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Editorial

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Breast Cancer-Related Lymphedema: The Primary/Secondary Conundrum

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For quite some time, within the pages of this journal[1–3] and elsewhere,[4,5] there has been a persistent theory that there might be systemic and other predispositions to the secondary (or acquired) lymphedema that is encountered frequently as a sequela of breast cancer therapeutics. In addition, it has recently been observed that the presence of a lymphatic disorder such as breast cancer-associated lymphedema can alter the patterns of associated systemic disease expression that exist as comorbidities.[6] These phenomena help to blur the distinction between ''primary'' and ''secondary'' lymphedema.

In the current issue of *Lymphatic Research and Biology*, we provide three additional sets of original observations that help to expand insights into this hypothesis.

In the first of these, Kim and colleagues have explored rates of incidental subclinical lymphedema in the contralateral arm of patients with unilateral postsurgical secondary upper extremity lymphedema. In their study, magnetic resonance imaging of the upper extremities was utilized to examine patients with unilateral upper extremity clinical lymphedema. Axial STIR MR images of the symptomatic and contralateral arms were retrospectively reviewed and edema severity was graded by the investigators. In these 78 examined subjects, contralateral abnormalities were detected in 14.1%. Although the direct conclusion was to emphasize the importance of evaluation of the contralateral limb, the interpretation, by extension, is that there is a disturbance in lymphatic anatomy or function that extends beyond the direct lymphatic trauma of cancer therapeutics.

The second investigation, by Furlan and colleagues, examines the phenomenon of blood flow abnormalities in the limb that precede the development of overt lymphedema. In a cohort of 200 subjects, Doppler ultrasound was utilized to examine the axillary and brachial arteries. In these patients, there was detection of higher mean flow velocity and end-diastolic velocity as early as 1 month after surgery. The end-diastolic velocity demonstrated a 73.7% sensitivity and 71.2% specificity as a predictor of long-term lymphedema, with a negative predictive value of 57.6%.

The third of these three new investigations proposed a pilot investigation of abdominal fat ratio in subjects with breast cancer-related lymphedema. Here, Nakipoğlu and colleagues investigated the impact of central obesity to the occurrence of this lymphedema presentation. They investigated cohorts of postsurgical subjects with a matched control cohort that differed only in the distribution of BMI. The abdominal circumference measurement demonstrated a modest predictive utility, with a predictive specificity of 89%.

In aggregate, these three newly published investigations continue to tantalize us with the increasingly tenable hypothesis that the appearance of acquired lymphedema (in this case following breast cancer therapies) may, and likely does, depend upon systemic factors that predict the likelihood of disease evolution. Continued exploration of these phenomena will, ideally, result in enhanced risk factor stratification, diagnostic evaluation, and, with good fortune, improved risk factor reduction strategies.

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