# Clinical staging and conservative management of peripheral lymphedema

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## INTRODUCTION

Lymphedema is defined as accumulation of fluid and fibroadipose tissues due to disruption of lymphatic flow. Lymphedema can be primary (congenital lymphedema, lymphedema praecox, lymphedema tarda) or, more commonly, secondary (ie, acquired) ( table 1). The main underlying causes of secondary lymphedema include interruption of lymphatics by surgery and/or radiation therapy (RT), malignant obstruction of the lymphatics, and infection. Lymph node dissection and/or radiation of the axilla or groin region for breast cancer or melanoma are the most common causes of secondary lymphedema in developed countries, while filariasis is the most common cause of secondary lymphedema worldwide.

Conservative, multimodal therapy for lymphedema consists of general measures for monitoring and self-care, which are applicable to all stages of lymphedema, along with varying levels of compression therapy and physiotherapy, with the choice of specific management dependent upon the clinical stage of disease (mild, moderate, severe).

Conservative therapies for managing lymphedema based upon its clinical severity are reviewed here. The clinical manifestations and diagnosis of lymphedema and surgical treatment of lymphedema are discussed separately. (See "Clinical features and diagnosis of peripheral lymphedema" and "Surgical treatment of primary and secondary lymphedema".)

## CLINICAL CLASSIFICATION

**Clinical stage** — We suggest using the staging system of the International Society of Lymphology (ISL) to characterize the severity of lymphedema [1]. Several other classification systems are also used to describe the severity of lymphedema, including the Campisi staging system ( table 2), and those of the American Physical Therapy Association (APTA) and the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE) [2,3]. These schemes generally only refer to the physical condition of the extremity. Classifications that may also include physiologic or genotypic information are evolving. These classifications describe the physical condition of the extremity. (See "Clinical features and diagnosis of peripheral lymphedema", section on 'Extremity measurements'.)

The International Society of Lymphology (ISL) combines two criteria to diagnose and classify lymphedema: the "softness" or "firmness" of the limb (reflecting fibrotic soft tissue changes) and the outcome after elevation. Stage "0" lymphedema is a subclinical or latent condition where swelling is not evident despite impaired lymphatic transport. Within stages I through III, severity is based upon volume differences, which are assessed as mild (<20 percent increase), moderate (20 to 40 percent increase), or severe (>40 percent increase) [1].

- Stage 0 – Stage 0 (or Ia) lymphedema is a subclinical or latent condition where swelling is not yet evident despite impaired lymph transport, subtle alterations in tissue fluid/composition, and changes in subjective symptoms. Most patients are asymptomatic, but some report a feeling of heaviness in the limb. Stage 0 can be transitory or may exist months or years before overt lymphedema occurs (ie, stage I, II, or III below).

- Stage I – Stage I lymphedema represents an early accumulation of fluid relatively high in protein content (in comparison with "venous" edema) that subsides with limb elevation, usually within 24 hours ( picture 1). Pitting may occur. An increase in various types of proliferating cells may also be seen. This is sometimes called reversible edema. Stage I corresponds to a mild grade of lymphedema above.

- Stage II – Stage II lymphedema involves more changes in solid structures, limb elevation alone rarely reduces tissue swelling, and pitting is manifest ( picture 2). Later in Stage II, the limb may not pit as excess subcutaneous fat and fibrosis develop. This is sometimes called spontaneously irreversible lymphedema. Stage II corresponds roughly to a moderate grade of lymphedema above.

- Stage III – Stage III lymphedema encompasses lymphostatic elephantiasis where pitting can be absent and trophic skin changes such as acanthosis, alterations in skin character

and thickness, further deposition of fat and fibrosis, and warty overgrowths have developed ( picture 3). Stage III corresponds to a severe grade of lymphedema above. It should be noted that a limb may exhibit more than one stage, which may reflect alterations in different lymphatic territories.

