The Incidence of Lymphedema

WOW!

In the U.S. Medicare age population, the number of persons afflicted with lymphedema, or at risk of developing it, exceeds 6.8 million individuals.

Introduction

“How many people have lymphedema?” In 2007 this question was put to Robert Weiss, M.S., who is well known as “the Lymphedema Advocate.”

Upon completion of a literature review, the following is his response and the data he made available to be shared with Lymph Notes members and visitors.

Background

There is a TOTAL lack of information on the prevalence of lymphedema, so I was forced to make what I hope is a credible estimate using the literature. I am behind in reviewing the literature of the last couple of years, but I believe that the following is still valid.

Credible estimates of the incidence of lymphedema are difficult to find. Few consistent surveys appear in the literature as the occurrence of lymphedema is so dependent on patient genetic predisposition, the patient’s general health and lymphatic system health, the nature and extent of lymphatic trauma and lack of a standard clinical definition of the condition.

Methods used

An extensive literature search was performed on over 1900 references to primary and secondary lymphedema. Over 200 references which cited the incidence of lymphedema from any cause were abstracted and the relevant statistics collected into a matrix citing:

1. The reference
2. Cause of the lymphedema
3. Appropriate statistic
4. Number of cases
5. Year of treatment
6. Length of study
7. Lymphedema measure used

Results

The incidence of lymphedema compared and contrasted, with an attempt to derive consistent estimates for individual procedures or causes. The majority of the estimates relate to breast cancer treatment protocols, but
the survey includes pelvic and inguinal treatment protocols as well as estimates of primary lymphedema incidence.

Dispersion between references is demonstrated to be caused by changing diagnosis and treatment during studies, lack of standard measurement and grading criteria, prolonged course of toxicity, therapeutic interventions during the study, physicians' viewpoints and knowledge, inadequate contemporary documentation, selection criteria of patients for study and non-use of actuarial estimates.

**Onset of lymphedema** is shown to vary as a function of the method of measurement and the causative therapeutic procedure. Toxic effects of radiotherapy do not become fully evident until many years after treatment. Using sensitive 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 mixed cohorts.

**Swelling after breast cancer treatment** can occur at a number of sites, and the restriction of measurements to one particular 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 have remained 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 with and without radiotherapy, the standard until the 1970's, resulted in upper limb lymphedema rates of 22-44% without and with radiotherapy. With the ascendency of the less radical Modified Radical Mastectomy in the 1970's and 1980's lymphedema rates fell to 19-29% without and with radiotherapy [Schünemann & Willich 1997].

The 1990's 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 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 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].

Conclusions
This systematic review of lymphedema references results in an estimate of lymphedema incidence overall and by causative factor. We can use these incidence statistics to estimate prevalence.

- **INCIDENCE:** The incidence of lymphedema as a consequence of breast cancer treatment (surgery and/or radiation) ranges from 10 to 40%.
- **PREVALENCE:** The prevalence of invasive cancer survivors in the U.S in 2002 has been estimated by the National Cancer Institute as 9.6 Million, of whom 61% (5.86 Million) are over 65 years of age.
- Add to this number an estimate of how many persons underwent surgeries known to lead to lymphedema. For example, coronary artery bypass grafts (277,000 over 65 in 2002), hip and knee replacements (314,000 over 65 in 2002), and cellulitis (374,000 over 65 in 2002), and the population of afflicted and at risk persons of Medicare age exceeds 6.8 million in the U.S.
- **A 20% incidence of lymphedema** yields a potential of 1.36 million cases of Lymphedema of the upper limbs, lower limbs, head and neck, breast and torso in this Medicare population. Note that this estimate does not include probably an equal number of patients suffering from lymphedema secondary to chronic venous insufficiency.

Acknowledgement and Gratitude
Our thanks to Robert Weiss, M.S. The LymphedemaAdvocate, who compiled this information. He can be contacted by e-mail at LymphActivist@aol.com.

Got a question or comment? Post in the **Are You at Risk for Lymphedema?** forum.

Category: Are You at Risk for Lymphedema? Updated: 2009-11-13
FAQ’s for Health Professionals

1. What is Lymphoedema?

Lymphoedema is the accumulation of excessive amounts of protein-rich fluid resulting in swelling of one or more regions of the body. This is due to a mechanical failure of the lymphatic system and occurs when the demand for lymphatic drainage exceeds the capacity of the lymphatic circulation. The condition usually affects the limb(s) although it may also involve the trunk, breast, head and neck or genital area.

