Lymphoedema: estimating the size of the problem

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Lymphoedema is a problem frequently encountered by professionals working in palliative care. This article reviews the evidence on the magnitude of the problem of lymphoedema in the general population and provides evidence on specific high risk groups within it. Prevalence is a good indicator of the burden of disease for chronic problems such as lymphoedema, as it indicates the numbers of patients who require care. Incidence is indicative of changes in the causes of lymphoedema and the success of any prevention programmes. Both are important means of assessing the current level of need and the potential for the changing needs in managing this condition. Problems exist in all studies in relation to precise definitions of lymphoedema, inconsistent measures to assess differential diagnosis and poorly defined populations. While there is some evidence of high rates in relation to breast cancer therapy, the total burden of lymphoedema in the general population is largely unknown. Palliative Medicine 2005; 19: 300–313

Key words: chronic oedema; epidemiology; prevalence; Lymphoedema; incidence

Introduction

Lymphoedema is a chronic swelling arising from the accumulation of fluid and other tissue elements that would otherwise drain via the lymphatic system. It can be a grossly disfiguring condition, usually affecting a limb, which causes discomfort and may cause pain, and can be complicated by recurrent infections often requiring hospital admission. Untreated, limbs can become huge and the term elephantiasis illuminates their appearance. Sufferers report the psychological impact of the condition to be considerable. Causes include cancer treatment, parasitic infection and congenital problems in the development of the lymphatic system. In addition, lymphoedema frequently occurs in patients with other chronic diseases e.g., spina bifida, rheumatoid arthritis and stroke.

While not exclusive to palliative care services, the association between cancer therapy and lymphoedema has led to many services being located within the palliative care system. The emphasis of treatment is on helping the patient to achieve as much self-sufficiency and independence as possible, given the chronic nature of their condition and to reduce the incidence of co-morbidity and the need for intensive therapy and hospitalisation.

This article will review the epidemiology of lymphoedema, with particular reference to the prevalence and incidence of the condition.

Epidemiology definitions

Epidemiology is defined as the study of disease in relation to populations. Within this there are a number of key measures that are important in defining the disease burden (prevalence) and the number of new cases that develop over a specified time period (incidence). Both measures are important to services providing care to patients since they will indicate the potential care requirements of a population and examine how the disease profile is likely to change over time as new cases add to this burden. The task of obtaining accurate figures for lymphoedema incidence and prevalence is, however, complex and the literature is limited. This paper will discuss some of the difficulties associated with exploring lymphoedema incidence and prevalence and review relevant literature related to specific types of lymphoedema and lymphoedema-associated conditions.

Defining cases of lymphoedema

In evaluating the prevalence and incidence of a condition it is essential to describe precisely how the disease is defined. A repeatable, valid and accepted definition will allow for comparisons between and within ‘at risk’ populations to evaluate temporal and geographical differences and give some indication of the nature of the disease. Whilst definitions are essential to determine the consistency of measurement, lymphoedema is rarely defined in precise terms. In a previous review, Logan highlighted some of the problems inherent in ascertaining rates in lymphoedema. Amongst various studies there are inconsistencies in methods used to determine the
presence of swelling, quantify the degree of swelling and assess skin and tissue changes.

In a recent publication we have used a general definition of chronic oedema/lymphoedema to describe the overall presence of swelling to health professionals. Population studies of this nature frequently rely on clinical classification of a condition, which may be confirmed at a later date using more objective invasive and non-invasive tests.

'Clinic oedema is a broad term used to describe oedema which has been present for more than 3 months and involves one or more of the following areas: limb/s, hands/feet, upper body (breast/chest, shoulder, back), lower body (buttocks, abdomen), genital (scrotum, penis, vulva), head, neck or face. Oedema which develops as a result of a failure in the lymphatic system is referred to as lymphoedema but chronic oedema may have a more complex underlying aetiology. At this stage we do not expect to make a differential diagnosis but need to record the actual numbers of people with oedema suggestive of chronic oedema/lymphoedema, even if a medical diagnosis has not been confirmed.13

This recent prevalence study used a case ascertainment method in an urban health authority and identified a prevalence figure of 1.33 per 1000. However, the authors suggest this may underestimate the actual number as the ascertainment of patients through health professionals is limited where not all patients are likely to be receiving treatment for their condition. Nevertheless, it is similar to the 1.44 per 1000 prevalence of chronic oedema in Norway reported by Petlund.4

Differential diagnoses
There are a number of problems in establishing a differential diagnosis in lymphoedema, particularly in relation to primary lymphoedema.5 Although lymphoscintigraphy is an invaluable tool in assisting in the diagnostic process, investigative methods are not universally standardized and can be inadequate. In some instances, several contributory factors, such as obesity and venous insufficiency, may confuse the clinical picture and make accurate diagnosis difficult.5

Despite these difficulties, attempts have been made over several decades to provide a classification for lymphoedema.6 9 Browse and Stewart suggested that only those with obvious abnormality of the large vessels or aplasia/dysplasia of the peripheral channels should be considered as having primary lymphoedema and describe these as genetically determined or acquired later in life.8 9 It is clear that identification of primary lymphatic abnormalities can be problematic due to the varying presentations and difficulties with investigation and differential diagnosis.

