

# Breast Cancer–Related Lymphedema: Attention to a Significant Problem Resulting From Cancer Diagnosis

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Effective treatments for breast cancer have resulted in a significant increase in the number of survivors.<sup>1</sup> Many of these women, however, must adjust to the unintended adverse effects of cancer and the treatments that have saved their lives. One feared, yet relatively understudied, treatment-related adverse effect is lymphedema of the ipsilateral arm/hand.

Lymphedema can occur anywhere in the body where the lymph system has been disturbed as a result of surgery or radiation. This disruption can cause a backup of lymph fluid in the interstitial area, causing swelling, pain, or loss of sensation. Historically, this condition has not been well studied, resulting in a lack of documented estimates of incidence and prevalence, a paucity of prospective studies examining predictors of incidence, the use of variable measurement techniques and mixed definitions of lymphedema, the inability to assess the impact of lymphedema on quality of life and physical functioning, few ways to prevent the development of lymphedema, and lack of awareness of this condition by women at risk. Lymphedema has been the most widely studied adverse effect secondary to breast cancer treatment.

The study by Ahmed et al<sup>2</sup> in this issue of *Journal of Clinical Oncology* directly addresses many of these issues and provides some new information on this condition, as well as validates results from prior studies. The participants included in this article come from the Iowa Women's Health Study, a population-based sample of women who developed breast cancer during the follow-up period. Lymphedema prevalence was assessed in a cross-sectional fashion among the following three groups of women: those diagnosed with lymphedema, those only with arm symptoms, and those with neither. Eight percent of women self-reported an official diagnosis of lymphedema, and 37.2% self-reported arm symptoms.

Previous studies have found rates of lymphedema of 0% to 56%,<sup>3</sup> depending on how lymphedema was defined and measured, how long the sample was observed after cancer diagnosis, and the characteristics of the sample. This variability argues for adoption of standards in definition and assessment of lymphedema. For example, in reporting estimates of lymphedema in studies where only self-reports are used, can authors state that these women indeed have lymphedema, or should terms such as swelling or arm symptoms be used, as in the Ahmed et al<sup>2</sup> article? Given that measurements may be unrealistic for all studies investigating lymphedema, common agreement of terminology is important. Norman et al<sup>4</sup> have developed a validated

self-administered questionnaire that correlates well with actual measurements of lymphedema, perhaps solving this problem. Armer and Stewart,<sup>5</sup> however, found that four different definitions (and measurements) of lymphedema were not equivalent and that self-report of signs and symptoms was not as good as using the definition of a 2-cm increase in arm circumference.

As reported in two other studies,<sup>6,7</sup> Ahmed et al<sup>2</sup> found that women with arm/hand swelling had a reduction in health-related quality-of-life (HRQOL) scores. Thus, to date, the literature is consistent on the detrimental effects of lymphedema on physical and mental HRQOL. Compounding these HRQOL effects has been the lack of knowledge women have about lymphedema.<sup>8</sup> Early studies performed by our group documented this fact,<sup>9</sup> which has now been validated by the current study by Ahmed et al,<sup>2</sup> where knowledge of lymphedema was low among women without diagnosed lymphedema. These findings underscore the fact that many cancer survivors are not aware of what lymphedema is, even though they are at risk of developing this condition. Qualitative interviews with women suffering from lymphedema paint a picture of effects on marital status, occupation, and overall well-being.<sup>9</sup> Insurance coverage of the costs of treatment services and compression garments is not uniform, and as a result, not all women have access to treatment services. These results point to the need for interventions to improve awareness of lymphedema and to prevent this condition.

Consistent risk factors for the development of lymphedema include obesity, cellulitis or infection, full axillary node dissection, radiation to the axilla, and chemotherapy.<sup>6</sup> Thus, prevention strategies could be developed to address these factors. For example, surgical practice has changed to allow sentinel lymph node biopsy for women without positive axillary nodes.<sup>10</sup>

Recently, several studies have tested different interventions to prevent lymphedema. Most popular have been exercise interventions, although many studies have been limited by small sample size.<sup>11,12</sup> In general, some benefits of exercise have been observed<sup>13</sup> with no reported adverse effects.<sup>14</sup> A second strategy tested has been weight reduction,<sup>15</sup> which also has shown some benefit. Lastly, Campisi et al<sup>16</sup> tested a complex intervention of lymphatic scintigraphy performed preoperatively and up to 5 years postoperatively. Although effective, these types of interventions might not be feasible for many women because of lack of access, insurance or financial resources, and awareness.

Cancer and Leukemia Group B (CALGB) has embarked on a lymphedema prevention study, the first large-scale randomized study of its kind. CALGB 70305 tests whether an intervention focusing on improving arm function by providing lymphedema education and awareness, using light arm weights with exercise, using a light compression sleeve at times of vigorous arm use, and practicing regular breathing exercises reduces the incidence and severity of arm or hand lymphedema after a full axillary lymph node dissection. This study builds on prior work in CALGB and is designed to overcome some of the limitations of prior research in lymphedema by incorporating pretreatment arm/hand measurements, large sample size, randomized design, and prospective assessment of the impact of lymphedema on HRQOL. This study is still recruiting participants, so results will not be available for several years.

Lymphedema has been an understudied adverse effect of cancer treatment. More studies like the one in this issue by Ahmed et al<sup>2</sup> must be performed to provide some answers for cancer survivors at risk for this condition. In addition, providers should routinely make patients aware of their risk of developing lymphedema and what to do if signs and symptoms appear. Lastly, methodologically rigorous research studies are needed to convince all insurers to cover the costs of prevention and treatment for lymphedema. Further research into this area will help ensure the best possible HRQOL for all survivors.

#### AUTHOR'S DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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