The lymphatic system is a network of vessels and nodes throughout the body that transports fluid (lymph) from the body tissues back to the bloodstream. The functions of the lymphatic system are to maintain the volume and protein concentration of the extracellular fluid in the body and to assist the immune system in destroying pathogens and removing waste products from the tissues.

2. What causes lymphoedema?

Lymphoedema may arise because the lymphatic vessels or nodes have been damaged or were not formed correctly.

Secondary lymphoedema is the most common type developing following damage to the lymphatic system. The damage may occur as a result of some cancer treatments including the removal of lymph nodes, following radiotherapy to lymph node groups or with the progression of malignant disease. The onset of lymphoedema may be at any time. It may occur within months of the damage or it may appear years later.

Secondary lymphoedema may also arise without a cancer diagnosis when one or more of the following conditions occur:

- Trauma and tissue damage
- Venous disease
- Immobility and dependency
- Factious – self harm
- Infection such as cellulitis
- Filariasis - Lymphatic Filariasis is a major cause of lymphoedema in the subtropical areas of the world. Parasitic filarial worms are transmitted through mosquito bites. The parasites lodge in the lymphatic system causing destruction of the healthy vessels and nodes, resulting in lymphoedema. More information can be found on the WHO web site: [http://www.who.int](http://www.who.int)
- Obesity

Primary Lymphoedema in comparison to Secondary Lymphoedema is the result of a congenital condition that affects how the lymph vessels where formed. This may result in hypoplasia of lymphatic vessels (a reduced number of lymphatic vessels), hyperplasia of lymphatic vessels (vessels that are too large to be functional) or aplasia (absence) of some part of the lymphatic system. This form may be presents at birth (congenital), develop at the onset of puberty (praecox), or not become apparent for many years into adulthood (tarda). It may be associated with other congenital abnormalities/syndromes.

Primary and secondary lymphoedema can occur together.

3. What is the incidence of lymphoedema?

The National Breast and Ovarian Cancer Centre (NBOCC) review of research evidence on Secondary Lymphoedema states “conservative estimates suggest that 20% of breast, genitourinary, gynaecological, or melanoma survivors will experience secondary lymphoedema.

More specifically the incidence of secondary lymphoedema associated with vulval cancer is estimated at 36-47%, breast cancer 20%, cervical cancer 24% and melanoma 9-29%. (1)

The incidence of lymphoedema following sentinel lymph node biopsy (SLNB) is reported to range from 4-8%. (4)
At birth, about one person in every 6000 will develop Primary Lymphoedema. (2)

4. What are the risk factors for developing lymphoedema?
The consensus document suggests that patients at risk of lymphoedema will be encountered in a wide variety of health care settings, primary, secondary and tertiary. Key risk factors identified by NBOCC for secondary lymphoedema include, the extent of surgery, lymph node dissection and radiation treatment. Other factors involve trauma, infection, increased body mass index (BMI) and immobility. Any major damage to the lymphatic system causes a life long risk of lymphoedema. For further information about identifying the patient at risk see [http://www.mepltd.co.uk/oneoffs.html](http://www.mepltd.co.uk/oneoffs.html) p 3-5.

For those with Primary Lymphoedema a referral to genetic counselling maybe indicated to ascertain the risk of lymphoedema.

5. What are the early warning signs of lymphoedema?
Subjectively these may include transient swelling of a limb or other region of the body. Other symptoms may include aching, heaviness, stiffness, limitation of movement, tightness or temperature changes. Clothing, jewellery or shoes may feel tighter. Lymphoedema is not usually a painful condition but some people report pain and tension in an affected limb or body part.

Clients report that the swelling associated with lymphoedema is often aggravated by heat, at the end of the day, with overuse, with sustained positions and prolonged inactivity. They report that gentle exercise, elevation, massage and compression can ease their symptoms.

Many conditions may cause these symptoms to occur and any of the changes described will need to be assessed by a doctor in order for an accurate diagnosis to be achieved.

6. How is lymphoedema diagnosed?
An accurate diagnosis is essential for appropriate therapy. This is determined from the clinical history and physical examination. Co-morbid and confounding conditions of morbid obesity, lipoedema, cardiac disease, renal disease, metabolic disorders, infection, and venous insufficiency will require thorough medical evaluation.

