Survivorship care: Understanding the sequelae of breast cancer treatment

Management of posttreatment risks, including arm lymphedema, cosmesis, and chronic pain, may help patients navigate their recovery after breast cancer treatment.

**ABSTRACT:** Survivorship care has improved as the sequelae of breast cancer treatment have become better appreciated and understood in an era of increasing focus on patient-centred care. Development of arm lymphedema is a risk following axillary treatment. The introduction of less-invasive surgical procedures has resulted in decreased rates of lymphedema. It is now recognized that physical activity and routine medical procedures on the treated arm are safe and do not increase the risk of lymphedema. Patient education regarding early detection of lymphedema and timely referral to physiotherapy may be beneficial. Cosmesis may represent another survivorship concern. The appearance of the treated breast may impact self-image and recovery. The decision between breast conserving therapy and mastectomy is complex and is best supported through patient education and a patient-centred process of care. Lastly, chronic posttreatment pain may affect certain individuals. The optimal management of posttreatment pain involves a multimodal early-intervention strategy. This approach can be instituted in the pretreatment, intraoperative, and postoperative phase, using balanced multimodal analgesics, self-management techniques, and upper body physical recovery. This article reviews current approaches to arm lymphedema, posttreatment cosmesis, and reducing posttreatment pain.

An increasing number of patients in British Columbia are survivors of breast cancer and are navigating life in their “new normal.” Survivorship care is an evolving field that strives to recognize, understand, and manage the issues that arise in the posttreatment phase. For some women, the sequelae of treatment have a significant and long-lasting impact on their physical, emotional, and psychological health. Some concerns in survivorship care are arm lymphedema, cosmesis, posttreatment pain, and cancer surveillance.

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Arm lymphedema
The reported incidence of arm lymphedema following breast cancer treatment is highly variable. The estimated risk for patients undergoing axillary lymph node dissection (ALND) is 20%, compared with 5% for sentinel lymph node biopsy (SLNB). However, a more clinically meaningful and relevant interpretation of risks is the presence of severe edema alone (defined as more than a 5-cm difference in arm circumference), which has an estimated incidence of 3.0% for ALND and 0.5% for SLNB. The use of axillary radiation is an independent and added risk factor for development of clinically significant lymphedema, with an incidence of 8% in patients undergoing combined axillary surgery and radiation. The onset of lymphedema is typically seen within 3 years of axillary intervention, while the ongoing risk beyond 3 years is estimated at 1% per year to at least 20 years. Prevention strategies focus on reducing axillary intervention and other risk factors. Once lymphedema is diagnosed, management efforts focus on preventing progression and addressing associated symptoms.

Diagnosis
Arm circumference is a commonly utilized and simple clinical measurement for assessing lymphedema. Measurements are taken at 15 cm above and below the medial epicondyle. Diagnosis is based on the difference between the treated and untreated arm, or between the preoperative and postoperative arm. Differences greater than 2 cm indicate clinical lymphedema, which is further classified as mild (2 to 3 cm), moderate (3 to 5 cm), or severe (more than 5 cm).

Risk factors
The mechanism leading to lymphedema following axillary intervention is not well understood but is thought to involve posttreatment fibrosis obstructing remaining lymphatic channels. Once clinically evident lymphedema develops, the changes are generally irreversible. Although theoretically lymphedema can be reversed in the subclinical phase, there are currently no diagnostic or intervention tools available for common clinical use.

While avoidance of trauma to the treated extremity, including blood pressure measurement and skin puncture, may appear sensible, the evidence for this is extremely poor and a growing body of literature does not support these precautions. The impact of blood pressure measurement on lymphedema risk was addressed in four recent level 2 and 3 studies, three of which did not identify a significant association. Other studies evaluating the use of a pneumatic tourniquet during hand surgery in patients with previous axillary surgery did not demonstrate increased risk of lymphedema.

The risk of skin puncture leading to lymphedema has been considered in 11 studies. Those that endorsed avoidance of skin puncture were primarily historical retrospective observational studies or single-subject case reports. Among the three prospective cohort studies available, one identified a significant risk of lymphedema in patients with a history of skin puncture, although recall bias has since been raised as an issue, and subsequent studies have found no significant association between skin puncture and lymphedema.

Although using the untreated arm for medical procedures when possible remains a sensible precaution, repeatedly advising patients to limit use of the treated arm may cause unnecessary anxiety and restrict activities. Given the evidence, it is reasonable for medical teams to move away from overly restrictive advice. Patients can be reassured that studies have demonstrated that blood pressure readings and medical procedures on the treated arm do not increase the risk of lymphedema.

Prevention and management
The only risk factors for lymphedema identified consistently are axillary surgery, axillary radiation, high body mass index, and cellulitis.
Cellulitis represents a proven and widely accepted risk factor for lymphedema. Thus, early recognition and treatment of extremity infections is important. Avoidance of ALND when feasible may also reduce the risk of lymphedema.