The classification of secondary lymphoedema is also highly problematic. These may be post-traumatic, post-inflammation/infection, secondary to lymph node dissection and irradiation or result from a range of other factors.8 The development of swelling, particularly in those with advanced cancer, may sometimes be due to failure of more than one system. Lymphatic damage or insufficiency may be compounded by venous obstruction, cardiac, renal or hepatic failure. Swelling associated with chronic venous disease is often not recognised as a lymphoedema-type problem, despite the knowledge that ulceration and infection are likely to damage the lymphatic system. The term 'chronic oedema' has become widely used in describing a range of oedemas, some with a considerable lymphatic component and many of which have complicated aetiologies. Consideration of these other types of oedema clearly influences the data on incidence and prevalence.

While this paper concentrates on lymphatic problems associated with westernized countries, tropical lymphoedema is acknowledged as a significant problem in other parts of the world. Lymphatic filariasis and infestation by Wuchereria bancrofti is a major cause of lymphoedema in some areas of Africa and India and has significant implications for health services in these countries.10

Measuring lymphoedema
Various methods exist for the measurement and calculation of the degree of swelling.11 Measurement using water displacement, electric volumetry and skin circumferences are the most common techniques but are open to variations in their use. For example, skin circumferences may be taken at a wide range of sites on the limb. In the UK the most common technique consists of 4 cm circumferences extending distally to proximally, which are used to calculate the total volume of the limb as the sum of a series of cylinders. A number of studies have explored the validity and reliability of arm volume measured by these different methods and most conclude that while these methods are highly correlated and reliable, they are not interchangeable and cannot be mixed or substituted.12 14

In their review Stanton et al. highlight a volume of >200 ml as measured by water displacement as a sensitive indicator of arm lymphoedema and this definition is used in many studies.11 Clearly, reducing this cut-off figure to >100 ml may appear to increase the prevalence of lymphoedema, but it may also be argued that this also enables identification of mild oedema. Stanton et al., however, suggest that percentage differences are more universally applicable, allowing for easier comparison and, as such, a difference of 10% in volume may be an appropriate cut-off point.11 The potential accuracy of the volumes also requires standar-
dization and accuracy in protocols for measurement and calculations.\textsuperscript{16}

More recently, Bland \textit{et al.} have suggested the value of a 5\% or \textgreater{} 1 cm increase in arm circumference is a reliable detector of probable lymphoedema in the clinical setting.\textsuperscript{17} However, although circumferential measurements are widely used in the literature, many people with lymphoedema do not have uniform swelling throughout the limb and it is common for swelling to be localized to hand or upper arm.\textsuperscript{18,19} This indicates that reliance on the use of one or two circumferential measurements of the swollen limb is inadequate and also does not take in account any changes in limb circumference due to increased fat or muscle mass. Asymmetry in limb circumferences and volumes, due to arm dominance, should also be a consideration.\textsuperscript{20} Ideally, circumferences should be taken along the length of the limb and the total limb volume with possible proximal and distal limb segment volumes should be calculated. Many studies have used subjective reporting of swelling alone, though the correlation with objective measures is often poor.\textsuperscript{18,21}

\textbf{Time to lymphoedema development}

The length of time to lymphoedema development is also an important consideration. Most patients experience an acute post-operative oedema and this leads to temporary limb swelling. Persistent oedema for greater than three months duration is more likely to be lymphoedema and oedema prior to this point should be excluded. Additionally, studies need to be undertaken over an adequate time period as lymphoedema may develop at any stage post-treatment. Edwards \textit{et al.} showed the onset of lymphoedema to occur in the first 18 months postsurgery,\textsuperscript{21} while others report a thirty-nine month median time interval to lymphoedema development.\textsuperscript{22} This suggests that a longer follow up is required to ensure that a late lymphoedema is recognized.\textsuperscript{18,23}

\textbf{Literature search methodology}

A search was undertaken of PubMed, Medline (from 1966), CINAHL (from 1982), the Cochrane Database of Systematic Reviews up to December 2003 and The International Society of Lymphology Congress Proceedings. The terms lymphoedema, chronic oedema, prevalence, incidence and epidemiology were used. Filarial lymphoedema was omitted from the search as it was felt to be beyond the scope of this review.