**Extremity girth** — The American Physical Therapy Association (APTA) uses girth as an anthropometric measurement to classify lymphedema. The maximum girth difference between the affected and unaffected limb (typically upper extremity) is used to determine the class of lymphedema [2] (see "Clinical features and diagnosis of peripheral lymphedema"):

- Mild lymphedema – Maximum girth difference <3 cm
- Moderate lymphedema – 3 to 5 cm difference
- Severe lymphedema – Difference >5 cm

The International Society of Lymphology notes that some clinicians use volume differences (VD) between the affected limb and the normal contralateral limb (equally applicable to upper and lower extremities) to define the severity of lymphedema as mild: VD >10 percent but less than <20 percent; moderate: VD 20 to 40 percent; and severe: VD >40 percent [1].

**Clinical grade** — The National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) categorizes lymphedema based upon exam findings and the presence of functional impairment [3]. These correspond roughly to the clinical stages described below.

- Grade 1 – Trace thickening or faint discoloration
- Grade 2 – Marked discoloration, leathery skin texture, papillary formation, limiting instrumental activities of daily living (ADL)
- Grade 3 – Severe symptoms limiting self-care and activities of daily living

## OVERVIEW OF MANAGEMENT

Lymphedema is a chronic condition that can be managed but is generally not cured [1]. Lymphedema is often difficult to treat, particularly if progression to later stages has already occurred [4]. Left untreated, lymphedema tends to gradually progress over time and inhibits the activities of daily living [5]. Lifelong care, in combination with psychosocial support, is necessary to achieve optimal outcomes. The mainstay of treatment is conservative, typical multimodal therapy, which is aimed at improving patient comfort and reducing limb volume, since the

underlying disease cause cannot usually be corrected [1,6]. Conservative treatments are best administered in clinics with expertise in the treatment of lymphedema. A limited number of patients who fail conservative treatment options may be candidates for surgical therapy, which may include lymphatic surgery, or soft tissue reduction. (See 'Surgical referral' below and "Surgical treatment of primary and secondary lymphedema".)

Conservative, multimodal therapy consists of general measures for self-care (eg, monitoring, skin care, weight reduction), which are applicable to all stages of lymphedema, along with varying levels of compression therapy (compression bandaging, compression garments, intermittent pneumatic compression) and physiotherapy (manual lymphatic drainage, complete decongestive therapy), with the choice of specific intervention depending upon the stage of disease (mild, moderate, severe) [1,7-9]. It is important to note that there is limited and predominantly low-quality evidence to support any of the treatment options discussed below [1,7,8,10]. For moderate-to-severe lymphedema, we agree with the consensus statement from the ISL and others that recommend complete decongestive therapy, as a multimodality regimen [1,6]. (See 'General measures' below and 'Compression therapy' below and 'Physiotherapy' below.)

**General measures** — General measures for self-care are aimed at minimizing the degree of edema and slowing the rate of progression. Although there is no scientific evidence supporting the efficacy of any of these measures, we agree with the guidelines from the International Society of Lymphology (ISL) that suggest self-monitoring, limb elevation, maintenance of ideal body weight, avoidance of infection/injury, and avoidance of constricting garments/extremity cuffs for all patients with lymphedema regardless of severity, and for those at risk for lymphedema following surgery [1,11].

**Self-monitoring** — Patients should be taught how to monitor their lymphedema, including serial measurement of limb circumference. They should be counseled to promptly report any changes in size, sensation, color, temperature, or skin condition.

**Limb elevation** — Simple elevation of a lymphedematous limb may reduce swelling, particularly in the early stage of lymphedema [1]. However, elevation alone is not an effective long-term therapy [12]. Patients should avoid positioning the limb in a gravity-dependent position for prolonged time periods; this includes prolonged standing, sitting, or crossing legs.

