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# BREAST CANCER

# in brief

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**Disclosures:** Donna M. Kinzler, DNP, ACNP-BC, AOCNP, and Kandace P. McGuire, MD, report no relationships with proprietary entities producing health care goods or services. Atilla Soran, MD, MPH, FACS, receives research support from ImpediMed. G. van Londen, MD, MS, receives research support from NIH, the Pittsburgh Affiliate of Susan G. Komen for the Cure, and John A. Hartford Foundation.

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## Survivorship Case Study

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M.S. is a 68-year-old Caucasian, female breast cancer survivor. She has undergone a segmental mastectomy followed by radiation therapy and has been prescribed adjuvant endocrine therapy. She has no evidence of disease recurrence.

Her past medical history includes depression, hypothyroidism, metabolic syndrome, and osteopenia. She works full time as a receptionist and lives with her husband and grandchild for whom she is the primary caregiver. As a result, she states that she does not have time to exercise. She also consumes two alcoholic beverages per day as a coping mechanism. Her medications include anastrozole, aspirin, bupropion, hydrochlorothiazide, levothyroxine, and naproxen as needed. She is not consuming calcium or vitamin D.

### Surveillance

During her first postsurgery visit, she hesitantly brought up a few concerns that are important to her. She expressed concern related to surveillance testing to monitor her for cancer recurrence. Her health care provider explained that the American Society of Clinical Oncology (ASCO) has created official cancer surveillance guidelines for both

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## SURVIVORSHIP CASE STUDY (continued)

professionals, as well as cancer survivors. Currently, in general, ASCO does not recommend the performance of any laboratory tests (including tumor markers) or imaging (except for mammograms) to detect recurrence of cancer before it causes symptoms. These surveillance tests have not been found to extend survival, compared to those whose cancer recurrence was diagnosed through clinical presentation. In addition, surveillance testing may be costly, induce anxiety, and can be associated with radiation exposure.

ASCO recommends that breast cancer survivors undergo intermittent history and physical examinations (initially more frequent and tapered as the years pass), annual mammogram (as applicable, while some survivors may benefit from individualized imaging frequencies/modalities), monthly breast self-examination (although evidence of its effectiveness is limited), and age/gender-appropriate health maintenance ([www.asco.org/guidelines/breastfollowup](http://www.asco.org/guidelines/breastfollowup)). This explanation provides reassurance and empowerment for the cancer survivor.

### Symptoms

M.S. started anastrozole after her first postsurgical visit. She expressed doubt about whether she should take this medication. She developed new and worsening of preexisting symptoms shortly after she began taking anastrozole. These symptoms included vasomotor symptoms, memory loss, musculoskeletal symptoms, mood swings, decreased sexual desire, and dyspareunia. Upon hearing her concerns, her health care provider decided to counsel her. Open communication about adherence-related issues is crucial; adherence to adjuvant endocrine therapy is low, as only 50% of cancer survivors still adhere upon completion of the five-year term<sup>12</sup>. Decreased adherence has been shown to be related to decreased survival benefit<sup>3</sup>.

Adherence is influenced by one's belief in the risk/benefit ratio and is affected by issues such as the understanding of/belief in its ability to reduce cancer recurrence risk, pricing, and adverse effects<sup>4</sup>. Therefore, in order to allow her to make a fully informed decision about continuing to take anastrozole, her health care provider re-explained the benefits of adjuvant endocrine therapy, and validated and provided support towards her symptoms.

Symptoms in cancer survivors are prevalent, clustering, and persistent<sup>5-7, 8-10</sup>. Experiencing chronic symptoms without sufficient relief can result in a vicious cycle of discouragement, decreased self-help, and worsening of physical and emotional symptoms<sup>11,12</sup>. Therefore, validation and support are important. Expectations should be set to avoid disappointment. Total relief of symptoms may not be achievable, but the focus is on achieving tolerability. Sometimes, behavioral interventions that target self-care and empowerment, delivered face-to-face or virtually, may be required to overcome this cycle, as demonstrated in prostate<sup>13</sup> and breast cancer<sup>14</sup> survivors and persons at high risk for depression<sup>15</sup>.

Following is a brief synopsis of supportive approaches for the most commonly encountered symptoms:

**Psychosomatic symptoms:** The most common symptoms breast cancer survivors suffer from include, but are not limited to, cognitive dysfunction<sup>16-20</sup>, adjustment disorder, or other psychosocial distress<sup>8,10,12,21-24</sup>,

vasomotor symptoms<sup>25-28</sup>, insomnia and fatigue<sup>23,29-34</sup>. Before attributing these symptoms exclusively to cancer and/or related treatments and procedures, including anesthesia, an individualized workup should be performed to assess for the presence of other factors that may contribute and, more importantly, may be reversible. These may include, but are not limited to, vitamin deficiencies, anemia, organ dysfunction, and endocrine, metabolic, or intracranial abnormalities. The workup may include blood work, imaging studies, and neuropsychological testing. The latter may allow for particular insight into the presence and degree of cognitive impairment and its potential relationship with emotional symptoms.