\textbf{Primary lymphoedema}

At present there are no published figures to confirm prevalence and incidence of primary lymphoedema. However, a small number of audits and reviews in the UK have provided some evidence on the numbers of patients with primary lymphoedema of those attending lymphoedema clinics. A national study by the British Lymphology Society reported that 8\% of 603 patients newly referred to 27 UK lymphoedema clinics over a three-month period suffered from primary lymphoedema.\textsuperscript{24} Williams \textit{et al.} estimated that 12\% of the 714 patients attending a lymphoedema clinic over the previous five years suffered from primary lymphoedema.\textsuperscript{25} Furthermore, an audit of the 908 patients attending a clinic over a four-year period, reported 218 (24\%) having non-cancer lymphoedema.\textsuperscript{26} Of these 218, 62 (28\%) were diagnosed with primary lymphoedema, although only 14 had unequivocal evidence of a primary lymphatic disorder, the remainder having a history suggestive of a primary lymphatic cause. However, those already attending clinics are likely to represent 'the tip of the iceberg' and it is likely that patients with primary disease will be under-represented due to poor diagnosis and services that often concentrate on patients with cancer related disease. This is illustrated by the long lead time from disease onset to referral for treatment.\textsuperscript{24}

Other studies outside the UK have adopted a more epidemiological approach to investigations of primary lymphoedema. A retrospective evaluation of primary lymphoedema in Minnesota (USA) between 1955 and 1974 estimated an annual incidence rate of 1.15/100 000 in the population aged under 20.\textsuperscript{27} More recently, a national epidemiological study in Spain surveyed 308 centres such as surgical and vascular units.\textsuperscript{28} From 2743 people with lymphoedema identified by these units, 1009 (36.8\%) were reported as having primary lymphoedema. Of these, 2\% were recognised as having congenital lymphoedema (present from birth), 30\% were estimated to have lymphoedema praecox (swelling developing around puberty) and 68\% were reported as having lymphoedema tarda (lymphoedema developing in later life). The apparently high number with lymphoedema tarda indicates that many of these may in fact have secondary lymphoedema.

\textbf{Lipoedema}

Rudkin and Miller reviewed 250 cases of lower limb lymphoedema and showed that around 4\% exhibited unique characteristics representative of lipoedema, a condition distinct from lymphoedema but often diagnosed as primary lymphoedema.\textsuperscript{29} Again, there are no clear figures indicating the numbers affected by this condition that is frequently associated with, but often mistaken for, lymphatic insufficiency.
Secondary non-cancer-related swelling

There may be a range of factors contributing to the development of lymphoedema, including chronic venous disease, trauma, inflammation, infection and conditions such as arthritis. However, prevalence and incidence data on these secondary causes are limited. One small study in the UK explored the prevalence of oedema in leg ulcer patients in hospital and the community.\(^{30}\) It suggested that oedema was present in 55% of the 56 patients, although the prevalence in the community-based patients was much greater at 77%. Another study of 689 chronic leg ulcers identified 17 cases of ulceration due to lymphoedema.\(^{31}\)

Blankfield et al. investigated the causes of bilateral leg oedema in 45 primary care patients in the USA.\(^{32}\) Investigation with ECG and duplex scan of the legs identified 33% with cardiac cause, 42% with pulmonary hypertension and 22% with venous insufficiency. Other causes of leg swelling included medication, nephrotic syndrome and hypoalbuminemia. The researchers concluded that leg swelling, particularly in those over 45-years-old, requires investigation as problems such as congestive cardiac failure and pulmonary hypertension are poorly recognised, particularly in their early stages.

Cancer-related lymphoedema

Lymphoedema related to cancer and/or cancer treatment may be readily identified as patients usually have an obvious clinical history and have regular follow up after their cancer treatment. In the audit by Sitzia et al.,\(^{24}\) 80% of the 603 newly assessed patients were estimated to have cancer-related lymphoedema, this group suffering from swelling for a much shorter period than those with primary lymphoedema.

Lymphoedema is most commonly associated with surgery and/or irradiation to the lymph nodes. Shaw and Rumball reviewed the case notes of 208 patients who underwent cervical, axillary or inguinal lymphade-nectomy in order to study the incidence of complications.\(^{33}\) Their classification distinguished between early (less than one month) and late (more than one month) onset. They reported an overall incidence of late lymphoedema as 14.9% and identified lymphoedema as the most common long-term complication, particularly in patients who underwent groin dissection. The study did not identify how lymphoedema was defined or measured.

Breast cancer-related lymphoedema

In 1921, Halstead recognised the problems of arm swelling following breast surgery and assumed this ‘surgical elephantiasis’ was due to streptococcal infection.\(^{34}\) A summary of the literature on breast cancer related lymphoedema is given in Table 1.\(^{15,18,21–23,42–66}\)

It is clear from Table 1 that there have been a large number of investigations of breast cancer related lymphoedema. The majority of these studies have attempted to identify factors in the treatment of the breast cancer that predispose patients to develop lymphoedema. The studies indicate that there is a wide range of incidences, much of which may be explained by differences in case definition and sampling procedures. There appear to be a number of themes around the risk factors associated with lymphoedema development, particularly, the use of irradiation,\(^{15,36,37,39,45,47,49,54–56}\) the extent of axillary node dissection,\(^{35,36,40,54,56,59–61,63,65,66}\) combined axillary surgery and irradiation,\(^{22,41,43,46,48,50,51,60,62}\) obesity,\(^{21,35,36,45,57,61}\) surgical wound infection,\(^{37,40,45,57}\) tumour stage and extent of surgery.\(^{21,48,49,51,56}\)