**Diet and exercise** — Maintenance of ideal body weight should be encouraged. Besides being a contributory factor for the development of lymphedema, obesity may also limit the effectiveness of compression pumps or sleeves [13,14]. Exercise and weight training are generally safe and should be allowed, with a properly fitted compression garment worn during

exercise. In a small trial, 21 patients with breast-cancer-related lymphedema were randomly assigned to dietary advice for weight reduction or to receive a booklet on general healthy eating [14]. At the end of the 12-week study, the weight reduction group experienced a significant reduction in body weight, body mass index, and excess arm volume compared with the control group. (See "Clinical features and diagnosis of peripheral lymphedema", section on 'Obesity'.)

Following axillary or groin lymph node dissection, exercise is safe, and exercises are generally recommended to restore the full range of motion in the affected extremity [1,10,15-18]. A small study of patients with lower extremity lymphedema following cancer surgery found no significant difference between limb volume differences before and after lower extremity weight training (ie, volume not exacerbated) [19]. A systematic review also found evidence that progressive resistance exercise therapy does not appear to increase the risk of developing lymphedema following breast surgery [10]. However, in contrast to early studies, which did not recommend exercise during the immediate recovery phase of lymph node surgery and/or radiation therapy (because of concerns that the increase in blood flow may worsen the edema) [17], this later review did not find any evidence to suggest a higher risk of lymphedema when starting shoulder mobilizing exercises early after breast surgery compared with a more delayed start (ie, seven days after surgery) [10].

For patients with established lymphedema, participation in sports involving repetitive movements against resistance, such as rowing, tennis, or golf, has traditionally been discouraged. However, there is accumulating evidence from randomized trials of the safety of exercise and weight training in the affected limb and of other benefits associated with exercise, such as improvements in cardiovascular fitness and quality of life [17,19-23]. One trial compared twice-weekly progressive weight lifting to no lifting over a one-year period (supervised for the first 13 weeks) in 141 breast cancer survivors with stable lymphedema of the arm [22]. Weightlifting reduced the number and severity of arm and hand symptoms, increased muscular strength, and significantly reduced the incidence of lymphedema exacerbations (14 versus 29 percent). For patients with lower extremity lymphedema, weight training did not affect limb volume at five months, but bench press and leg press strength increased, and there were improvements in walking distance; however, no improvement was seen in quality of life [19].

The National Lymphedema Network position statement for exercise recommends that individuals with lymphedema wear a properly fitted compression garment during exercise, including aerobic and resistive training, while individuals at risk for developing lymphedema may consider obtaining a compression garment [11]. (See 'Compression garments' below.)

**Avoid skin infection/injury** — Meticulous skin hygiene and nail care should be maintained to prevent a portal of entry for infection that may result in cellulitis. Patients should be encouraged to use skin moisturizers and topical antibiotic solutions after small breaks in the skin as may be induced by a paper cut or abrasions, pinpricks, insect bites, or pet scratches. Exposed skin should be protected, including use of sunscreen and wearing of gloves while doing activities that may cause skin injury. Similarly, whenever possible, patients should avoid medical procedures in the affected limb that might introduce infection, such as vaccination, acupuncture, phlebotomy, intravenous lines, and venography. The patient should also avoid exposure to temperature extremes, which may increase the risk of injury to the tissue in the lymphedematous limb. In addition, lymphedema may be exacerbated in patients who use saunas, steam baths, or hot tubs.

All episodes of cellulitis should be treated. Antibiotics that have adequate coverage for gram-positive cocci should be promptly administered for cellulitis. Severe cellulitis, lymphangitis, or bacteremia requires intravenous antibiotics. If patients experience three or more episodes of cellulitis in a year, we suggest an extended period of oral antibiotic therapy. (See "Acute cellulitis and erysipelas in adults: Treatment".)

**Avoid limb constriction** — Recommendations to avoid limb constriction (eg, tight fitting clothing, blood pressure cuffs) are pervasive but are based on limited scientific evidence [24]. Those who support limb constriction as a risk factor for developing lymphedema hypothesize that constriction (no matter how brief) can increase pressure in the limb, increasing lymph production, and potentially leading to stenosis and fibrosis of the lymphatic vessels. On the other hand, others have challenged recommendations to avoid limb constriction, observing that limb compression is commonly used in the management of lymphedema.

