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NLN
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The NLN Mission Statement

The mission of the NLN is to create awareness of lymphedema through education and to promote and support the availability of quality medical treatment for all individuals at risk for or affected by lymphedema.

The NLN is dedicated to:

- *promoting research into the causes, prevention and treatment of lymphedema;*
- *securing adequate insurance coverage for medically necessary, safe and effective treatment;*
- *expanding the number and geographical distribution of lymphedema treatment facilities and certified therapists.*

To achieve these goals, the NLN disseminates information about lymphedema to health care professionals so they can appropriately counsel their patients on its avoidance, and prescribe safe, effective treatment for those affected by this condition. The NLN also provides this information to the general public.

Lymphedema in Melanoma Patients

By Janice N. Cormier, MD,MPH, Latunya Davidson, MPH, Wendy J. Evans, MS(N),RN,AOCN, and Jane M. Armer, RN,PhD

BACKGROUND

Melanoma is a growing public health problem with an estimated 132,000 cases diagnosed annually worldwide.[1] It is the 6th most common malignancy among Americans[2] and accounts for more than 79% of all skin cancer-related deaths.[3,4] Fortunately, the majority of patients diagnosed with melanoma present with early stage disease that is cured by surgical excision alone. For others, presenting with regional or distant metastatic disease, the prognosis is not as favorable. The most critical factors for determining the prognosis of patients with melanoma are primary tumor thickness and the status of regional lymph nodes. Both of these elements are incorporated into the American Joint Committee on Cancer (AJCC) staging system for melanoma.[5]

SURGICAL TREATMENT

The most important information for determining surgical treatment of melanoma is the thickness (Breslow thickness), which is measured in millimeters and is determined by pathologic examination of a biopsy of the primary tumor. Current surgical guidelines[6] include a wide local excision (WLE) of the primary tumor. Regional lymph nodes are the most common first site of melanoma metastases. Over the last decade, sentinel lymph node (SLN) biopsy has emerged as a reliable technique for identifying micrometastatic disease in clinically negative regional lymph node basins. SLN biopsy is a highly accurate, minimally invasive surgical procedure based on the theory that lymphatic metastases associated with melanoma follow an orderly progression through lymph channels from the primary tumor to a particular lymph node (designated the "sentinel" lymph node) before spreading into other regional ("non-sentinel") lymph nodes.[7]

Current guidelines outlined by the National Comprehensive Cancer Network for the treatment of patients with melanoma recommend SLN biopsy for all patients with primary melanomas greater than 1 mm thickness and subsets of patients with high-risk thin (<1 mm) melanomas.[8] In patients with a SLN that tests negative for presence of cancer, no further surgical therapy is recommended. In patients with metastases identified in the SLN, a complete lymph node dissection is performed. This combination of surgical treatments, a WLE of a primary tumor along with SLN biopsy and possible subsequent complete lymph node dissection, results in multiple sites of lymphatic disruption.

Unlike axillary ("armpit") node dissection for patients with breast cancer, which includes dissection of level I and II lymph nodes, axillary node dissection for patients with melanoma of the upper extremity or trunk includes the routine dissection of level I, II and level III lymph nodes. Level III lymph nodes are the highest axillary nodes (apical). A standard lymph node dissection for patients with lower extremity or truncal melanomas draining to the inguinal region includes the removal of lymph nodes located in the inguinofemoral (groin) region. In addition, subsets of melanoma patients with bulky nodal disease undergo an additional deep pelvic dissection.

The surgical treatment of melanoma results in varying degrees of lymphatic disruption resulting in a lifetime risk for developing lymphedema. It is postulated that lymphedema may occur more frequently in patients with melanoma because of: (1) multiple

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surgical sites (e.g. primary tumor excision on an extremity in conjunction with lymph node biopsy or dissection), (2) extent of nodal dissections, and (3) anatomic sites, particularly the lower extremity which may be at increased risk due to physiologic reasons.