Lymphoedema usually has a gradual onset. However when lymphoedema has an acute onset appropriate tests to exclude, deep venous thrombosis (DVT), recurrence of cancer and infection may be necessary. Sometimes lymphoscintigraphy will be offered to confirm a clinical diagnosis of Primary Lymphoedema.

Whether primary or secondary, lymphoedema develops in stages, from mild to severe. Methods of staging are numerous and inconsistent. They ranged from three to as many as eight stages. In Australasia, the most commonly used stage scale is that adopted by The International Society of Lymphology (ISL) (3), which identifies the following stages:

**Stage 0** A latent or subclinical state where swelling is not evident despite impaired lymph transport.

**Stage I** This represents early onset of the condition where there is an accumulation of tissue fluid with higher protein content, which subsides with limb elevation. The oedema may be pitting at this stage.

**Stage II** Limb elevation alone rarely reduces swelling and pitting is manifest. In later Stage II the limb may or may not pit as fat and fibrosis supervenes.

**Stage III** The tissue is hard (fibrotic) and pitting is absent. Skin changes such as thickening, hyperpigmentation, increased skin folds, fat deposits and warty overgrowth develop. Stage III encompasses lymphostatic elephantiasis. At this stage, the swelling is spontaneously irreversible and usually the limb(s) is very large.

7. Are there any complications that can arise with lymphoedema?
Lymphoedema is understood to be a progressive disease and early intervention is recommended to minimise time and age related changes.

The swelling may progress without treatment. The skin is prone to thickening and the development of fibrosis and other secondary changes.
When the lymphatic impairment causes the lymph fluid to exceed the lymphatic system's ability to transport it, an abnormal amount of protein-rich fluid collects in the tissues of the affected area. Left untreated, this stagnant, protein-rich fluid causes tissue channels to increase in size and number, reducing the availability of oxygen. This interferes with wound healing and provides a rich culture medium for bacterial growth that can result in infections: cellulitis, lymphangitis, lymphadenitis, (in severe cases sepsis) and skin ulcers.

It is vital for lymphoedema patients to be aware of the symptoms of infection and to seek treatment at the first signs, since recurrent infections, in addition to their inherent danger, further damage the lymphatic system and set up a vicious cycle. The ALA has developed best practice guidelines in relation to cellulitis - The Management of Cellulitis in Lymphoedema available here.

Very rarely, in certain exceptionally severe cases, lymphoedema untreated over many years can lead to a form of cancer known as Lymphangiosarcoma.

8. What can be done to cure or treat lymphoedema?

Lymphoedema cannot be cured but it can be reduced and managed with appropriate intervention. The stage, location and severity of the lymphoedema together with the individual circumstances of the client will influence the most appropriate intervention. Early intervention is recommended. For further information about management and treatment options see lymphoedema management.

References


BACKGROUND

Of the 2 million breast carcinoma survivors, perhaps 15-20% are living currently with posttreatment lymphedema. Along with the physical discomfort and disfigurement, patients with lymphedema also must cope with the distress derived from these symptoms.

METHODS

To review the medical literature for the question of lymphedema incidence, a comprehensive, computerized search was performed. All publications with subject headings designating breast carcinoma-related lymphedema from 1970 to the present (116 reports) were found, and each summary or abstract was read. Of the 116 reports, 35 discussed the incidence of lymphedema. Of these, seven reports since 1990 from five countries with the most relevance to current patients were then chosen for greater analysis and comparison.

RESULTS

The incidence of lymphedema ranged from 6% to 30%. The source of patients, length of follow-up, measurement techniques, and definition of lymphedema varied from report to report. In general, reports with shorter follow-up reported lower incidences of lymphedema.

CONCLUSIONS

The definitive study to determine the incidence of lymphedema has not been performed to date. There has been no prospective study in which patients have been followed at intervals with accurate measurement techniques over the long term. Cancer 1998;83:2776-2781. © 1998 American Cancer Society.

In a recent statement to the press,1 the director of the National Cancer Institute reported that 8.5 million Americans are living after the diagnosis of cancer, of which a large fraction, about 2 million, are breast carcinoma survivors. With such large numbers, it behooves clinicians and scientists to study the health-related quality of life after breast carcinoma treatment. Except for breast carcinoma recurrence, no event is more dreaded than the development of lymphedema.