For patients with lymphedema or significant risk factors for its development (eg, axillary node dissection), we support a recommendation to measure blood pressure in the contralateral arm, particularly in any setting in which blood pressure is being closely monitored (eg, in an intensive care unit, recovery room, or during procedures). This recommendation is based upon several factors. Blood pressure measurement in an enlarged extremity will be inaccurate if the cuff is not properly sized, and the cuff causes a high-pressure focal compression (in contrast to pneumatic compression devices used for lymphedema treatment, for which the compression is applied sequentially) [25,26]. Among the rare patients who have undergone bilateral axillary lymph node dissection, routine blood pressure measurements can be obtained in the lower extremity. If the patient has had bilateral axillary lymph node dissection and there is not an option of obtaining blood pressure measurements in the lower extremity, then a manual (but not automatic) blood pressure cuff can be used intermittently, but inflated to only just above

the expected level of systolic blood pressure [25]. (See "Blood pressure measurement in the diagnosis and management of hypertension in adults", section on 'Leg blood pressure'.)

Patients who do not have lymphedema, or who have undergone sentinel lymph node biopsy rather than a full axillary lymph node dissection, may have blood pressure measurements taken from either extremity. One study prospectively investigated the association between factors thought to increase the risk for lymphedema in 632 patients treated for breast cancer and screened routinely for lymphedema [27]. On multivariate analysis, there was no significant association between increases in arm volume and blood pressure readings. Significant factors included body mass index ≥25, axillary lymph node dissection, regional lymph node irradiation, and cellulitis. There was no association between blood pressure readings on the ipsilateral arm and cellulitis. (See "Clinical features and diagnosis of peripheral lymphedema", section on 'Epidemiology and risk factors'.)

**Conservative treatment by severity** — Our approach to treatment of lymphedema is based upon severity.

**At risk for postoperative lymphedema** — For all patients who are at risk for lymphedema following surgery (ISL stage 0) ( table 3), in additional to general measures, we suggest physiotherapy to improve mobility.

The treatment of cancer-treatment-related lymphedema at a very early stage or even before it manifests may potentially prevent progression of the condition. (See 'Clinical stage' above.)

For patients treated by axillary lymph node dissection for breast cancer, the approach to and efficacy of prophylactic strategies including physiotherapy and compression are discussed elsewhere. (See "Breast cancer-associated lymphedema" and "Breast cancer-associated lymphedema", section on 'Exercise, physiotherapy and compression'.)

The technical approach to these strategies is discussed in the sections below. (See 'Techniques' below.)

**Mild lymphedema** — For all patients with mild lymphedema (ISL stage I) ( table 3), in addition to general measures, we suggest physiotherapy (simple lymphatic drainage, a commonly taught self-help maneuver) and compression garments. The degree of compression should be guided by the patient's vascular status and their ability to tolerate compression. (See 'General measures' above and 'Compression garments' below.)

For women following breast cancer surgery, the efficacy of compression therapy was illustrated in a randomized trial of 90 women with unilateral lymphedema that compared the use of

multilayered short-stretch bandaging for 18 days followed by elastic hosiery for 24 weeks versus the use of elastic hosiery alone for 24 weeks [28]. Combined therapy was approximately twice as effective in reducing limb volume (31 versus 16 percent at 24 weeks).

Manual lymphatic drainage is safe and may offer an additional benefit to compression therapy for reducing limb volume in those with lymphedema following breast surgery [29]. For symptoms such as pain and heaviness, 60 to 80 percent of participants reported feeling better regardless of which treatment they received [30-35].

**Moderate lymphedema** — For all patients with moderate lymphedema (ISL stage II) ( table 3), in additional to general measures, we suggest intensive physiotherapy, usually in the form of complete decongestive therapy, rather than less intense therapy, for those without specific contraindications. (See 'General measures' above and 'Complete decongestive therapy' below and 'Contraindications' below.)