REVIEW OF THE LITERATURE

The data estimating the incidence of lymphedema in patients with melanoma are far from complete. We have systematically reviewed the literature and found a total of 25 studies performed between 1972 and 2004 pertaining to melanoma and lymphedema.[9-33] Of these 25 studies, 12 (48%) were retrospective, 10 (40%) prospective, 2 (8%) clinical trials, and 1 (4%) case series. As with the reported incidence of post-surgical lymphedema for breast cancer patients, [34,35] the reported incidence of lymphedema in patients with melanoma varies widely with reported rates ranging from 2% to 67%. The disparity likely relates to the heterogeneity of the reports which will be discussed below.

MEASUREMENT METHODS

Volume measurement using water displacement has historically been regarded as the most sensitive and accurate measure; however, clinicians rarely use this cumbersome approach.[36,37] Two of the 25 studies used water displacement alone[24] or in combination with circumference measurements.[18] Circumference measurements were utilized in five of the studies.[10,22,23,26,27] The remaining fifteen studies reported on lymphedema in melanoma patients using clinical definitions with no objective measurement criteria.

LYMPHEDEMA CLASSIFICATION

In one study in which significant lymphedema was defined as greater than 1 inch difference (measured at the ankle or mid-calf) between the affected and unaffected limb, lymphedema was reported in 80% of patients 5 years after surgery.[26] Two other studies reported rates of 21%- 26% when 2-4 cm^{22} or 3-4.5 cm^{23} differences were used as criteria.

SURGICAL PROCEDURES

In 235 patients who underwent SLN biopsy in the axillary or inguinofemoral regional, only 5 patients (2%) were reported to have lymphedema on an average of 6 weeks after surgery (range of 2-10 weeks).[12] Three studies reported lymphedema in 20% to 45% of patients undergoing inguinofemoral dissections, with no difference noted between superficial dissections alone or in combination with deep pelvic dissections.[11,16,18] Postoperative wound complications are often associated with extensive nodal dissections particularly in the inguinal region. Seven studies reported postoperative wound complications including cellulitis in 6% to 33% of patients.[9,10,14,16,18,21,22]

ANATOMIC VARIATION— UPPER VERSUS LOWER EXTREMITY

It is difficult to make direct comparisons of rates of lymphedema at various anatomic sites among studies given the heterogeneity of the reports. Of the studies, which examined lymphedema, associated with axillary versus inguinofemoral nodal dissections, similar trends were noted. The reported range of upper extremity lymphedema was 5% to 8%[22,38] compared to 14% to 29% for lower extremity lymphedema.[9,10] It appears from these reports that the incidence of lower extremity lymphedema may be twice as high as upper extremity lymphedema.

TIME HORIZON

It has been noted that breast cancer lymphedema studies with the shortest follow-up (12 months) report the lowest incidence (6%)[34] while studies with the longest follow-up have the highest incidence. Similar trends are noted in this review with the lowest lymphedema rates (upper and lower extremity) noted in studies which examined patients six months post-operatively,[12] while the highest incidence (67%, lower extremity lymphedema) had the longest follow-up (20 years).[26] High rates (44%) were also noted when lymphedema was defined as swelling lasting more than 6 months.[17]

DISCUSSION

All persons diagnosed with melanoma are at a lifetime risk of developing lymphedema because of the extensive lymphatic disruption associated with surgical treatment. Lymphedema and its sequelae is a much understudied morbidity associated with cancer treatment, particularly in patients with melanoma. In breast cancer patients, lymphedema has been described as an overlooked, under-diagnosed, and undertreated condition which other than tumor recurrence is the most feared effect of treatment.[39] The same can likely be said of melanoma and lymphedema.

Lymphedema is a significant problem. In addition to the symptoms and risks, the associated challenges may also lead to post-treatment psychosocial distress. Although researchers have documented the psychological sequelae of breast cancer treatment,[40] we know little about

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such issues in patients with melanoma, especially those that may involve lymphedema of the lower extremity. A conclusion by Maunsell, et al.[41] still stands: "The impact of lymphedema problems on patient quality of life has not been quantitatively assessed."[41] This research has been hampered by the traditional view that quality of life is less important than the eradication of cancer and detection of recurrence. Unfortunately, lack of attention to lymphedema by health professionals has not only meant that many persons go undiagnosed and fail to receive basic preventive information,[41] but this lack of attention has also hindered the development of effective psychosocial and physiological therapeutic interventions.

