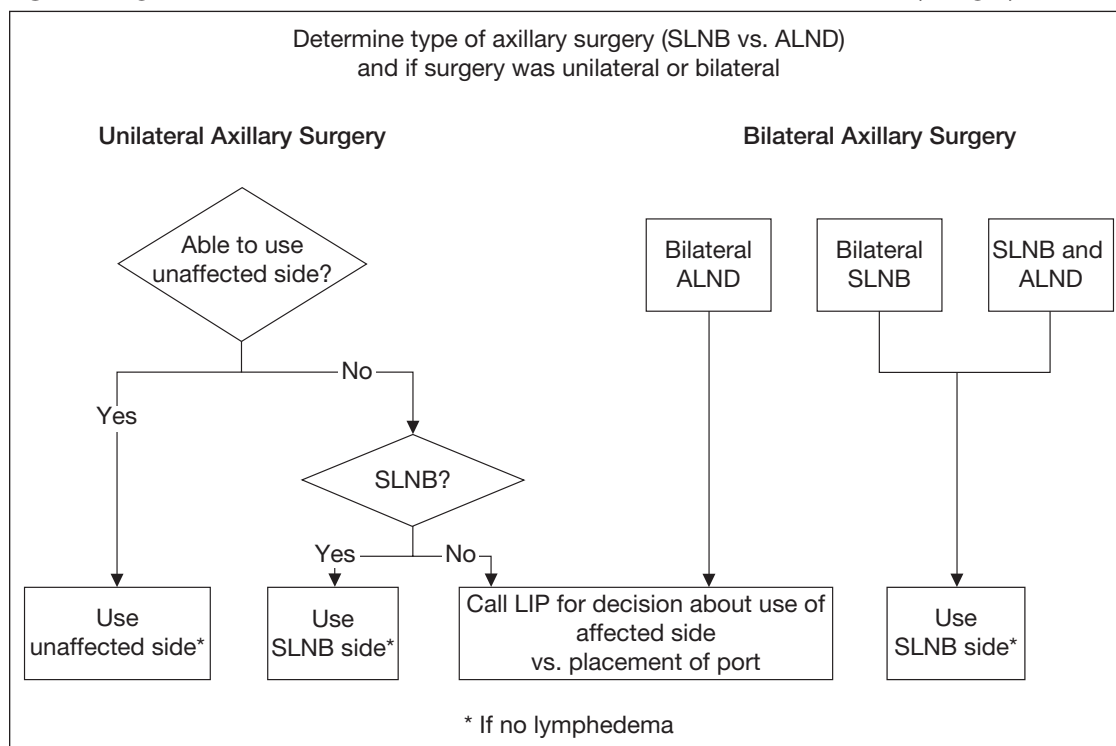
Cervical radiculopathy, which results from cervical nerve root compression, is a common cause of neck pain, upper extremity pain, and upper extremity

Table 2. Clinical Features That Differentiate Radiation-Induced Brachial Plexopathy (RIBP) from Tumor Recurrence³⁵

Characteristics	RIBP	Tumor Recurrence
Clinical presentation	Late	Late
Associated with Horner syndrome? ^a	No	Yes
Likely trunk area affected	Upper	Lower
Prevalence of entire trunk involvement	25%	25%

^aHorner syndrome, which results from the disruption of a nerve pathway from the brain to the face, typically causes unilateral pupillary constriction, ptosis, and anhidrosis.

Figure 2. Algorithm for Intravenous Line Placement in Patients Who Have Had Axillary Surgery



ALND = axillary lymph node dissection; LIP = licensed independent practitioner; SLNB = sentinel lymph node biopsy.

Postaxillary procedure guidelines were developed at the Memorial Sloan Kettering Cancer Center and are published with permission.

weakness in breast cancer survivors. Although it is not believed to be related to breast cancer or its treatment, it can worsen other disorders that result from breast cancer treatment, thereby contributing to upper body pain and dysfunction in this population. Providing patients with an explanation of the cause underlying the associated discomfort can alleviate their anxiety and help them understand the goal of recommended treatments.