The treatment of moderate lymphedema (stage II) is similar to that of mild lymphedema, but with a more intensive treatment schedule for physiotherapy and compression, and generally under the care of a physiotherapist, rather than self-directed. Patient compliance is required for long-term success. In one study evaluating patients with upper or lower extremity lymphedema, at least 90 percent of the lymphedema reduction was maintained in compliant patients at an average follow-up of nine months, while noncompliant patients lost approximately one third of the initial benefit [36]. (See 'General measures' above and 'Manual lymphatic drainage' below.)

For established lymphedema following breast cancer surgery, support for the efficacy of manual lymphatic drainage (MLD) comes from both observational studies [37-40], and from small randomized trials [30-34]. However, not all studies have found a benefit for MLD over standard management for reducing limb volume [35,41]. (See 'Mild lymphedema' above.)

However, MLD as a component of multimodal therapy in the form of complete decongestive therapy does appear to reliably reduce limb volume [42]. In observational studies, the reduction in limb volume ranged from 33 to 68 percent and was associated with improved pain, cosmesis, and/or function [36,37,43-48]. In a small phase III trial, 53 patients with lymphedema after breast cancer treatment were randomly assigned to complete decongestive therapy (MLD, multilayer compression bandaging, elevation, remedial exercise, and skin care) versus standard physiotherapy (bandages, elevation, head-neck and shoulder exercises, and skin care) [49]. The group receiving complete decongestive therapy had a significantly greater improvement in edema as measured by circumferential and volumetric measurements.

However, another trial suggested that the benefit is minimal for complete decongestive therapy compared with compression therapy as a first-line treatment for lymphedema [50]. In this trial, 95 female breast cancer survivors with lymphedema (defined as an absolute increase in arm volume of at least 10 percent between the affected and unaffected arm) were randomly assigned to complete decongestive therapy or the use of compression garments alone. Compared with compression garment use, complete decongestive therapy resulted in a significantly greater absolute reduction in arm volume (250 versus 142 mL), but the mean reduction in arm volume was not significantly different (29 versus 23 percent). There were no differences in severe adverse events, which consisted of a temporary rash or mild to moderate pain in the affected arm.

**Severe lymphedema** — For all patients with severe lymphedema (ISL stage III) ( table 3), in addition to general measures, we suggest intensive physiotherapy, usually in the form of complete decongestive therapy, rather than less intense therapy, for those without specific contraindications. (See 'General measures' above and 'Complete decongestive therapy' below and 'Contraindications' below.)

Patients with severe lymphedema may also benefit from intermittent pneumatic compression (IPC), in addition to general measures and intensive physiotherapy. If the lymphedema is controlled and can be reduced with IPC, a compression garment should be worn to maintain limb girth and prevent further swelling. (See 'Intermittent pneumatic compression' below.)

In early observational studies examining the benefit of IPC, limb measurements reduced with the use of this then novel device [4,51]. However, an early trial of 80 patients with mild-to-moderate lymphedema found no significant difference in limb circumference comparing pneumatic compression to controls (prophylactic hygiene only; 1.9 versus 0.5 cm) [52].

A number of subsequent studies evaluated the role of intermittent pneumatic compression, in combination with complete decongestive therapy, for moderate-to-severe upper extremity [34,38,52-55] and lower extremity lymphedema [56-61]:

- A benefit was illustrated in a trial of 27 patients with previously untreated lymphedema following treatment for breast cancer who were randomly assigned to complete decongestive therapy alone or with adjunctive IPC (30 minutes daily for 10 days) [54]. Combined therapy was associated with a significantly greater reduction in limb volume during initial treatment (45 versus 26 percent with complete decongestive therapy alone) [54]. A second randomization of the trial evaluated the efficacy of maintenance IPC therapy (self-administered 60 minutes daily) added to complete decongestive therapy in 11 patients with unilateral breast-cancer-associated lymphedema who had previously

been treated with a multimodality program of complete decongestive therapy [54]. At 6 to 12 months, a significant reduction in mean limb volume was found for combined therapy compared with an increased limb volume with complete decongestive therapy alone (-90 versus +33 mL).