In general, careful listening to the survivor's concerns, education, and multifactorial support, tailored to survivor's needs, might have significant therapeutic value. Multifactorial support can include any combination of pharmacological therapy (such as antidepressants or stimulants) and non-pharmacological interventions, including physical therapy, psychological support, physical activity, nutritional counseling, and complementary medicine. Living a healthier lifestyle, regaining control of one's life, and resuming pleasurable activities that contribute to inner peace and quality of life can all positively impact psychosomatic symptoms.

Given the current limited availability of head-to-head comparisons of pharmacological and non-pharmacological therapies, an informed conversation might help outline an individualized management approach that accounts for prior treatments, evidence when available, patient preferences, and insurance coverage. Choosing treatment that affects multiple symptoms simultaneously is preferable. For example, increasing physical activity not only improves functional status, fitness, and survival, but also helps improve severity and tolerance of emotional, cognitive, and physical symptoms while improving quality of life<sup>23</sup>.

Some breast cancer survivors may prefer non-pharmacological treatments to avoid further pharmacological adverse effects. However, non-pharmacological management can be challenging, as it often requires active participation of the survivor in the way of time, expenses, motivation, and effort. For example, cancer survivors might be challenged in their pursuit to initiate, resume, or increase the level of physical activity by logistical barriers, acquired physical limitations, and/or a fear of harm<sup>7,35</sup>. In these instances, a certified cancer exercise trainer<sup>36</sup> or a physical therapist might be a valuable resource.

Cancer survivors, although often very motivated to improve their situation, are often already very stressed. Instituting new interventions that are intended to provide relief might also further increase the degree of stress experienced. A brief course of psychological therapy focused on stress management and any changes in how they view themselves after a cancer diagnosis may prove helpful<sup>37</sup>.

Most breast cancer survivors cope well with their worry about the possible recurrence of their cancer, though at least periodic fears of risk of recurrence are a near-universal experience at some point in the post-treatment period<sup>5</sup>. For some cancer survivors, however, this fear of a recurrence can become disabling. Counseling survivors on actions they can take to reduce their risk actually may empower them by increasing their sense of control. Psychological support may be beneficial to improve

coping skills<sup>38</sup>. In addition, a recent diagnosis of an illness, such as cancer, can be eye-opening and result in a teachable moment to improve one's health behaviors. Currently, evidence shows that breast cancer survivors can reduce their risk of recurrence by limiting alcohol intake, smoking habits, as well as obtaining and maintaining a healthy weight via eating wisely and regularly participating in physical activity<sup>39,40</sup>.

**Musculoskeletal symptoms** are very prevalent among breast cancer survivors, whether due to chemotherapy, menopausal transition, or aromatase inhibitor therapy. More than 50% of breast cancer survivors upon initiation of an aromatase inhibitor experience a musculoskeletal syndrome that presents as diffuse arthralgias and myalgias, which are either new or worsened and improve within two to three months<sup>41-49</sup>. Although a causal relationship is likely to be due to cancer treatment or menopausal transition, new diagnoses, such as autoimmune or crystalline arthritis should not be overlooked. Treatment approaches are similar to osteoarthritis (e.g. non-pharmacological, such as physical therapy, local heat, and/or acupuncture in combination with pharmacological therapy, such as NSAIDs given short-term, either systemically or topically). For those aromatase inhibitor-related symptoms, despite best supportive efforts, about 25% of patients' symptoms become unbearable, necessitating a change in therapy regimen.

In addition, breast cancer survivors often undergo locoregional treatment with surgery, with or without radiation therapy, which predisposes more than 75% to develop fibrosis, rotator cuff pathology, and altered body habitus, leading to pain, limited range of motion, and impaired function in daily life<sup>50-57</sup>. Axillary web syndrome is the most extreme case among these symptoms<sup>50,54</sup>. Physical and massage therapists are of great value since they are able to provide great symptom relief by administering an intense regimen of massage, stretching, and exercises, minimizing a need for surgical therapy. In addition, psychological support that improves coping by treating concurrent emotional symptoms can be very helpful as well.

**Sexual dysfunction<sup>26-28,58-61</sup> and urinary complaints:** More than one half of breast cancer survivors, in particular those on adjuvant endocrine therapy or who have undergone cancer therapy-induced premature menopause, may suffer from sexual dysfunction and urinary symptoms<sup>62-64</sup>. Sexual dysfunction may include vaginal atrophy, diminished libido, or pain during intercourse. Changes in libido can be due to multiple causes, including mood, pain, body image, fatigue, relationship issues, and estrogen deprivation. Urinary issues may include overactive bladder with urgency, with or without incontinence. Management options partially overlap. Sexual complaints are often supported through a combination of local non-hormonal applications (moisturizers, lubricants, vitamin E), a low-dose of topical estrogens (usually as a last resort and only upon an informed conversation), physical therapy (pelvic floor muscle exercises), gynecologic strategies (vaginal dilatational mechanical measures) and psychological care (e.g. exploring causes of decreased libido, coping strategies, and partner communication). Urinary complaints can often be helped by pelvic floor muscle exercises, topical estrogen, and, in some cases, a referral to a urogynecologist.