Despite improvements in surgical technique it is difficult to see reductions in the incidence of lymphoedema, with more recent studies still exhibiting high rates of development in excess of 30% of women treated.\(^{18,63,64}\) However, this may be a consequence of detecting more mild cases in isolated parts of the arm, such as the hand or forearm.\(^{18}\)

Lymphoedema secondary to groin dissection

The study by Shaw and Rumball reported a 40% incidence of lymphoedema following groin dissection confirming a previous study of 55% of 90 patients who underwent ilioinguinal dissection.\(^{33,67}\) When 33 of the previous 90 patients were followed up at a review clinic, 26 (79%) reported some experience of swelling, often worse in the first six months after surgery. Twenty-two (67%) of the 33 patients had persistent lymphoedema at the time of review, a follow up period ranging from one to eight years post-treatment.

Lymphoedema secondary to malignant melanoma

Commonly the management of malignant melanoma involves ilio-inguinal lymph node dissection and a study from 1977 reported a lymphoedema incidence of up to 80% in these patients.\(^{68}\) Other studies have identified lymphoedema in 23 and 26% of patients, respectively and
Table 1  Summary of papers/studies of breast cancer-related lymphoedema and reported risk factors

<table>
<thead>
<tr>
<th>Author/s and dates</th>
<th>Details</th>
<th>Reported incidence</th>
<th>Measurement method</th>
<th>Definition of oedema</th>
<th>Risk factors described</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fitts et al. (1954)53</td>
<td>Review of papers and study of 130 women following radical mastectomy</td>
<td>8–95% (reviewed papers). 49% (study group)</td>
<td>Clinical examination</td>
<td>Not defined</td>
<td>Obesity; number of axillary nodes removed; wound margin necrosis</td>
</tr>
<tr>
<td>Treves (1957)36</td>
<td>Study of 768 women following mastectomy</td>
<td>41%</td>
<td>Circumferential measurements</td>
<td>≥3 cm Circumference increase compared with contralateral limb</td>
<td>Axillary surgery; obesity; irradiation</td>
</tr>
<tr>
<td>Britton and Nelson (1962)37</td>
<td>Review of 19 papers 1908–1960 and study of 114 lymphoedema patients</td>
<td>6.7–62.5% (reviewed papers)</td>
<td>Circumferential measurements</td>
<td>≥2 cm Circumference increase compared with contralateral limb</td>
<td>Post-op wound complications; delayed healing; cellulitis; irradiation damage to skin</td>
</tr>
<tr>
<td>Howell-Hughes and Patel (1966)38</td>
<td>Review of 11 papers 1944–1960</td>
<td>41–80%</td>
<td>Not discussed</td>
<td>Not defined</td>
<td>Lymphatic and venous obstruction due to fibrous tissue irradiation; inadequate nutrition leading to delayed wound healing</td>
</tr>
<tr>
<td>Markowski et al. (1981)39</td>
<td>Study of 58 women following mastectomy; 39% had irradiation</td>
<td>31%</td>
<td>Circumferential measurements at five sites</td>
<td>≥1.5 cm Circumference increase at two or more sites compared with contralateral limb</td>
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<tr>
<td>Penzer et al. (1986)40</td>
<td>Study of 74 women following breast conserving surgery and breast irradiation; 86% had axillary node dissection (AND) and 24% had axillary irradiation</td>
<td>14% overall; 7% (those &lt;60 years) 25% (those &gt;60)</td>
<td>Circumferential measurements at two sites (forearm and upper arm)</td>
<td>≥2.5 cm Circumference increase compared with contralateral limb or pitting oedema in dorsum of hand</td>
<td>Age &gt;60 years; axillary node dissection; wound infection; surgical splitting of pectoralis minor muscle in &gt;60 years</td>
</tr>
<tr>
<td>Rytov et al. (1988)41</td>
<td>Study of 57 patients following mastectomy; 23% had irradiation</td>
<td>11% (surgery alone); 46% (surgery and irradiation)</td>
<td>Circumference 10 cm above epicondyle</td>
<td>≥2.5 cm Circumference increase compared with contralateral limb</td>
<td>Adjuvant irradiation in those with metastatic axillary nodes</td>
</tr>
<tr>
<td>Badr El Din et al. (1989)42</td>
<td>Review of files of 100 patients with stage 3 breast cancer treated 1974–1988; all had neo-adjuvant irradiation and 74% had neo-adjuvant chemotherapy; 92% had mastectomy</td>
<td>22%</td>
<td>Not discussed – case study review</td>
<td>Not defined</td>
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<tr>
<td>Aitken et al. (1989)43</td>
<td>Study of 94 patients; 42% had mastectomy and axillary clearance; 58% had mastectomy and axillary sampling and 52% of these had irradiation</td>
<td>8–32%</td>
<td>Circumference at 15 cm above and 10 cm below olecranon</td>
<td>Not defined</td>
<td>Combined axillary surgery and irradiation</td>
</tr>
<tr>
<td>Hoe et al. (1992)44</td>
<td>Study of 118 patients; 51% had mastectomy and axillary clearance; 49% had wide local excision and axillary clearance then breast irradiation</td>
<td>7.6%</td>
<td>Water displacement</td>
<td>≥200 ml Increase compared with contralateral limb</td>
<td>Similar risk with axillary sampling and clearance</td>
</tr>
<tr>
<td>Segerström et al. (1992)45</td>
<td>Study of 136 women following mastectomy and AND; 63% had irradiation</td>
<td>21–89% (depending on factors studied)</td>
<td>Water displacement</td>
<td>≥150 ml Increase compared with contralateral limb</td>
<td>Obesity; oblique skin incision; infection; irradiation</td>
</tr>
<tr>
<td>Thompson et al. (1995)46</td>
<td>Study of 121 patients following wide local excision and axillary surgery; 61% had irradiation</td>
<td>21% (axillary sampling); 30% (axillary sampling and irradiation); 29% (axillary clearance); 54% (axillary clearance and irradiation)</td>
<td>Water displacement, Circumferences at 10 cm distal and 15 cm proximal to olecranon</td>
<td>≥200 ml Increase compared with contralateral arm</td>
<td>Combined axillary surgery and irradiation</td>
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Table 1 (Continued)