- A benefit for pneumatic compression devices in patients with lymphedema was further supported by a retrospective review of 718 patients with lymphedema (374 with cancer and 344 without cancer) who were commercially insured and Medicare Managed care enrollees from a large national United States managed healthcare insurer and who received an Advanced Pneumatic Compression Device (APCD) between 2007 and 2013 [62]. Outcomes were compared for the 12 months before and after APCD purchase. Specifics regarding the severity of the lymphedema, whether it was upper or lower extremity, and the other modalities being applied for lymphedema treatment were not provided. In both the cancer and noncancer cohorts, use of an APCD was associated with a significant reduction in the rates of cellulitis (from 21 to 4.5 percent in the cancer cohort, and from 29 to 7 percent in the noncancer cohort), a decrease in the need for lymphedema-related manual therapy (from 59 to 41 percent in the cancer cohort, and from 53 to 31 percent in the noncancer cohort), and an overall reduction in total lymphedema-related costs per patient.

Thus, intermittent pneumatic compression appears to be an effective addition to a multimodality lymphedema treatment. However, given the logistical problems with application, particularly for patients with lower extremity lymphedema, we tend to reserve this therapy for patients with severe lymphedema. For patients with mild-to-moderate lymphedema, there is little need for IPC; however, it may be used as an adjunct in those with lower stage disease who are unable to perform self-manual drainage or in those with allergies to components of compression garments (eg, latex).

## TECHNIQUES

### Compression therapy

**Compression bandaging** — In early stages of lymphedema, external compression is used to diminish ultrafiltration and is achieved with repetitively applied, multilayered padding materials and short-stretch (also called low-stretch) bandages [6,28,63,64]. For more severe disease, compression bandaging is applied to the affected limb after manual lymphatic drainage is performed and is worn around the clock during the treatment phase (phase 1) of complete

decongestive therapy [6]. (See 'At risk for postoperative lymphedema' above and 'Mild lymphedema' above and 'Phases' below.)

Short-stretch bandages apply pressure during movement, but not at rest [6]. The pressure induced by muscle contraction within the bandage appears to reduce lymphedema via mechanical stimulation of the smooth muscle of the lymphatic vessels, resulting in increased lymph flow. The multilayered bandage may also soften the edematous tissue, thereby increasing the efficacy of manual lymphatic drainage.

A possible alternative to standard bandages is Kinesio tape (also called K-tape), which is made of a highly elastic woven fabric that stretches only along its longitudinal axis and has been used for rehabilitation after sports injuries [65,66]. An initial randomized trial of 41 patients with breast cancer and unilateral lymphedema of the arm found equivalent efficacy with K-tape and short-stretch bandages but better patient acceptance of K-tape, manifested by less difficulty in usage and increased comfort and convenience [65].

**Compression garments** — Once the lymphedema reaches its nadir, compression garments (lymphedema compression sleeve and gauntlet or hosiery) are used to provide maintenance therapy (phase 2 of complete decongestive therapy) to prevent fluid reaccumulation. (See 'Moderate lymphedema' above and 'Severe lymphedema' above and 'Phases' below.)

Fitted elastic knit two-way low-stretch compression garments generate greater pressures distally than proximally, thereby promoting mobilization of the edema fluid [6,67]. Compression garments deliver 20 to 50+ mmHg of pressure [1,6]. The highest compression tolerated by the patient is likely to be the most beneficial [1].

A prescription is necessary to obtain compression garments, and these garments need to be provided by a fitter with appropriate expertise. For the upper extremity, a compression hand piece, either a glove or a gauntlet, is necessary when wearing a compression sleeve to prevent swelling in the hand. Similarly, in the lower extremity the foot is an integral part of compression hosiery. It is important to note that compression bandages or garments may lead to the onset or progression of lymphedema if they are restrictive or not properly fitted. When correctly fitted and worn properly, compression garments may reduce swelling [68]. If off-the-shelf garments do not provide a proper fit, custom-made garments will be necessary. However, as fluid shifts occur, even custom-made garments may no longer fit. Garments should be replaced every three to six months or sooner if they lose elasticity. Use of compression garments during exercise is discussed below. (See 'Diet and exercise' above.)

