The Risk of Breast Cancer Related Lymphedema Over Time

I am very grateful to Carol Doeringer, lymphedema patient and advocate, who submitted this interesting and very insightful contribution on the risk factors contributing to breast cancer related lymphedema. The material is excerpted from a self-study course Carol has developed with the support of friends and experts in the lymphedema and nursing communities. The course is called Breast Cancer-Related Lymphedema: The Nurse's Role in Care and Prevention, the program will soon be available at no charge to any interested nurse. Those interested can learn more by visiting the Lymphedema Speaks website

The Risk of Breast Cancer Related Lymphedema Over Time

Most women developing breast cancer related lymphedema (BCRL) will do so within three years after breast cancer diagnosis. Survivors not developing near-term BCRL retain a small lifetime risk. Norman et al (2009) found the five-year cumulative incidence of BCRL was 42%. Of the affected women, 80% developed lymphedema within two years and 89% within three years (1). Petrek et al (2001) followed 263 patients after mastectomy and complete axillary dissection. At 20 years after treatment, 49% reported lymphedema. Of those, 77% noted onset within three years after surgery, and the remaining women developed arm swelling at a rate of almost 1% per year (2).

Breast cancer treatments and BCRL risk

BCRL risk factors seem to be additive: A woman with breast conserving surgery and no other treatment has less BCRL risk than a woman receiving breast conserving surgery with axillary node dissection and radiation. Increasing the number of nodes removed also increases BCRL risk (Paskett et al)(3). Sentinel node biopsy, which removes one to seven nodes, brings a lower risk than axillary node dissection, when 25 or more nodes might be removed. Shah and Vicini (2011) summarized incidence ranges with various treatments, in their BCRL-study review: (4)

Breast Cancer Treatment	**Incidence Range**
Lumpectomy alone	0-3%
Lumpectomy with SLN and breast RT	3-23%
Lumpectomy with ALND and breast RT	1-61%
Lumpectomy with regional nodal RT	9-65%
Mastectomy with SLN, no RT	3-23%
Mastectomy with ALND, no RT	30-47%
Mastectomy with regional nodal RT	58-65%
ALND with axillary RT	32%

ALND = axillary node dissection SLN=sentinel node RT=radiation therapy

Most BCRL studies focus on arm lymphedema, which is readily measured once past Stage 0, or subclinical BCRL. However, many breast cancer patients develop lymphedema of the breast or trunk, with or without arm lymphedema. One year after surgery, Ronka et al (2004) found breast edema identified by clinical examination in 48% of patients with axillary clearance/ positive nodes; in 35% with axillary clearance/ negative nodes; and in 23% with sentinel node biopsy. Using ultrasound, they found subcutaneous breast edema in 69-70% of the axillary clearance node patients and 28% of the sentinel node biopsy patients (5). Sentinel node biopsy reduces arm lymphedema risk compared to axillary clearance, but it poses a significant risk for breast lymphedema.

Additional cancer and related factors that influence BCRL risk

Additional factors include cancer stage at diagnosis, chemotherapy, seroma, and cording. Kwan et al (2010) found both advanced stage breast cancer and chemotherapy to be associated with increased BCRL risk (6). Fu et al (2011) found that patients with seroma requiring needle aspiration had 7.78 and 10.64 times the odds of developing arm swelling and chest/breast swelling, respectively, compared to patients without symptomatic seroma (7). Cording (axillary web syndrome) is the appearance of painful cord-like structures below the skin in an affected arm.

Key points

- 42-49% of breast cancer patients develop arm lymphedema within three years, but BCRL is a lifetime risk.
- Node removal, radiation, surgery, chemotherapy, seroma and cording are important, additive risk factors.
- Breast /trunk lymphedema is very common, but difficult to measure. Ultrasound has detected subcutaneous breast edema in up to 70% of breast cancer patients a year after surgery.
- Sentinel node biopsy reduces but does not eliminate arm lymphedema risk, and it poses a significant risk for breast lymphedema.

Personal factors that influence BCRL risk

Many women with multiple risk factors will never develop lymphedema, and some women with very low suggested BCRL risk (such as mastectomy only) develop the condition despite their seemingly favorable odds.

Why does one woman with statistically low BCRL risk develop lymphedema, and another woman with multiple treatment-risk factors does not? A partial answer may lie in two personal risk factors. Obesity at time of diagnosis is known to be a significant risk factor for BCRL. In addition, recent research suggests there may be a genetic predisposition to the condition.

Obesity is a known risk for developing BCRL. One study that followed 138 breast cancer patients for 30 months found that those with body mass indices of 30 or higher at the time of diagnosis were 3.6 times more likely to develop lymphedema. The study found that weight gain after the breast cancer diagnosis was not related to BCRL incidence (8). Of course, asking a patient to engage in significant weight loss efforts at the time of breast cancer treatment is not a realistic short-term means to reduce her BCRL risks. Even so, knowing that her body weight adds to her BCRL risk may help ensure that a breast cancer patient thinks of lymphedema and discusses early, pre-clinical symptoms with her doctor instead of dismissing them as not important.

Genetics likely also play a role in who develops and who avoids BCRL. Lymphedema after breast cancer treatment is considered *secondary* lymphedema, i.e. caused by damage or disruption to the lymphatic system. *Primary* lymphedema is caused by abnormal development of the lymphatic system, a rare genetic condition whose symptoms may occur at birth or later in life. Lymphedema clinicians have long hypothesized that some breast cancer survivors may have more robust lymphatic transport capacity than others, so that women born with a 'four-lane highway' versus a 'two-lane highway' will be less susceptible to BCRL after damage to their lymphatic nodes and/or vessels.

Recent studies may well support that hypothesis, identifying genetic mutations in some women with BCRL. For example, Finegold et al (2012) (9) studied 188 women diagnosed with breast cancer and sequenced candidate lymphedema genes for mutation. Mutations were identified in individuals having secondary lymphedema following breast cancer treatment but not in breast cancer controls or women without breast cancer. The authors conclude that their findings 'challenge the view that secondary lymphedema is solely due to mechanical trauma and support the hypothesis that genetic susceptibility is an important risk factor for secondary lymphedema.'

Key points

- Obesity at the time of breast cancer diagnosis is a known important risk factor for developing BCRL.
- Genetics likely play a role in determining who will develop BCRL.

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