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<tr>
<td>Ferrandez et al. (1996)</td>
<td>Study of 683 women following mastectomy, axillary node sampling and irradiation</td>
<td>41%</td>
<td>Circumference at eight sites on arm</td>
<td>≥ 1.5 cm Circumference increase at two or more adjacent sites compared with contralateral limb</td>
<td>Axillary irradiation; delayed wound healing; thoracic fibrosis</td>
</tr>
<tr>
<td>Kissin et al. (1996)</td>
<td>Study of 200 patients following mastectomy (35%) or wide local excision (WLE) (65%); 44% had irradiation</td>
<td>8.3% (axillary irradiation); 9.1% (axillary sampling and irradiation); 7.4% (axillary clearance); 38.3% (axillary radiotherapy and irradiation)</td>
<td>Circumference at 15 cm above lateral epicondyle and water displacement</td>
<td>≥200 ml Increase compared with contralateral limb</td>
<td>Combined axillary surgery and irradiation; breast irradiation; nodal status; tumour stage</td>
</tr>
<tr>
<td>Mortimer et al. (1996)</td>
<td>Review of 1077 women following mastectomy (93%) and WLE (7%) for unilateral breast cancer without recurrence; 467 (43%) had irradiation</td>
<td>28–38%</td>
<td>Self reported questionnaire – method validated</td>
<td>Self reported</td>
<td>Irradiation; mastectomy has greater risk than WLE</td>
</tr>
<tr>
<td>Suneson et al. (1996)</td>
<td>Study of 362 women with breast cancer comparing those treated in 1983 (94% mastectomy; 6% WLE) and those treated in 1988 (71% mastectomy; 29% WLE); irradiation in 48% (1983) and 52% (1988)</td>
<td>8–15%</td>
<td>Not discussed</td>
<td>Not defined</td>
<td>Number of +ve axillary lymph nodes; combined axillary dissection and irradiation</td>
</tr>
<tr>
<td>Schunemann and Willich (1997)</td>
<td>Study of 5868 women treated 1972–1995; various combinations of surgery and irradiation</td>
<td>44.4% (overall); 22.3–44.4% (depending on cancer treatment)</td>
<td>Circumferential measurements 10 cm above and 10 cm below olecranon</td>
<td>≥2 cm Circumference increase compared with contralateral limb</td>
<td>Combined surgery and irradiation; radical breast surgery</td>
</tr>
<tr>
<td>Petrek and Heelan (1998)</td>
<td>Review of seven papers and study of 272 women treated 1976–78</td>
<td>6–30% (reviewed papers); 28% (study group)</td>
<td>Self reported circumferential measurements at two sites below and above the olecranon – method validated</td>
<td>Not identified</td>
<td>Not identified</td>
</tr>
<tr>
<td>Kissane et al. (1999)</td>
<td>Study of 303 women treated for early stage breast cancer</td>
<td>4.3%</td>
<td>Water displacement</td>
<td>Not identified</td>
<td>Not identified</td>
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<tr>
<td>Berlin et al. (1999)</td>
<td>Study of 226 women following mastectomy in 1979–1983 (five year follow up); unknown number had irradiation</td>
<td>20%</td>
<td>Water displacement</td>
<td>≥100 ml Increase compared with contralateral limb</td>
<td>+ve axillary lymph nodes requiring irradiation</td>
</tr>
<tr>
<td>Hajri et al. (2000)</td>
<td>Study of 84 women following mastectomy and axillary node dissection for stage 1 and 2 breast cancer; high risk patients had adjuvant irradiation and/or chemotherapy</td>
<td>26% (subjective report)</td>
<td>Circumference 15 cm above and 10 cm below the olecranon. Also used nine circumferential measures to calculate volume</td>
<td>≥200 ml Increase compared with contralateral limb</td>
<td>Axillary dissection; non-significant increased risk in irradiated group</td>
</tr>
<tr>
<td>Tengrup et al. (2000)</td>
<td>Study of 110 women T1, N0 staging following mastectomy and axillary dissection; 68% had irradiation</td>
<td>19%</td>
<td>Self reported and water displacement</td>
<td>Not defined</td>
<td>Not defined</td>
</tr>
<tr>
<td>Edwards (2000)</td>
<td>Study of 201 women treated 1994–6; 57% had mastectomy (22% irradiated); 43% WLE (72% irradiated)</td>
<td>11%; (23.4% subjective)</td>
<td>Water displacement and self reported. Volume adjusted to address natural asymmetry of arms</td>
<td>≥10% Increase in arm volume in relation to pre-operative volume</td>
<td>High BMI; axillary surgery; mastectomy &gt;risk than WLE; tumour size and grade</td>
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<td>Herd-Smith et al. (2001)</td>
<td>Study of 1278 women; mastectomy (24%); 19% had WLE and axillary node dissection without irradiation; 57% had WLE, axillary node dissection and breast irradiation</td>
<td>15.9%</td>
<td>Arm circumference six 6 sites to calculate% difference</td>
<td>&gt;5% Increase in sum of the differences between the two arms</td>
<td>Post-operative breast irradiation; T2 tumour classification; (&gt;30 lymph nodes removed borderline risk)</td>
</tr>
<tr>
<td>Petrek et al. (2001)</td>
<td>Study of 263 women treated 1976–8 and followed up over twenty years</td>
<td>13%; (49% self-reported)</td>
<td>Circumferences at four sites – self measurement</td>
<td>Circumference increase any one site compared with contralateral limb; ≥2 inches defined as severe but noted 50% had mild swelling defined as increase of &lt;0.5 inches</td>
<td>Infection; injury; weight gain</td>
</tr>
<tr>
<td>Duff et al. (2001)</td>
<td>Study of 100 women with unilateral breast cancer; 64% had mastectomy; 36% had WLE and axillary node clearance</td>
<td>10%</td>
<td>Optoelectronic volumeter</td>
<td>&gt;200 ml Increase compared with contralateral limb</td>
<td>No association between lymphoedema and type of surgery or number of lymph nodes removed</td>
</tr>
<tr>
<td>Sener et al. (2001)</td>
<td>Study of 420 women treated with mastectomy or WLE; 72% had sentinel lymphadenectomy (SL); 28% had level 1–2 axillary clearance due to metastatic disease in sentinel nodes</td>
<td>3% (SL); 17% (SL and axillary dissection)</td>
<td>'Arm measurements' taken pre- and post-operatively but no detail given</td>
<td>&gt;20% Volume increase compared to contralateral arm</td>
<td>Extent of axillary staging; tumour in upper outer quadrant of breast; post-operative trauma and/or infection to arm</td>
</tr>
<tr>
<td>Albrecht et al. (2002)</td>
<td>Study of 655 women following WLE and axillary dissection or irradiation; compared to others treated elsewhere with combined axillary surgery and irradiation</td>
<td>1% (axillary irradiation); 26% (axillary dissection)</td>
<td>Circumferential measurements – not detailed</td>
<td>&gt;1 cm Increase in circumference compared with contralateral arm (&gt;2 cm if dominant arm)</td>
<td>Axillary dissection in post-menopausal women</td>
</tr>
<tr>
<td>Kwan et al. (2002)</td>
<td>Study of 112 patients treated 1993–7 with WLE and breast irradiation or mastectomy; most had level 1 or 2 axillary dissection; high risk patients had irradiation to supravacular and axillary nodes</td>
<td>12.5%; 5% (axillary surgery); 30% (axillary surgery and irradiation)</td>
<td>Self report questionnaire, Water displacement, Circumferences at four sites</td>
<td>&gt;200 ml Increase compared with contralateral limb. Self reported</td>
<td>Axillary dissection and irradiation</td>
</tr>
<tr>
<td>Meric et al. (2002)</td>
<td>Study of 234 patients treated 1990–92 with WLE; all had breast irradiation; 88% had axillary dissection; 44% had irradiation to axillary and supravacular nodes</td>
<td>13.6%; 18% (surgery with breast and axillary irradiation); 10% (following surgery alone)</td>
<td>Circumferential measurements 10 cm above and 10 cm below lateral epicondyle, subjective reporting</td>
<td>Any increase in circumference compared to contralateral arm</td>
<td>Axillary node dissection; high body weight</td>
</tr>
<tr>
<td>Nagel et al. (2003)</td>
<td>Study of 106 women treated 1995–6; 73% had mastectomy; 27% had WLE; 10% had irradiation</td>
<td>13%</td>
<td>Water displacement, Circumference 15 cm above and 10 cm below olecranon, Questionnaire</td>
<td>&gt;200 ml Increase in volume compared to contralateral arm</td>
<td>Axillary lymph node dissection; adjuvant axillary irradiation</td>
</tr>
<tr>
<td>Querci della Rovere et al. (2003)</td>
<td>Study of 198 women following level 1 and 2 axillary dissection; with oedema for &gt;6 months; 20% had mastectomy and axillary dissection; 71% had WLE and AD; 10% had only AD</td>
<td>32.8%; (27.8% were mild to moderate); (5% were severe) Oedema seen in single sites but not affecting whole of arm in most cases e.g., hand, forearm</td>
<td>Circumferences at 15 cm above and 10 cm below elbow, Subjective assessment by patient, nurse and doctor</td>
<td>&gt;5% Increase in circumference compared to contralateral arm (mild); moderate = &lt;10%; severe = &gt;10%</td>
<td>Nodal status; affected dominant arm; right sided cancer increases risk of forearm oedema; non-consultant surgeon</td>
</tr>
</tbody>
</table>
Table 1 (Continued)