**Bone health:** It is estimated that osteoporosis affects one in every three postmenopausal women, with a 40% lifetime risk of fracture and about a

21%<sup>65</sup> risk of one-year mortality after hip fracture. Breast cancer survivors are at even higher risk of bone loss due to chemo-toxic effects on the bone, treatment induced hypogonadism, and supportive therapies that include steroids<sup>64,66-70</sup>. Fracture risk is not only determined by bone mass, as measured by a DXA-scan, but also by the propensity to fall due to chemotherapy-induced neuropathy, deconditioning, urinary incontinence, vitamin D deficiency and cognitive impairment. Simple measures such as weight-bearing exercises, minimal or no consumption of nicotine/alcohol, and an adequate daily intake of calcium (600 mg PO bid, to be obtained via diet, as well as needed supplements) and vitamin D (800 i.u./day) are crucial in fracture risk reduction. Given the evidence of an association between calcium intake and acceleration of coronary artery disease<sup>71</sup>, it might be prudent to individualize the degree of oral supplementation by adapting it to one's dietary intake, with help from a dietitian.

As far as pharmacological interventions to support bone health, the selection of an agent and timing of its initiation remain challenging. Gralow et al. have created an algorithm that includes the FRAX calculator in an effort to individualize the initiation of bone medications based on a survivor's 10-year fracture risk<sup>69</sup>. An informed conversation between the survivor and provider about the pros and cons of bone medications is essential. Survivors should be monitored with baseline and surveillance DXA scans every two years.

**Cardiovascular health:** Breast cancer survivors are at increased risk of cardiovascular events. Its cumulative incidence may be as high as 33%<sup>72</sup>, depending on events, such as having experienced premature, chemotherapy induced menopause<sup>73,74</sup>; receiving aromatase inhibitor therapy<sup>75-80</sup>; or receiving left-sided chest wall radiation<sup>80</sup>. Cardiac toxicity is not only limited to coronary artery disease but also can include cardiomyopathy, thromboembolism, arrhythmias, and valvular and pericardial disease<sup>72</sup>. An attempt should be made to achieve optimal assessment and control of cardiovascular risk factors, including weight, physical fitness, lipid profile, and glucose tolerance. A dietitian, psychologist, personal trainer, and/or physical therapist may help facilitate these efforts. Evidence indicates that for a subset of breast cancer survivors, the benefit/risk ratio may not necessarily warrant aromatase inhibitor therapy<sup>77</sup>, requiring an informed consent conversation at the time of prescription.

### Health Behaviors and Lifestyle

During one of her subsequent office visits, our cancer survivor expressed her desire to improve health behaviors (better nutrition, increased physical activity, decreasing alcohol and nicotine intake). Having been diagnosed with cancer motivates her to try to improve her health behaviors. Her health care provider makes use of this small window of opportunity, encouraged by data that has shown that health behaviors impact overall, as well as breast cancer-related outcomes<sup>39</sup>. Being overweight, obese, or underweight can increase the risk of breast cancer recurrence and death<sup>81</sup>. Nutritional counseling can provide education about which products to avoid or seek out, given one's breast cancer diagnosis, initiate the creation of an individualized weight management plan, and address the use of herbal and vitamin supplements. It is important to relativize this by stressing that healthier behaviors will not be 100% protective, as some cancer survivors may partake in excess. Resumption or initiation of

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## SURVIVORSHIP CASE STUDY (continued)

physical activity might be challenging post-cancer treatment, due to pain, lymphedema, limited range of motion, or fear of causing harm to oneself. Involvement of a cancer-certified personal trainer or even physical therapist may facilitate one's ability to participate in physical activity<sup>82</sup>. Alcohol usage should ideally be limited to three consumptions/week, not more than one/day<sup>83,84</sup>.

The UPMC Cancer LiveWell Survivorship Program (UPMCCancerCenter.com/livewell) is created for disease-free cancer survivors or their providers who seek special expertise on important cancer survivor-related topics and/or a return to living well. LiveWell provides support for emotional and physical symptoms, cancer treatment adherence, and health behaviors. Patients will first visit with a medical oncologist for a comprehensive assessment to help prioritize concerns and create an efficient and feasible management plan. Referrals can involve a comprehensive team of LiveWell providers, including dietitians, physical therapists, and psychologists. Additional services include e.g. coordination and continuity of care by maintaining close contact with current health care providers, facilitation of access to comprehensive research studies relevant to cancer survivors, and educational activities.