The pain associated with radiculopathy can be neuropathic, following the dermatomal distribution of the affected nerve root or roots, or myofascial, resulting from muscle spasms within the myotome of the affected root or roots. Both types of radiculopathy are common, with distribution of the pain depending on the affected roots. Treatment recommendations vary widely and largely depend on the severity of the symptoms, particularly pain. For patients with minimal pain and no weakness, conservative treatment with antiinflammatory drugs and physical therapy is usually effective.⁴¹ Physical and occupational therapy can reduce pain and improve strength, fine motor skills, and performance of activities of daily living. Patients with more severe pain and weakness may require intervention with epidural steroid injections.³⁵ Patients with severe weakness or

spinal cord compromise due to radiculopathy may be considered for surgery, which has been shown to be helpful in 70% to 90% of patients.⁴²

Brachial plexopathy is commonly seen in breast cancer survivors, either as a result of radiation therapy or neoplasm.⁴³ The brachial plexus innervates all the muscles of the upper extremity, except the trapezius and levator scapula. Risk of radiation-induced brachial plexopathy is increased with radiation therapy doses greater than 55 Gy, with reported incidence as high as 73%.⁴⁴ When cumulative radiation therapy doses are less than 40 Gy, however, incidence drops to less than 1%.

Brachial plexopathy presents with pain, paresthesias (sensation of burning or tingling), sensory loss (numbness), weakness, and new-onset arm edema.⁴⁵ It is important to remember that both radiation-induced brachial plexopathy and tumor recurrence can occur simultaneously, and that accurate diagnosis generally requires clinician judgment, radiology, and collaboration (see Table 2³⁵). Early diagnosis is crucial in order that, if tumor recurrence is the underlying problem, antineoplastic therapy can be initiated before symptoms become debilitating.

No medical treatments are known to be effective against radiation-induced brachial plexopathy,

a disorder that often progresses to “flail arm,” with severe muscle wasting and weakness. Physical and occupational therapy focuses on helping patients maximize their strength and develop adaptive strategies. Rehabilitation may also include skin desensitization and proprioceptive techniques. Nerve stabilizers, such as duloxetine or pregabalin (Lyrica), may be used to treat neuropathic pain. If there is musculoskeletal involvement (rotator cuff syndrome or adhesive capsulitis, for example), NSAIDs may be used as well. Opioids may be prescribed for severe pain.

INTEGRATIVE MEDICINE AND THERAPEUTIC EXERCISE

There has been little definitive research into the effects of holistic approaches on chronic pain and dysfunction in breast cancer survivors, as double-blind, randomized, placebo-controlled studies are lacking and interventions tend to include multiple modalities used simultaneously that evolve in response to patient progress or lack thereof. Acupuncture and massage therapy, however, have been shown to benefit some cancer survivors with treatment-related pain syndromes⁴⁶ and to reduce peripheral neuropathy following chemotherapy.⁴⁷ While potentially beneficial, such interventions should be incorporated into an integrative program that includes therapeutic exercise. Evaluation by a physical therapist or physiatrist familiar with the sequelae of cancer treatment and treatment-related pain management offers cancer survivors the greatest potential for restoring function and quality of life.

IMPLICATIONS FOR NURSES

Nurses in nononcology settings are frequently involved in the care of women who have been treated for breast cancer. They will often be asked to provide expertise and advice on managing treatment sequelae such as chronic lymphedema or upper body pain and dysfunction. Patients may ask if it is safe to exercise the affected arm or to use it for routine medical interventions or in day-to-day lifting activities.

For decades, women who had axillary lymph node dissections were instructed to practice “arm precautions.” They were told not to let anyone take a blood pressure reading, give an injection, draw blood, or insert an intravenous catheter into the arm on the side of the surgery site and to refrain from lifting anything heavy with the affected arm. In recent years, however, clinical trials have shown that weight lifting and resistance exercise is safe for breast cancer survivors and can improve strength, muscle endurance, and quality of life in women with or at risk for lymphedema after breast cancer treatment.¹⁸ Evidence on the effect of venipuncture in the affected arm is mixed; for this reason, nurses should continue to use the contralateral arm for such routine medical interventions as blood draws, injections, and intravenous catheters (see Figure 2).⁴⁸ At the Memorial Sloan Kettering

Cancer Center in New York City, blood pressure measurement on the side of the surgery site is permitted if there is no evidence of lymphedema.

Nurses should continue to counsel patients who are at risk for lymphedema about healthy lifestyle choices, including weight management, as obesity is associated with increased lymphedema risk.⁴⁸⁻⁵⁰ They should also remind patients with lymphedema to follow recommendations for physical therapy or occupational therapy and identify barriers to adherence. By increasing patients’ awareness of lymphedema risks while emphasizing self-care and preventive strategies following surgery, nurses can help patients maintain quality of life and minimize cosmetic, functional, psychological, and emotional complications.

Despite the adoption of more conservative surgical approaches and focused radiation therapy, morbidity after breast cancer treatment remains a significant clinical problem for survivors. Strategies to prevent and manage lymphedema, address pain, and improve quality of life in survivors are evolving. With increased emphasis on improved quality of life in cancer survivorship and posttreatment sequelae, optimizing function after cancer treatment can be expected to emerge as an increasingly important public health issue. Nurses are uniquely positioned to educate breast cancer survivors, alleviate their fears, and help them find appropriate resources to address the late and long-term effects of treatment. ▼

For 128 additional continuing nursing education activities on cancer topics, go to www.nursingcenter.com/ce.