Early detection and intervention hold the greatest promise of reducing this widespread condition.[42,43] The range of findings in the literature reflects inconsistent criteria for defining lymphedema, small studies, retrospective analyses, and short follow-up.

We must clearly identify epidemiological and clinical factors associated with risk and incidence to build a foundation for preventive interventions. ❐

FOR A COMPLETE LIST OF REFERENCES, CONTACT THE NATIONAL LYMPHEDEMA NETWORK AT 510-208-3200.
A REPRINT OF THE ENTIRE ARTICLE WITH REFERENCES IS ALSO AVAILABLE.

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Research Perspectives...

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lymphoscintigraphic measures of lymphedema, Campisi [2003] shows early effects of breast cancer treatment at 3-6 months (range <1 to 24 months). The delayed effects of radiotherapy are demonstrated [Pierquin 1986] with median onset at 7 (range 2-37) months with surgery alone, 12 (1-52) months with surgery and radiation and 25 (6-156) months with radiation alone. Other researchers demonstrate medians between 1 and 2 years, with maximum times of onset of 3 to 10 years for cohorts with a mix of treatments.

Swelling after breast cancer treatment can occur at a number of sites, and measurement of swelling at one site such as the forearm, upper arm or entire arm and hand results in an underestimation of the incidence of lymphedema. Arm swelling may account for only about half of the patient-reported swelling [Bosompra et al. 2002]. Other reported sites include the breast, chest, underarm and back. But measurement of these sites is very difficult and so remains largely unreported. Breast lymphedema incidences of 70% using measurement of dermal swelling have been demonstrated [Rönkä 2004] while clinical examination detects only 35% in the same cohort. Changes in the mix of breast cancer surgery and radiotherapy over the last 50 years have resulted in a change in the incidence of lymphedema, since each therapy has a different associated morbidity. Halsted Radical Mastectomies, the standard until the 1970s, resulted in upper limb LE rates of 22-44%, with and without radiotherapy. With the ascendancy of the less radical Modified Radical Mastectomy in the 1970s and 1980s, lymphedema rates fell to 19-29% without and with radiotherapy [Schünemann & Willich 1997]. The 1990s brought Breast Conserving Surgery from a small percentage to approximately half of the surgeries performed [Yoshimoto et al. 2004] with a further drop in upper limb lymphedema rates to 7-10% without and with radiotherapy [Schünemann & Willich 1997].

Breast lymphedema started to receive attention in 1982 with Kissin reporting clinical rates of 8% and Clarke reporting rates of 41% using skin measurements. Recent reports estimate the rates at 1-9% based on subjective reporting [Fehlauer 2003; Højris 2000], 10-19% based on clinical examination [Fehlauer 2003; Goffman 2004] 20-48% [Rönkä 2004; Senofsky 1991], and 30-70% based on skin thickness measurement [Rönkä 2004].

Lower limb lymphedema rates are likewise a strong function of the extent of the surgery and radiation used for treatment of reproductive and pelvic cancers, as well as lower limb melanomas. Whereas there are many different methods commonly used to evaluate upper limb swelling, there are very few methods reported to measure lower limb swelling. Lower limb lymphedema is reported in medical records only when it is severe enough that compression is not adequate, or it causes disablement. Reported lower limb lymphedema ranges from zero [Coblenz 2002] to 60-80% [Balzer 1993] [James 1982] [Papachristou 1977] with many reports between these extremes.

Lymphedema of the genitals has been reported as 2-5% [Gaarenstroom 2003] [Nelson 2004] and 18% (combined with lower limb) [Lieskovsky 1980]. Genital lymphedema among users of pneumatic pumps on the lower limb has been reported at 43% [Boris 1998]. Prevalence of primary lymphedema has been estimated as 1.15/100,000 persons under 20 years [Smeltzer 1985]

This systematic review of lymphedema references results in an estimate of lymphedema incidence overall and by causative factor. ❐

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