For more information about the unique health needs of cancer survivors, visit UPMCCancerCenter.com/livewell or call 412-641-4530.

This case study is adapted from *Breast Cancer Management, January 2013*, Vol. 2, No. 1, Pages 71-81 with permission of Future Medicine Ltd.

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# Navigation Services for Breast Cancer Patients

Judy Herstine, MBA

An important aspect of the Magee-Womens Cancer Program is to provide women with emotional support and guidance with regard to the many demands of their cancer diagnosis, treatment, recovery, and survivorship. The Oncology Patient Navigation Services at Magee, which include licensed social workers, oncology nurses, and community resources, can help.

The program is a critical part of the cancer care team at Magee, providing individualized assistance to patients, families, and caregivers to help address and overcome health system barriers and facilitate timely access to quality medical and psychosocial care. Navigators provide support with everything from linking women to necessary community resources to ensuring that a patient gets to multiple appointments and receives the care they need.

## Navigators work with patients' families and friends to:

- Guide patients through the healthcare system.
- Identify and mobilize strengths.
- Support coping capacities.
- Make connections to community resources.
- Alleviate stressors that can hinder recovery.

## Breast Surgery Concierge Services

A new service of Oncology Patient Navigation Services is the establishment of a Breast Surgery Concierge Service, which provides for a more streamlined approach between breast cancer diagnosis and timely access to surgical consultation and additional testing; better communication between the referring physicians; and more individualized education, so women with a new diagnosis are less anxious and better prepared to make decisions about treatment options available to them.

Women who have used Oncology Patient Navigation Services express relief and gratitude that the support of their navigator has given them a powerful ally as they move through their diagnosis and treatment.



Referrals to Patient Navigation can be made by any member of the health care team by calling 412-641-1926.

## CASE STUDY: PREMENOPAUSAL BREAST CANCER

Kandace P. McGuire, MD

L.P. was a 28-year-old newlywed when she went for her annual gynecologic exam. During her breast exam, the doctor noticed a mass in her left breast. L.P. and her doctor were concerned, as her mother had passed away in her early 40s from breast cancer, and her maternal grandmother had also had breast cancer.

She was quickly scheduled for a mammogram, which led to an ultrasound and a biopsy, eventually leading to a breast cancer diagnosis. L.P. soon learned that she had a triple (estrogen, progesterone, and HER2 receptor) negative breast cancer, a particularly aggressive form of breast cancer that had already metastasized to a lymph node. Holding her new husband's hand, she presented to the surgeon's office with many questions. Will I live? Why did I get cancer so young? Can I have children? How do we treat this cancer?

She was referred to a Magee-Womens Breast Cancer Program medical oncologist with a special interest in treating women with premenopausal breast cancer, and was offered the option of neoadjuvant (preoperative) chemotherapy to shrink the tumor in her breast and minimize the amount of disease in her axillary lymph nodes. The six months of chemotherapy also gave her time to undergo genetic testing. There she learned she had a mutation in one of the BRCA genes, which significantly increased her risk of breast and ovarian cancer. She also had a very high risk of a second breast cancer.

She met again with her breast surgeon and a gynecologic oncologist to discuss options to manage her risk for breast and ovarian cancer. With her breast surgeon, L.P. decided to undergo a bilateral mastectomy. Through the coordinated efforts of her breast oncologist, plastic surgeon, the radiologists who performed and interpreted the pre- and post-therapy MRIs of her breasts, and the radiation oncologist at Magee, she was ensured a low likelihood of needing radiation following surgery, allowing her the option of nipple sparing mastectomy and immediate reconstruction.

L.P. celebrated her first wedding anniversary in the operating room undergoing a nipple-sparing mastectomy. Surgical pathology confirmed a complete response to chemotherapy, increasing her odds for long-term survival. Long-term survival is excellent. L.P. can now move on with life as a newlywed and will soon be enjoying a second honeymoon with the promise of a family. She will continue to be followed closely by all of her physicians, and will one day likely have her ovaries removed, so that she can continue to live a long, cancer-free life.

The physicians who worked together to treat L.P. are all part of a new initiative offered at Magee focused on the coordination of services for premenopausal women who have been diagnosed with breast cancer.

In 2011, more than 55,000 women in the United States under the age of 50 were diagnosed with breast cancer. Approximately 5,000 died of the disease in the same time period. Young women diagnosed with breast cancer have a five-year relative survival rate of 84%, as opposed to older women with a rate of 90%. This survival rate gap increases as age at diagnosis decreases<sup>1</sup>. Numerous studies have established a poorer prognosis in premenopausal breast cancer (breast cancer age <50)<sup>2-7</sup>. Some have related this outcome to poorer prognostic features in this age group<sup>7</sup>. Factors such as higher stage and grade at diagnosis<sup>4,6,7</sup>, a preponderance of triple negative tumors<sup>5</sup>, and lymphovascular invasion/nodal involvement<sup>4-7</sup> have been found to be common among premenopausal breast cancer patients. These features portend a poorer outcome in all age groups, and thus, age has been seen as a surrogate for other prognostic markers<sup>7</sup>.