Randomized controlled trials (RCTs) have shown upper extremity exercise and weight training to be safe following axillary intervention, with no increased risk of lymphedema in patients without lymphedema at baseline.13 Physiotherapy and/or manual lymphatic drainage produced encouraging results in modifying the risk of lymphedema,14,15 while patient education regarding early recognition of lymphedema, timely referral to physiotherapy, and use of compression sleeves were shown to be useful management strategies.14-16

Cosmesis

Once a cancer is surgically excised, patients must live with the new appearance of the treated breast. Using patient-reported outcomes, researchers have demonstrated the importance of cosmesis and its impact on self-image and recovery.17 Of the numerous validated psychometric patient-reported outcome measures (PROMs) available, the BREAST-Q17 has become one of the most widely utilized for breast reconstruction and breast conserving surgery (BCS).18

Breast conserving surgery versus mastectomy

The nononcologic goals of breast conserving surgery include preservation of the breast’s esthetic appearance, sense of wholeness, and sensation. The likelihood of achieving these goals with BCS, mastectomy with reconstruction, or mastectomy alone is discussed with the patient. Patients with small tumors, relatively large breasts, and/or lesions in the upper outer breast quadrant are considered more suitable candidates for BCS.19,20

The relationship between cosmetic outcome, psychological adjustment,21,22 and quality of life23 has been well demonstrated. Reports evaluating patient satisfaction with cosmesis after BCS with radiation and after mastectomy with reconstruction have shown differing results. While some studies comparing patient satisfaction favor BCS,24 others favor mastectomy with reconstruction,21,25 and others have observed no difference.26 These findings are likely due to the varied cosmetic results achieved with both procedures, and the complexity of individual perception and expectations. However, regardless of procedure, factors associated with lower patient satisfaction and/or cosmesis are high body mass index (BMI),22,25,26 delayed wound healing or postoperative complications,22,26,27 axillary surgery,22 and radiation boost to the tumor bed.27 Age did not correlate with satisfaction with cosmesis.22,26

Most studies have found that mastectomy alone is associated with the lowest patient satisfaction when compared with BCS or mastectomy with reconstruction.21,24-26 Guidelines state that all patients undergoing mastectomy should be offered consultation with a plastic surgeon regarding immediate reconstruction.28 Immediate reconstruction has particular benefits compared with delayed reconstruction, including a reduction in the number of surgeries, superior cosmesis,
visible breast volume loss, and/or nipple displacement. Unfortunately, the options for posttreatment surgical correction are limited. Immediate oncoplastic approaches may help to mitigate some of these undesirable effects. Simple approximation of the parenchymal flap at the time of lumpectomy represents an effective method of distributing the volume loss and providing tissue coverage with resultant reduced retraction and change in breast contour. Complex oncoplastic procedures may be undertaken with the participation of a plastic surgeon. These coordinated procedures include a lumpectomy combined with a planned reduction mammoplasty, recentralization of the nipple-areolar complex, and volume replacement. For patients who are candidates for neoadjuvant chemotherapy, preoperative systemic treatment may reduce the primary tumor size prior to BCS and improve cosmesis.

**Posttreatment pain**

Chronic pain following breast cancer treatment has been reported to affect between 25% and 60% of patients and has been variably defined. As the surgical management of breast cancer has changed over time, particularly regarding the axilla, such historic reports of pain incidence must be interpreted with caution. In a large national cohort study, chronic posttreatment pain was observed in 47% of patients, with a mean time of 26.0 months from surgery to data collection. On a scale of 0 to 10, with 0 representing no pain and 10 representing worst imaginable pain, 48% had light pain (1 to 3), 29% had moderate pain (4 to 6), and 13% had severe pain (7 to 10). In a continuation of this cohort study at a mean time of 72.5 months from surgery, 36% of patients who initially reported pain had persistent pain at follow-up.

**Causes**

The development of posttreatment pain is multifactorial and may result from neuropathic stimuli of surgically damaged nerves, muscular changes at the surgical site, and referred pain from related connective tissues. Factors that can intensify pain and disability and have a negative impact on quality of life include intrinsic nervous system changes (central sensitization), inflammatory processes, and psychosocial factors affecting recovery or timely access to services.

**Assessment**

Patient risk factors for the development of posttreatment pain include pre-existing pain, psychosocial determinants, biology, and genetics. Assessment can aid in identifying patients at risk and allow for implementation of risk-reducing and early intervention strategies.

Pre-existing pain in the breast as well as other anatomic areas not related to the surgery can potentially cause sensitization in the nervous system and changes that are further altered postoperatively. Existing pain may be evaluated using a standard numeric rating scale or a screening instrument for neuropathic pain such as the DN4 questionnaire. Neck and arm range of motion should be assessed and the torso and upper extremity musculature should be palpated to identify dysfunctional movement patterns or tender trigger points that might be aggravated by surgery and need to be addressed preoperatively.