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REFERENCES

1. National Cancer Institute, Surveillance, Epidemiology, and End Results Program. *SEER stat fact sheets: female breast cancer*. 2012. <http://seer.cancer.gov/statfacts/html/breast.html>.
2. Tevaarwerk AJ, et al. Survival in patients with metastatic recurrent breast cancer after adjuvant chemotherapy: little evidence of improvement over the past 30 years. *Cancer* 2013; 119(6):1140-8.
3. Altman LK. The doctor's world. *New York Times* 1981 Sep 8. <http://www.nytimes.com/1981/09/08/science/the-doctor-s-world.html>.
4. Halsted CP, et al. A historical account of breast cancer surgery: beware of local recurrence but be not radical. *Future Oncol* 2014;10(9):1649-57.
5. Fisher B, 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(16):1233-41.

6. American Cancer Society. *Cancer facts and figures 2016*. Atlanta; 2016. <http://www.cancer.org/acs/groups/content/@research/documents/document/acspc-047079.pdf>.
7. American Cancer Society. Breast cancer facts and figures 2015-2016. Atlanta; 2015. <http://www.cancer.org/acs/groups/content/@research/documents/document/acspc-046381.pdf>
8. Beckjord EB, et al. Population-level trends in posttreatment cancer survivors' concerns and associated receipt of care: results from the 2006 and 2010 LIVESTRONG surveys. *J Psychosoc Oncol* 2014;32(2):125-51.
9. Collins LG, et al. Perceptions of upper-body problems during recovery from breast cancer treatment. *Support Care Cancer* 2004;12(2):106-13.
10. Sagen A, et al. Changes in arm morbidities and health-related quality of life after breast cancer surgery—a five-year follow-up study. *Acta Oncol* 2009;48(8):1111-8.
11. McLaughlin SA, et al. Trends in risk reduction practices for the prevention of lymphedema in the first 12 months after breast cancer surgery. *J Am Coll Surg* 2013;216(3):380-9.
12. BreastCancer.org. *Stages of lymphedema*. 2016. <http://www.breastcancer.org/treatment/lymphedema/how/stages>.
13. Golshan M, Smith B. Prevention and management of arm lymphedema in the patient with breast cancer. *J Support Oncol* 2006;4(8):381-6.
14. Shih YC, et al. Incidence, treatment costs, and complications of lymphedema after breast cancer among women of working age: a 2-year follow-up study. *J Clin Oncol* 2009;27(12):2007-14.
15. Tsai RJ, et al. The risk of developing arm lymphedema among breast cancer survivors: a meta-analysis of treatment factors. *Ann Surg Oncol* 2009;16(7):1959-72.
16. Damstra RJ, Partsch H. Compression therapy in breast cancer-related lymphedema: a randomized, controlled comparative study of relation between volume and interface pressure changes. *J Vasc Surg* 2009;49(5):1256-63.
17. National Comprehensive Cancer Network. *NCCN clinical practice guidelines in oncology (NCCN guidelines): survivorship version 2.2015*; 2015. NCCN Guidelines; http://www.nccn.org/professionals/physician_gls/pdf/survivorship.pdf.
18. Cormie P, et al. Is it safe and efficacious for women with lymphedema secondary to breast cancer to lift heavy weights during exercise: a randomised controlled trial. *J Cancer Surviv* 2013;7(3):413-24.
19. Dayes IS, et al. Randomized trial of decongestive lymphatic therapy for the treatment of lymphedema in women with breast cancer. *J Clin Oncol* 2013;31(30):3758-63.
20. Lin CH, et al. Vascularized groin lymph node transfer using the wrist as a recipient site for management of postmastectomy upper extremity lymphedema. *Plast Reconstr Surg* 2009;123(4):1265-75.
21. Ito R, Suami H. Overview of lymph node transfer for lymphedema treatment. *Plast Reconstr Surg* 2014;134(3):548-56.
22. Yeung WM, et al. A systematic review of axillary web syndrome (AWS). *J Cancer Surviv* 2015;9(4):576-98.
23. Bergmann A, et al. Incidence and risk factors for axillary web syndrome after breast cancer surgery. *Breast Cancer Res Treat* 2012;131(3):987-92.
24. Leidenius M, et al. Motion restriction and axillary web syndrome after sentinel node biopsy and axillary clearance in breast cancer. *Am J Surg* 2003;185(2):127-30.