To individualize treatment for premenopausal patients, we must first understand the unique characteristics of breast cancer in premenopausal women at all levels, from genomic and cellular differences to global health perspectives. At Magee, physician-researchers are actively investigating these and other related topics, so that we may provide opportunities for premenopausal breast cancer patients to participate in, and possibly benefit from, clinical trials designed specifically for patients in this subset.

Currently, the Magee-Womens Breast Cancer Program has open clinical trials investigating the use of a PARP inhibitor for patients with a BRCA mutation and chemo-resistant breast cancer, as well as a registry for those patients who chose nipple-sparing mastectomy. Plans are in development to offer a research registry that will include data specifically recorded with the purpose of studying premenopausal breast cancer patients and their clinicopathologic data, including any available genetic or genomic testing information. However, research alone cannot help serve the needs of today's young breast cancer patients.

At Magee, we know that many young women who are diagnosed with cancer feel isolated at a time when what they need most is support, help with issues that are specific to them, and a sense of community. This new initiative is designed to help patients feel connected and valued as individuals who have unique needs and desires in dealing with breast cancer and in their lives beyond cancer treatment.

We already know that premenopausal cancer differs from postmenopausal breast cancer in many ways. First, there is the issue of risk. Are premenopausal women at risk for breast cancer? What might increase a woman's likelihood of developing breast cancer at a young age? We know that women who develop breast cancer at a young age tend to have a higher risk of a BRCA or genetic mutation that not only causes breast, but ovarian cancer<sup>8</sup>. These mutations also can lead to triple-negative breast cancer, which can be particularly aggressive.

Do younger women choose or require different surgical or medical treatment for breast cancer? How can we ensure a speedy and accurate diagnosis for these women? We know that young women with breast

cancer may have especially dense breasts and may need more advanced imaging techniques such as breast MRI or tomosynthesis, in order to properly diagnose and treat their cancer. We know that young women with breast cancer tend to have mastectomies more so than women with the same type and stage of cancer who are older and tend to undergo contralateral prophylactic mastectomy and reconstruction more often<sup>9</sup>. These patients also often request and are excellent candidates for new modalities of care, like preoperative chemotherapy and nipple sparing mastectomy<sup>10</sup>.

What are the social and emotional needs of a young woman with breast cancer? We know that young women with breast cancer may not be done having families and often desire the opportunity to preserve their fertility in a variety of ways<sup>11</sup>. We know that the younger a woman is when she develops her breast cancer the more likely it is to recur, thus changing the shape of her follow up and survivorship<sup>12</sup>. We also know that women who are diagnosed with breast cancer at a young age are balancing a career, a family, and now a serious disease. These women, more so than older women, find their stress levels to be extraordinarily high during treatment and recovery. They also find that with hormonal treatment for breast cancer, they experience early menopause with all the sexual dysfunction and changes in bone health that accompany that change<sup>13</sup>. We know they also have a limited social network that can understand what they are going through. When their friends are talking about wedding dresses, diapers, play dates, and soccer practice, young breast cancer patients are talking about chemotherapy, radiation, and prophylactic oophorectomy. When their colleagues are concerned about promotion and their next vacation, they are worried about their ability to keep and perform their job and the financial effects that sick leave will have on them and their family.

To meet the unique needs of premenopausal breast cancer patients, the Magee-Womens Breast Cancer Program offers services that address the difficult issues of genetic susceptibility to breast cancer, fertility preservation, reconstructive options, and survivorship, among other topics. In addition, patients will have access to nutritional and complementary medicine services, thus allowing them an opportunity to treat mind, body, and soul.

To aid young women through their journey from cancer diagnosis to wellness, access to these services will be available at Magee, by phone or email, to suit the needs of the busy and technologically savvy younger women who seek our help.

With support from the Glimmer of Hope Foundation, the program will enhance patient navigation services and our genetic testing services, so that young patients with breast cancer will have access to social and moral support through our Buddy Network, pairing survivors with patients with similar backgrounds and needs.

For more information or patient referrals, call the Magee-Womens Breast Cancer Program at 1-866-MYMAGEE (696-2433).

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# LYMPHEDEMA EDUCATION, MONITORING, EARLY DETECTION, INTERVENTION, AND PREVENTION AFTER BREAST CANCER TREATMENT

Atila Soran, MD, MPH, FACS

**What is lymphedema (LE):** LE is the accumulation of protein-rich fluid that occurs when the ability of the lymphatic system to transport interstitial fluid is exceeded. It is a chronic, progressive, and often debilitating condition.