<table>
<thead>
<tr>
<th>Author/s and dates</th>
<th>Details</th>
<th>Reported incidence</th>
<th>Measurement method</th>
<th>Definition of oedema</th>
<th>Risk factors described</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geller et al. (2003)</td>
<td>Study of 145 women; 62% had WLE; 39% had mastectomy; 86% had AND; 67% had irradiation</td>
<td>38%</td>
<td>Self-reported (telephone interviews)</td>
<td></td>
<td>Age &lt;50 years; axillary node dissection; cytotoxic chemotherapy; work outside home; lower risk if treated for hypertension</td>
</tr>
<tr>
<td>Kornblith et al. (2003)</td>
<td>Study of 153 women followed up at 20 years post adjuvant chemotherapy; 66% had mastectomy; unknown number had irradiation</td>
<td>39%</td>
<td>Self-reported (telephone interviews)</td>
<td></td>
<td>None described</td>
</tr>
<tr>
<td>Powell et al. (2003)</td>
<td>Study of 714 women (727 arms) women with stage 1 and 2 breast cancer and treated with breast conservation surgery and breast irradiation; 32% had irradiation to axilla and supraclavicular nodes; 15% had level 1-3 axillary dissection</td>
<td>4.1%; 10.7% (axillary surgery and irradiation)</td>
<td>Circumference of forearm at 10 cm below olecranon</td>
<td>&gt;2 cm Increase in forearm circumference compared with contralateral limb. &gt;4 cm = severe</td>
<td>Combined axillary node surgery and irradiation</td>
</tr>
<tr>
<td>Golshan et al. (2003)</td>
<td>Study of 125 women (node negative at time of surgery); 62% had sentinel lymph node biopsy and 91% of these had irradiation; 38% had AND; 77% of these had irradiation</td>
<td>2.6% (sentinel node biopsy and axillary sampling); 27% (axillary node dissection)</td>
<td>Circumferences at 10 cm above and 10 cm below olecranon</td>
<td>≤3 cm Increase in circumference compared with contralateral arm</td>
<td>Axillary node dissection has greater risk than sentinel node biopsy</td>
</tr>
</tbody>
</table>
a previous review has indicated a 6–20% incidence of lymphoedema in patients following combined inguinal and pelvic lymph node dissection for stage III melanoma.69–71