Preoperative psychological risk factors, including depression, anxiety, fear of pain, and catastrophizing, have been observed to affect pain perception and behavior. These factors may be identified with existing screening questionnaires for depression (e.g., Patient Health Questionnaire-9), anxiety (e.g., Generalized Anxiety Disorder-7), and functional decline (e.g., Brief Pain Inventory).

Young age is a commonly reported factor for posttreatment pain, which may be related to the physiological effects of age or differences in subjective pain expressions. High body mass index has also been observed to increase pain and sensory disturbances possibly due to the increased tissue trauma inherent in surgeries dealing with large breast and axillary volumes and obesity-related sequelae of reduced mobility and nutritional imbalance. Furthermore, genetic variation in individual responses to noxious stimuli and pharmacogenetic variations may influence the development of posttreatment pain and alter response to pain medications.

ALND has been associated with an increased risk of chronic pain when compared with SLNB. The underlying mechanism for this is not well understood but may arise from the surgical impact on the intercostobrachial nerves. Interestingly, studies have not identified a significant difference between BCS and mastectomy on the risk of posttreatment pain, although one study found proportionately more patients in the mastectomy group with moderate to severe pain. The finding of little difference between BCS and mastectomy may be explained by the common use of radiotherapy in patients undergoing lumpectomy, as the association between radiation treatment and chronic pain is well established.

**Preoperative interventions**

Interventions to prevent the development of chronic posttreatment pain can begin prior to surgery with a multimodal approach that optimizes preoperative health and conditioning. Studies have shown that active coping strategies such as self-man-
management (exercise, distracting activities, and positive self-statements) and obtaining emotional support from others are associated with reduced psychological distress, feelings of helplessness, catastrophizing, and fear, which have all been associated with increased postoperative pain and disability.36 A practical and simple technique that can be utilized to enhance coping is the box breath: an inspiration of 4 to 8 seconds followed by prolonged breath hold for 3 to 5 seconds, expiration over 4 to 8 seconds, and a rest period of 3 to 5 seconds.43 Analgesic benefits result from activating the baroreceptor reflex and producing a generalized inhibitory effect on the central nervous system, which includes a reduction in nociception.43

Treatment of pre-existing pain utilizing nonpharmacological methods helps reduce opioid use and medication side effects and can improve musculoskeletal function and self-management skills that will be useful in the posttreatment phase.42

Intraoperative considerations
Intraoperative local and regional nerve blocks may be effective methods to prevent chronic posttreatment pain. Initial reports on the use of paravertebral nerve blocks have shown decreased chronic pain incidence and pain intensity following breast surgery.44 Systemic lidocaine and magnesium sulfate have been found to reduce intraoperative and postoperative opioid needs and pain intensity. Intraoperative systemic lidocaine also improved postoperative functional recovery in one trial.45

Postoperative interventions
Effective strategies to manage chronic pain that were begun preoperatively can be continued postoperatively to prevent the progression of acute pain to chronic pain. Treatment includes rationalization of analgesics, functional restoration, graded physical reconditioning, and strategies to reduce the impact of pain on daily activities.42 Early recognition and intervention are key to preventing or reducing the disabilities caused by undertreated pain. Current management approaches are extrapolated from the literature on deactivation of receptors associated with hyperalgesia and neuropathic pain, and sleep improvement.36,47

Beyond the first 4 weeks, a graded functional restoration approach is recommended. Any patient who deviates from the expected pain recovery trajectory should be identified. Symptoms that raise concern include burning skin, intolerance to light touch, pain.</p>
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Surveillance
The object of surveillance is to identify new primary breast cancers and curable recurrences in the treated breast and axilla. Recommended posttreatment surveillance includes:

- Breast and nodal examination every 6 months for 5 years, then yearly thereafter.
- Annual diagnostic bilateral mammogram.

Routine CT imaging and blood tests for detection of incurable metastatic disease have not been shown to improve patient outcomes and are not recommended. Posttreatment investigations should be based on patient symptoms.

Summary
As our ability to treat and cure breast malignancies continues to improve, more women are navigating life as cancer survivors. For some, the treatment sequelae have significant and long-lasting effects on their physical, emotional, and psychological health. Understanding the long-term risks and impact of treatment can allow physicians to identify survivorship care issues such as arm lymphedema, cosmesis, and posttreatment pain, to base posttreatment cancer surveillance on patient symptoms, and to provide optimal support to patients as they recover from treatment.

Competing interests
Dr Lau is co-founder of the CHANGEpain Clinic, which charges fees for services not covered by MSP and accepts referrals for patients requiring pain management. Drs Chiu and Nichol have no competing interests to declare.

References
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