**Incidence of LE:** LE has been estimated to affect up to 3 million people in the U.S., with a high proportion developing the condition as a consequence of cancer or its treatment. The highest incidence of lymphedema occurs following breast cancer (BC) surgery, particularly among those who undergo radiation therapy following lymph node surgery. Among this group, up to 60% (average 25%) of patients develop some degree of upper extremity lymphedema. Currently, a woman living in the U.S. has a 12.5% or a 1 in 8, lifetime risk of being diagnosed with BC. In 2012, an estimated more than 225,000 new cases of BC were diagnosed among women, and about 50,000 patients suffered from some degree of breast cancer-related lymphedema (BCRL) in this period.

<b>Stage 1: Acute</b>	<b>Pitting edema; reversible with elevation of the arm. Usually, upon waking in the morning, the limb(s) or affected area is normal or almost normal size. “Spontaneously Reversible”</b>
<b>Stage 2: Chronic</b>	<b>Spongy consistency and is “non-pitting.” Fibrosis found in Stage 2 lymphedema marks the beginning of the hardening of the limbs and increasing size. “Spontaneously Irreversible”</b>
<b>Stage 3: Elephantiasis</b>	<b>Irreversible and usually the limb(s) is/are very large. The tissue is hard (fibrotic) and unresponsive; some patients consider undergoing reconstructive surgery called “debulking” at this stage.</b>

- **Grade O: Normal**
- **Grade I: Asymptomatic**
- **Grade II: Mild Lymphedema**
- **Grade III: Moderate Lymphedema**
- **Grade IV: Severe Lymphedema**

**What happens if not treated:** It is well established that without treatment, LE can lead to progressive swelling, fibrosis, physical and functional deficits, and chronic infections, which negatively affect quality of life and health care costs. It can cause seriously impaired limb function resulting from extensive limb swelling and discomfort that is chronic, progressive, and incurable. LE is difficult to manage for women. Treatment for LE remains suboptimal and is, in most cases, palliative, with a goal of preventing disease progression, rather than curing.

While there are differing degrees of severity when it comes to lymphedema, once it is present it can severely impact a person's quality of life, with complications ranging from fatigue, impairment of daily activities, recurrent bacterial infections, and embarrassment due to the size and shape of the effected limb.

**Risk factors:** The etiology and risk factors of BCRL in patients with BC are multifactorial and not fully understood. BCRL has risk factors that can be divided into three main categories:

- 1) Treatment related
- 2) Disease related
- 3) Patient related

Treatment-related factors include surgery, radiation therapy, chemotherapy, and combined treatments. Disease-related factors include tumor stage at time of diagnosis, pathologic nodal status, number of removed lymph nodes, and the location of the tumor in the breast. Patient-related factors include age at diagnosis, high body-mass index (BMI), history of infection or inflammation, hand dominance, and excessive use of the affected limb.

In a case-control study, nearly 75% of the patients with LE were overweight or obese (BMI greater than 25 kg/m<sup>2</sup> or 30kg/m<sup>2</sup>). BMI is a risk factor that increases the severity of LE, infection, and wound healing as well. LE can develop secondary to an infection, which interrupts normal lymphatic pathway function. A correlation between postoperative upper extremity infections and upper extremity edema was reported in several studies. Various studies have shown that cellulitis complicates LE. Level of hand use is a significant factor for BCRL. We published a modified classification system of the level of hand use by three objective criteria according to the status of occupational workload: Group I included working continuously less than 30 minutes at a time and equal to or less than eight hours per day. Group II included working continuously between 30 and 60 minutes at a time, and equal to or less than eight hours per day. Group III included working continuously for more than one hour and at least eight hours per day. Based on this new classification, we confirmed that occupation is an important risk factor for increased severity of BCRL, and occupations

requiring more upper extremity activity and long periods of work had an independent risk for more severe disease outcome. Therefore, patients with BCRL should be informed to adjust their daily use of upper extremities to prevent increased severity of BRCL.

Currently, breast-conserving surgery with sentinel lymph node (SLN) biopsy is a standard surgical management of early BC. SLN biopsy is an effective method of assessing axillary nodal status and avoiding unnecessary axillary lymph node dissection (ALND) in patients with node-negative BC, thereby preventing arm LE. Published studies demonstrated that the risk of LE is significantly lower in patients who underwent only SLN biopsy compared with routine ALND. Another treatment-related risk factor is axilla radiation therapy. Usually the axilla is radiated when more than three nodes are positive for cancer.