25. Torres Lacomba M, et al. Axillary web syndrome after axillary dissection in breast cancer: a prospective study. *Breast Cancer Res Treat* 2009;117(3):625-30.
26. Gärtner R, et al. Prevalence of and factors associated with persistent pain following breast cancer surgery. *JAMA* 2009;302(18):1985-92.
27. Hayes SC, et al. Prevalence of upper-body symptoms following breast cancer and its relationship with upper-body function and lymphedema. *Lymphology* 2010;43(4):178-87.
28. Stubblefield MD, Custodio CM. Upper-extremity pain disorders in breast cancer. *Arch Phys Med Rehabil* 2006;87(3 Suppl 1):S96-S99.
29. Merskey H, Bogduk N, eds. *Classification of chronic pain: descriptions of chronic pain syndromes and definitions of pain terms*. 2nd ed. Seattle: IASP Press; 1994. <http://www.iasp-pain.org/files/Content/ContentFolders/Publications2/FreeBooks/Classification-of-Chronic-Pain.pdf>.
30. Couceiro TC, et al. Prevalence of post-mastectomy pain syndrome and associated risk factors: a cross-sectional cohort study. *Pain Manag Nurs* 2014;15(4):731-7.
31. Smith WC, et al. A retrospective cohort study of post mastectomy pain syndrome. *Pain* 1999;83(1):91-5.
32. Alves Nogueira Fabro E, et al. Post-mastectomy pain syndrome: incidence and risks. *Breast* 2012;21(3):321-5.
33. McNeely ML, et al. A prospective model of care for breast cancer rehabilitation: postoperative and postreconstructive issues. *Cancer* 2012;118(8 Suppl):2226-36.
34. Ebaugh D, et al. Shoulder impairments and their association with symptomatic rotator cuff disease in breast cancer survivors. *Med Hypotheses* 2011;77(4):481-7.
35. Stubblefield MD, Keole N. Upper body pain and functional disorders in patients with breast cancer. *PM R* 2014;6(2):170-83.
36. Herrera JE, Stubblefield MD. Rotator cuff tendonitis in lymphedema: a retrospective case series. *Arch Phys Med Rehabil* 2004;85(12):1939-42.
37. Winters-Stone KM, et al. A prospective model of care for breast cancer rehabilitation: bone health and arthralgias. *Cancer* 2012;118(8 Suppl):2288-99.
38. Mao JJ, et al. Patterns and risk factors associated with aromatase inhibitor-related arthralgia among breast cancer survivors. *Cancer* 2009;115(16):3631-9.
39. Henry NL, et al. Pilot study of duloxetine for treatment of aromatase inhibitor-associated musculoskeletal symptoms. *Cancer* 2011;117(24):5469-75.
40. Wang ZY, et al. Efficacy and safety of duloxetine on osteoarthritis knee pain: a meta-analysis of randomized controlled trials. *Pain Med* 2015;16(7):1373-85.
41. Yoon SH. Cervical radiculopathy. *Phys Med Rehabil Clin N Am* 2011;22(3):439-46, viii.
42. Basho R, et al. Neck pain from a spine surgeon's perspective. *Phys Med Rehabil Clin N Am* 2011;22(3):551-5, x.
43. Jaeckle KA. Neurologic manifestations of neoplastic and radiation-induced plexopathies. *Semin Neurol* 2010;30(3):254-62.
44. Galecki J, et al. Radiation-induced brachial plexopathy and hypofractionated regimens in adjuvant irradiation of patients with breast cancer—a review. *Acta Oncol* 2006;45(3):280-4.
45. Kamenova B, et al. Effective treatment of the brachial plexus syndrome in breast cancer patients by early detection and control of loco-regional metastases with radiation or systemic therapy. *Int J Clin Oncol* 2009;14(3):219-24.
46. Glare PA, et al. Pain in cancer survivors. *J Clin Oncol* 2014;32(16):1739-47.
47. Schroeder S, et al. Acupuncture for chemotherapy-induced peripheral neuropathy (CIPN): a pilot study using neurography. *Acupunct Med* 2012;30(1):4-7.
48. Cemal Y, et al. Preventative measures for lymphedema: separating fact from fiction. *J Am Coll Surg* 2011;213(4):543-51.
49. Helyer LK, et al. Obesity is a risk factor for developing post-operative lymphedema in breast cancer patients. *Breast J* 2010;16(1):48-54.
50. Schmitz KH, et al. Impact of obesity on cancer survivorship and the potential relevance of race and ethnicity. *J Natl Cancer Inst* 2013;105(18):1344-54.