Lymphedema is distressing. Along with the deformity, the swelling causes discomfort and disability. Recurrent episodes of cellulitis and lymphangitis may be expected. Added to the physical symptoms is the pain caused unintentionally by the clinicians who, interested in carcinoma recurrence, trivialize the nonlethal nature of lymphedema. The appearance of arm swelling is more distressing than that of a mastectomy, because the latter can be hidden easily, but the disfigured arm/hand is a constant reminder of the disease to the woman herself and a subject of curiosity to others.
Lymphedema After Breast Cancer: Incidence, Risk Factors, and Effect on Upper Body Function

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Purpose Secondary lymphedema is associated with adverse physical and psychosocial consequences among women with breast cancer (BC). This article describes the prevalence and incidence of lymphedema between 6 and 18 months after BC treatment; personal, treatment, and behavioral correlates of lymphedema status; and the presence of other upper–body symptoms (UBS) and function (UBF).

Patients and Methods A population-based sample of Australian women (n = 287) with recently diagnosed, invasive BC were evaluated on five occasions using bioimpedance spectroscopy. Lymphedema was diagnosed when the ratio of impedance values, comparing treated and untreated sides, was three standard deviations more than normative data. UBF was assessed using the validated Disability of the Arm, Shoulder, and Hand questionnaire.

Results From 6 to 18 months after surgery, 33% (n = 62) of the sample were classified as having lymphedema; of these, 40% had long–term lymphedema. Although older age, more extensive surgery or axillary node dissection, and experiencing one or more treatment–related complication(s) or symptom(s) at baseline were associated with increased odds, lower socioeconomic status, having a partner, greater child care responsibilities, being treated on the dominant side, participation in regular activity, and having good UBF were associated with decreased odds of lymphedema. Not surprisingly, lymphedema
leads to reduced UBF; however, BC survivors report high prevalences of other UBS (34% to 62%), irrespective of their lymphedema status.

**Conclusion** Lymphedema is a public health issue deserving greater attention. More systematic surveillance for earlier detection and the potential benefits of physical activity to prevent lymphedema and mitigate symptoms warrant further clinical integration and research.

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Authors’ disclosures of potential conflicts of interest and author contributions are found at the end of this article.
Risk Factors of Arm Lymphedema in Breast Cancer Patients

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Chronic lymphedema is a life-long, potential complication of axillary treatment for breast cancer patients. In this article we focus on risk factors in the development of arm lymphedema and also discuss definition, type and stage, and incidence of arm edema.

REVIEW ARTICLE

In the industrialized countries, cancer and cancer treatment are the most common causes of lymphedema (1). This complication can develop at any time and has been reported as late as 30 years after treatment (2). Arm edema may be disfiguring and can therefore greatly affect quality of life. Once established lymphedema cannot be cured, therefore it is essential to prevent or minimize this condition. In this article we focus on risk factors in the development of lymphedema and also discuss the definition, type and stage, and incidence of arm edema in breast cancer patients.

DEFINITION, TYPE AND STAGE

Lymphedema is the result of the functional overload of the lymphatic system in which lymph volume exceeds transport capabilities. Lymphedema can be classified as primary or secondary, and acute or chronic (3) (Table 1). Primary lymphedema may be caused by the congenital absence or abnormality of lymph tissue. Secondary lymphedema occurs as a result of obstruction or interruption of the lymph system due to infection, malignancy, or surgical or radiation treatment. Acute lymphedema is usually transient and self-limiting and lasts for less than 3 to 6 months (4). Chronic lymphedema is present for at least 3 months, with noticeable skin changes, known as brawny edema (3). Three stages of lymphedema have been defined (1) (Table 2). Stage I (acute phase) is characterized by a pitting edema and is reversible with elevation of the arm. If the condition worsens, stage II or the chronic phase begins. This stage, which is not considered to be ‘spontaneously reversible’, constitutes protein-rich edema and a proliferation of connective tissue. There is much less or no skin pitting. Stage III is known as elephantiasis, characterized by massive swelling and cartilage-like hardening.

INCIDENCE

All women who have had surgical resection of the lymph channels are at risk for lymphedema. In Halsted’s time, lymphedema occurred in up to 62% of patients (5). Few recent trials of modern therapies have addressed this problem. The report from Germany is one of the largest on post-treatment lymphedema with long follow-up. The incidence of lymphedema was 24% in 5 868 patients with a median follow-up of 11 years (6). According to the analysis performed by Petrek & Heelan (7), the incidence of
lymphedema varied from 6% to 30%. They reported that the incidence of arm edema varied along with:
- the methods used to define lymphedema
- the source of the patients
- the completeness of the patient population follow-up
- the interval between axillary treatment and measurement of lymphedema.