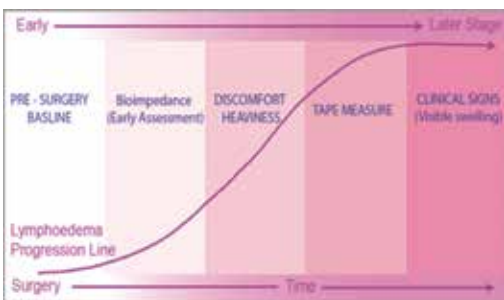
**Diagnosis of BCRL:** The diagnosis of BCRL remains a challenge. Many women who suffer from BCRL are undiagnosed until the condition causes significant morbidity. Traditional techniques used to aid in the diagnosis and monitoring of BCRL include circumference-based measurements, water displacement, perometry, and self-assessment. Self-assessment is limited in that it is unable to detect subclinical disease with relatively low sensitivity compared with newer techniques.

**Lymphedema Education, Monitoring, Early Detection, Intervention, and prevention Program goal:** Detect those patients with lymphatic congestion *prior* to clinical manifestation (Stage O and Grade I).

- A noninvasive procedure passing a small electrical current through the limb that measures impedance of extracellular fluid.
- L-Dex: A measurement system used to assist in the assessment of unilateral lymphedema.
- The affected limb is given an L-Dex Value.
- Enables comparison and tracking.



Recent data suggest that bioimpedance (BIS) represents an improvement in sensitivity over traditional assessment tools with an average detection of four months earlier and in some cases up to 10 months earlier. This is important because data from the National Institutes of Health (NIH) has confirmed that management of patients with subclinical BCRL can be done simply and effectively with minimal long-term morbidity, making it imperative to diagnose BCRL at the subclinical stage, in order to improve outcomes.



Magee-Womens Hospital of UPMC's *Lymphedema Education, Monitoring, Early Detection, Intervention, and Prevention Program* was established in 2010 and is the first such program. Based on the protocol, approximately 1,000 measurements were done and around 22% of patients were diagnosed with early-stage LE.

**Components of UPMC Lymphedema Program:**

- Individual consult with physician
- Effective one-on-one education
- Quarterly group meetings facilitate dialogue among health care providers and breast cancer survivors at risk for lymphedema.
- Physician
- Nurse coordinator
- Physical therapist
- Dietician

**2011 NAPBC Standard 2.15 Support and Rehabilitation:** *NLN lymphedema management and risk reduction practices (Lymphedema Screening and Treatment Recommendations)* (strongly recommended);

- All patients diagnosed with breast cancer have pretreatment measurements on both arms prior to treatment.
- All patients have posttreatment measurements on both arms at each visit.
- To reduce the occurrence of false negative or false positive results, ideally these methods have little room for user error and therefore, bioelectrical spectroscopy (BIS) or infrared perometry are highly desired methods of alternative measurements.

**The importance of early detection of lymphedema:**

- More treatment options
- Less swelling
- Extends duration to get extremity swelling
- Improvement
  - Aches/pain
  - Tightness
  - Cramps
- Infection rate decrease
- Increasing the desire to continue treatment
- Less cost
- QoL is better

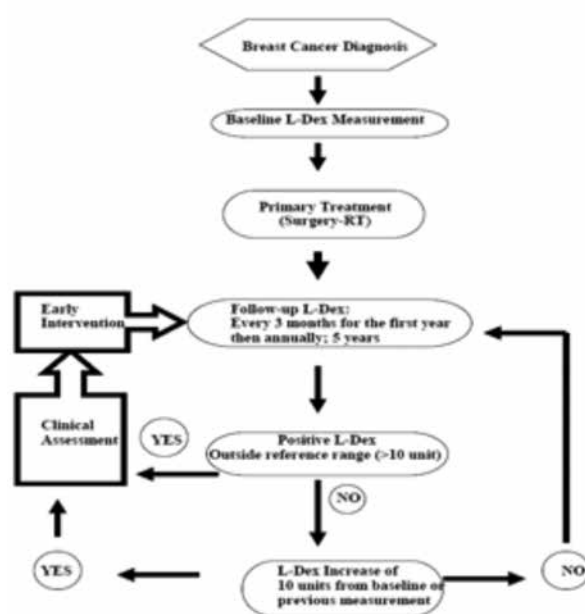
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# LYMPHEDEMA SCREENING (continued)