Karakousis et al. studied 77 patients following groin dissection, mainly for malignant melanoma.72 They identified oedema in 21% of these patients and reported those who had a primary tumour of the lower leg to be significantly more likely to develop swelling. They also showed that those who wore compression garments post-operatively were less likely to develop swelling. The same author later studied 205 patients following groin dissection and suggested that all had some localized oedema of the anteromedial thigh, with around 40% having swelling of the lower leg.73 Interestingly, Urist et al. also suggested lymphoedema to be mostly confined to the thigh.70

Strobbe et al. studied 71 patients with positive iliac and/or obturator fossa nodes, reporting mild/moderate lymphoedema in 19% and severe lymphoedema in 6% of patients.74 A study by Serpell et al. reviewed 73 lymphadenectomies in 64 patients, showing lymphoedema to be more common after groin dissection, occurring in 29% of patients following inguinal surgery compared to 6% of axillary dissections.75 This study defined lymphoedema as post-operative swelling persisting beyond three months and highlighted the use of post-operative prophylactic measures, such as seven days bed rest and six months use of below knee compression hosiery to reduce the risk of lymphoedema. To reduce the risk of lymphoedema, Wrone et al. suggest that sentinel node biopsy is associated with a 1.7% incidence of lymphoedema and Lawton et al. have described the use of a fascia-preserving technique when complete lymphadenectomy is indicated.76,77 This study reported permanent oedema in 8% of patients following axillary dissection and 14% of those having groin dissection. A transient oedema was also present in 48% of the groin dissection group, resolving over a median of twelve months. Factors including obesity, post-operative seroma and occult metastases have been described as contributing to the risk of lymphoedema in this group.75,76