RISK FACTORS
Risk factors in the development of arm lymphedema are still poorly understood, and there have been few trials.

Table 1
Types of lymphedema
<table>
<thead>
<tr>
<th>Type</th>
<th>Etiology</th>
<th>Duration</th>
<th>Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>Congenital obstruction</td>
<td>Infec</td>
<td>Within 6 weeks of surgery, less edema in morning more edema at night</td>
</tr>
</tbody>
</table>
| Secondary          | Acute | B3 – 6 months | Peau d’orange relating to this subject in the literature. Nevertheless, risk factors can be grouped into three main categories. The first category consists of treatment-related factors (these factors will not be discussed): surgery, irradiation, systemic treatment (chemotherapy, tamoxifen), and combined treatment; the second category consists of disease-related factors: stage at diagnosis, pathologic node status, the number of lymph nodes with positive pathologic findings, and the location of the tumor in the breast. The third category consists of patient- and clinical-related factors: patient age at diagnosis, obesity-body mass index, hypertension, history of infection-inflammation, handedness and excessive use of the limb, appearance of early lymphedema, and time interval since treatment (Table 3).

DISEASE-RELATED FACTORS
Advanced stage at diagnosis is a major predictive factor for developing lymphedema (6, 8, 9). A study from Germany, which is the largest on post-treatment lymphedema with long-term follow-up, demonstrated that the incidence of arm edema in patients with in situ carcinoma (Tis) tumors was 6.7%, whereas the incidence was 16.9% in patients with T1 tumors and 34.9% in patients with T4 tumors. Furthermore, the risk of lymphedema was 24.8% in patients with N1 tumors, compared with 44.4% for those with N3 tumors (6) (Table 4). According to the univariate analysis performed by Kissin et al. (8), T-stage was significantly associated with lymphedema (p = 0.002).

PATIENT AND CLINICAL-RELATED FACTORS
Pathological nodal status is the independent risk factor for developing lymphedema (8). Schunemann & Willich (6) reported that the incidence of arm edema was 17.9% for node-negative patients (N0), compared with 38.5% for node positive (N+) patients (Table 4). Despite these findings, it is difficult to distinguish them as independent risk factors, because they show nodal stage of the disease and, furthermore, patients with positive nodal disease receive more aggressive treatment.
The study from Sweden (10) demonstrated that the number of pathologically positive lymph nodes was the significant factor contributing to lymphedema, but others did not find a correlation between number of positive lymph nodes and lymphedema (9, 11).

Correlation between site of the primary tumor and development of arm edema has not been demonstrated (9, 12, 13).
In contrast to Werner et al. (9), Kiel & Rademacker (14) have reported that the most statistically significant factor leading to the development of arm edema is the age of the patient at diagnosis. The study showed that the actuarial incidence of arm edema at 3 years was 56% for women older than 55 years and 23% for women younger than 55 years ($p < 0.0005$), which suggests that the risk of developing lymphedema is higher in older patients. Marcks (3) claims that this may be attributed to the formation of lymphovenous anastomosis in younger patients. Autopsy results have shown that these lymphovenous anastomoses are much less common in older patients, because of the ageing process (13).

Table 2

<table>
<thead>
<tr>
<th>Stage</th>
<th>Severity</th>
<th>Difference in circumference</th>
<th>Symptoms and volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Mild</td>
<td>B3 cm (150–400 ml)</td>
<td>Pitting edema, reversible with elevation of the arm</td>
</tr>
<tr>
<td>II</td>
<td>Moderate</td>
<td>3–5 cm (400–700 ml)</td>
<td>Progressive hardening of the extremity; edema does not decrease with elevation</td>
</tr>
<tr>
<td>III</td>
<td>Severe</td>
<td>$\geq$5 cm ($\geq$750 ml)</td>
<td>Hardened tissue with skin changes</td>
</tr>
</tbody>
</table>


Fig. 1. Factors related to the development of lymphedema. RF: risk factor, AF: aggravating factor, BMI: body mass index.