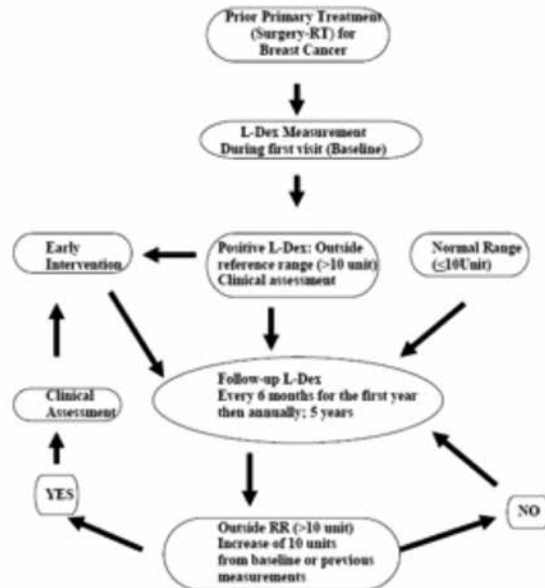
LE Screening Guidelines-5/1/2012

LE Screening Guidelines-5/1/2012

Clinical Practice Pathway and Algorithm  
A) Newly Diagnosed breast Cancer



B) Operated for Breast Cancer Previously: No Clinical Lymphedema



**Treatment of BCRL:** Therapies commonly used involve compression therapy, including new generation pumps, therapeutic exercises, laser therapy, surgery, and multimodality. Therapeutic exercise and MLD are two treatment options that often represent a bridge between compression sleeves and CDP. The exercises include those that aid lymph flow through repeated contraction and relaxation of muscles. These exercises should be individualized and should be performed while the edematous arm is bandaged. Ideally, these exercises are initiated by well-trained therapists and then continued at home. The 2010 *American College of Sports Medicine (ACSM) Exercise Guidelines for Cancer Survivors* stated benefits include:

- Improved flexibility
- Reduced fatigue
- Increased strength
- Improved body image and quality of life
- Improved body composition
- Decreased anxiety

Recent data found that active exercise further improves reduction in limb volume with standard therapy.

For severe LE, excisional operations and debulking procedures have been reported as effective methods to alleviate symptoms by removing fibrosclerotic connective tissue, excess adipose tissue, and excess skin. Liposuction was introduced as an excisional technique to remove

subcutaneous fat to reduce a limb's overall size. The preventive surgical strategies include lympho-venous shunts before a diagnosis of LE in high-risk patients. Contemporary advances have resulted in the development of microsurgical reconstruction enabling the creation of fine connections between lymphatics and subdermal venules (LVA). Early reports of LVA for the treatment have been promising. Lympho-lymphatic anastomosis and lymphatic grafting have been proposed as reconstructive techniques that are associated with improved patency over time.

The concept of *Axillary Reverse Mapping* is to map the drainage of the arm with blue dye to determine the anatomical variation in the lymphatics and thus have a roadmap for their preservation. This prevention of BCRL during surgery techniques is promising.

**Preventive recommendations for BCRL:** Physicians can play a pivotal role as educators by informing BC patients about the risk of secondary LE, prevention strategies, early signs and symptoms, and treatment options. Early subclinical symptoms of BCRL might include subjective reporting of:

- Limb heaviness, fullness
- Aching
- Tightness
- Fatigue in BC survivors

In fact, some of the current recommendations for prevention of LE are anecdotal with scant scientific evidence.

Recommendations should be categorized as:

- Avoid needle sticks
- Avoid limb constriction
- Elevate the limb
- Avoid air travel and wear compressive garments on flights
- Maintain a normal body weight (BMI less than 30kg/m<sup>2</sup>)
- Avoid extremes of temperature and sunburns
- Avoid vigorous exercise

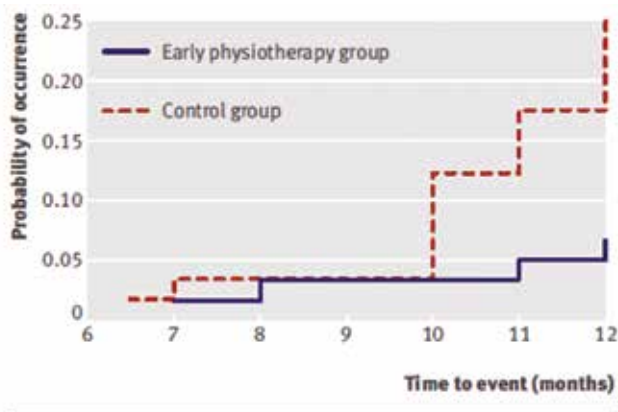


Fig. 4 | Failure time for development of secondary lymphedema by group.

**Conclusion:** LE of the arm and hand undoubtedly impairs quality of life after BC surgery. A number of promising treatments have been reported, but they have not yet been subjected to sufficient rigorous research to recommend as the standard of care. There are newer diagnosis techniques, including BIS. The most important benefit of BIS is allowing significant diagnostic potential of subclinical LE. BIS technology allows us to diagnose subclinical BCRL. It also facilitates early interventions, such as education and preventive recommendations, such as the use of over-the-counter compression sleeve, physical therapy consultation, daily exercise, and avoiding overuse of the affected arm. It allows clinicians to discuss further recommendations, such as maintaining BMI less than 30kg/m<sup>2</sup>. It also may postpone or eliminate more advanced LE in the future. This is important for women who already face general health-related issues and who live on a limited budget.

For more information or patient referrals, call **1-866-MY-MAGEE**.

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### Magee-Womens Breast Cancer Program of UPMC CancerCenter Pittsburgh, Pennsylvania

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### Cancer Genetics

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### Radiation Oncology

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