Lymphoedema secondary to genitourinary cancers

There is limited literature on this subject and Okeke et al. suggest that lymphoedema is uncommon from cancers of pelvic genitourinary organs, such as kidney and testes.78 However, in patients with advanced disease and complications, such as recurrence or pelvic tumour mass obstructing venous and lymphatic return, gross oedema of the legs and genitalia will often occur. Worldwide, the problem of genital lymphoedema is most common secondary to filariasis and is also associated with primary cancer-related lymphoedema and traumatic injury.79–87 Soto et al. reported lymphoedema in 100% of men following inguinal dissection for penile carcinoma.82 Martin Martinez et al. have also shown lymphoedema in 28.5% of these patients following inguinal lymphadenectomy and Ornellas et al. have reported a figure of 16% in this same group.84,85 Male circumcision has also been shown to be associated with lymphoedema.88

Henningsohn et al. have recently described the development of swelling or heaviness in the legs or lower abdomen in 20% of those following radical radiotherapy compared to 10% of those who had radical cystectomy and urostomy for carcinoma of the bladder.89 They indicated that lymphoedema is a minor problem in this group.

Lymphoedema secondary to gynaecological cancers

Nesvold et al. cited a lack of information after gynaecological surgery causing a delay in diagnosis and treatment of lymphoedema.90 In this study, 83 patients reported a 20% incidence of swelling following treatment for cervical and vulval cancers, similar to findings reported in other studies of these patients.91,92 In vulval cancer treatment, Leminen et al. established lymphoedema to be more common in women suffering a wound infection following radical vulvectomy including groin dissection, occurring in 48% of patients.93 Gould et al. also showed a 29.5% incidence in patients undergoing inguinal lymphadenectomy in the treatment of vulvar carcinoma similar to the 28% incidence reported by other authors.94,95 Preservation of the saphenous vein during inguinal lymphadectomy has been advocated as decreasing morbidity in relation to chronic oedema in this patient group in one study.96 Lymphoedema has also been shown to occur in three of 80 patients receiving palliative radiotherapy for ovarian cancer, although research is limited.97

More substantial literature is available in relation to cervical cancer. One study reported lymphoedema leading to distress in 14% of patients, regardless of whether surgery or surgery combined with radiotherapy was used.98 Relatively low rates (1%) of ‘severe’ lymphoedema have also been reported, although how severity was established is not specified.99 Martimbeau et al. studied 402 patients following treatment for Stage IB cervical cancer showing that 23.4% developed some degree of lymphoedema.100 A similar result was reported in a study by Gerdin et al. (21%) following hysterectomy and radiotherapy, where the risk of lymphoedema was also associated with external pelvic irradiation.101 Fiorica et al. also studied patients following treatment for Stage IB cervical cancer, with a median follow-up time of
Lymphoedema secondary to sarcoma treatment

Two studies of lymphoedema following sarcoma treatment have been reviewed. Lampert et al. observed 40 patients who had received wide local excision and radiotherapy, at least two years previously.109 They measured oedema using finger pressures to identify skin pitting and subjectively estimated that approximately 50% had some degree of oedema. Robinson et al. studied 54 patients at least two years post-treatment of soft tissue sarcoma of the lower limb or pelvis.110 Lymphoedema was assessed by pinch test and Stemmer's sign and categorized according to its extent up the limb. Lymphoedema was identified in 16 (30%) of the patients, although 21 (39%) had experienced swelling at some time. Interestingly, the authors discuss their rationale for avoiding limb circumferential measures suggesting these may be skewed by previous surgery.

Conclusion

This review highlights limitations in the current literature, both in terms of quality of studies and lack of sound incidence and prevalence data. Critical reviews of methods used raise awareness and insight into how subsequent research might be conducted and where the possible pitfalls may lie. There are still a number of areas to be addressed, namely the accurate identification of lymphoedema and the diagnostic criteria for making differential diagnoses between different types of lymphoedema and chronic oedemas. There is also a need to consider other problems not highlighted in previous studies, such as breast oedema. There is clearly a need to produce sound incidence data on particular ‘high risk’ groups, as these will contribute to the pool of new patients. This prevention and early detection strategy may help to prevent patients developing morbidities associated with the more chronic and severe conditions of some lymphoedema types. These data will also contribute to our understanding of the long-term impact of this progressive condition and provide direction for future service development.

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69 Ingvar C, Erichsen C, Jonsson PE. Morbidity following prophylactic and therapeutic lymph node dissection for melanoma — a comparison. Tumori 1984; 70: 529–33.


312  AF Williams et al.