Table 4

Frequency of lymphedema according to tumor size (T) and nodal stage (N) (6)

<table>
<thead>
<tr>
<th>T</th>
<th>Tx</th>
<th>Tis</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>T4</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>T</td>
<td>179</td>
<td>7</td>
<td>362</td>
<td>657</td>
<td>98</td>
<td>102</td>
<td>43.6</td>
<td>6.7</td>
</tr>
<tr>
<td>N0</td>
<td>525</td>
<td>443</td>
<td>241</td>
<td>82</td>
<td>28</td>
<td></td>
<td>17.9</td>
<td>38.5</td>
</tr>
</tbody>
</table>

noted that the incidence of arm edema in patients treated with both axillar surgery and irradiation was 35% among patients with normal blood pressure but 61% for patients with hypertension ($p < 0.005$).

A correlation between recurrent or late infections and arm edema has been reported in several studies (17, 19, 20), but it is difficult to accept this as a causative factor for lymphedema. The lymphedematous tissues are extremely sensitive to infections, and any simple burns and puncture wounds can develop into generalized erysipelas, which may produce further lymphatic destruction and blockage (4). Accumulated lymph in the edematous arm provides a rich culture medium for bacteria. As reported by Segerstro¨m et al. (17), the recurrent infections may be secondary to the edema, rather than the cause of the condition.

There is no evidence linking these factors with an increased risk for developing arm edema: handedness (operation on the dominant arm), excessive use of the limb, appearance of early lymphedema (8, 11, 17). Many trials (14, 21, 22) report that lymphedema has a significant tendency to increase with time. Moretimer et al. (21) noted that there was a significant increase in prevalence with increasing time since treatment in patients who had received radiotherapy, but not in patients treated with surgery alone. Moreover, they suggested that at least 3 years’ follow-up was required for this tendency to manifest itself, particularly following radiotherapy.

CONCLUSIONS

Owing to lack of studies performing multivariate analyses and to lack of prospective data, it is difficult to draw any definitive conclusions about risk factors from a review of the literature. Nevertheless, there seems to be a higher risk for developing lymphedema in patients with advanced disease at diagnosis, older age, greater BMI.
(obesity), and longer follow-up (see Fig. 1). Hypertension and infection are important comorbidities and may be initiating factors, but more likely they aggravate existing lymphedema.

In the literature there is support for the view that obesity is a risk factor in postmastectomy arm edema (11, 15–17). Few studies have examined the risk associated with obesity and increased patient size in patients treated conservatively. The study from Memorial Sloan Kettering Cancer Center showed that the most statistically significant predictive factor was body mass index (BMI) in patients treated with conservative surgery and radiotherapy (9). The findings of this study showed that in patients with BMIs greater than 29.2 kg/m², the 5-year incidence of lymphedema rose to 36% compared with 12% for those with lower BMIs. Although it is not clear that obesity is a direct risk factor for arm edema, it is certainly a risk factor for infection and poor wound healing (3).

In a series of studies by Bohler et al. (18), the effects of hypertension were investigated. Bohler and colleagues

Table 3

Classification of risk factors for lymphedema

<table>
<thead>
<tr>
<th>Main groups</th>
<th>Subgroups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment-related factors</td>
<td>Surgery</td>
</tr>
<tr>
<td>Irradiation</td>
<td></td>
</tr>
<tr>
<td>Systemic treatment (chemotherapy, tamoxifen)</td>
<td></td>
</tr>
<tr>
<td>Combined treatment</td>
<td></td>
</tr>
<tr>
<td>Disease-related factors</td>
<td></td>
</tr>
<tr>
<td>Stage at diagnosis</td>
<td></td>
</tr>
<tr>
<td>Pathologic node status</td>
<td></td>
</tr>
<tr>
<td>Number of lymph nodes with positive pathologic findings</td>
<td></td>
</tr>
<tr>
<td>Location of the tumor in the breast</td>
<td></td>
</tr>
<tr>
<td>Patient- and clinical- related factors</td>
<td></td>
</tr>
<tr>
<td>Obesity – body mass index</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
</tr>
<tr>
<td>History of infection-inflammation</td>
<td></td>
</tr>
<tr>
<td>Handedness and excessive use of the limb</td>
<td></td>
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<tr>
<td>Appearance of early lymphedema</td>
<td></td>
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<tr>
<td>Time interval since treatment</td>
<td></td>
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REFERENCES