Compression garments are typically worn during waking hours, with compression bandaging at night, if necessary [6]. Nighttime compression garments consist of padding materials with

compression applied over the padding with short-stretch bandages, elastic sleeves, or Velcro bandages.

**Intermittent pneumatic compression** — Intermittent pneumatic compression (IPC; also called sequential pneumatic compression) is another method of compression therapy. IPC may be most effective in addition to a multimodality lymphedema treatment. IPC may also be an alternative maintenance program for lymphedema patients who have difficulty in performing self-manual lymphatic drainage secondary to weakness, fatigue, or range of motion deficits. It may also be beneficial for lymphedema patients that are unable to use compression bandaging or garments due to skin allergies from the materials used in these compression products. (See 'Severe lymphedema' above.)

These devices use a plastic sleeve or stocking that is intermittently inflated over the affected limb. Most pneumatic compression pumps sequentially inflate a series of chambers in a distal-to-proximal direction. Some pumps permit adjustment of the amount of pressure in a particular chamber; however, for the management of patients with lymphedema, the ideal pressure for the pump is not known. Some investigators have suggested that a pressure greater than 60 mmHg may injure lymphatic vessels. IPC is usually applied daily or five times per week. The optimal duration of IPC is also unknown. Among the various studies, sessions have varied in length (90 minutes to as long as six hours) and duration (two to three days to four weeks) [4,28,34,51,52,54,69]. After external compression therapy is completed, a form-fitting, low-stretch elastic knit sleeve is usually applied to maintain edema reduction [1]. (See 'Compression garments' above.)

**Physiotherapy** — Manual lymphatic drainage (MLD) is a massage-like technique that is performed by specially trained physical therapists. A multimodality program combining MLD with meticulous skin and nail care, therapeutic exercise, and limb compression using repetitively applied multilayered padding materials and short-stretch bandages is referred to as complete decongestive therapy.

**Manual lymphatic drainage** — MLD is a massage-like technique that is performed by specially trained physical therapists [1,6]. Light pressure is used to mobilize edema fluid from distal to proximal areas in an attempt to enhance filling of the cutaneous lymph vessels, promote dilation and contractility of lymphatic conduits, and recruit watershed pathways for lymph flow. Upon completion of manual lymphatic drainage, patients should wear compression garments during waking hours and, as necessary, perform self-compression bandaging of the limb at night. (See 'Compression bandaging' above and 'Compression garments' above.)

Manual techniques such as MLD are typically included as a component of complete decongestive therapy despite the low quality of the evidence supporting benefit. There are some concerns that MLD may dislodge and promote the spread of tumor cells among those with secondary lymphedema related to cancer [1,45]. These concerns and other contraindications to manual lymphatic drainage are described below. (See 'Contraindications' below.)

Lymphatic drainage may also be promoted by gentle therapeutic exercise of the affected limb. When possible, patients and family members should be instructed on self-manual lymphatic drainage techniques [1,6].

**Complete decongestive therapy** — The term complete decongestive therapy (also called complex decongestive therapy, complex decongestive physiotherapy, or decongestive lymphatic therapy) refers to an empirically derived, multicomponent technique that is designed to reduce the degree of lymphedema and to maintain the health of the skin and supporting structures [1,6].

**Phases** — Complete decongestive therapy generally consists of a two-phase treatment program that can be used in both adults and children [1,6]. Success is dependent in part upon the availability of physicians, nurses, and physical therapists who are trained in these techniques.

- The first phase (treatment phase) includes meticulous skin and nail care to prevent infection, therapeutic exercise, a massage-like technique called manual lymphatic drainage (see 'Manual lymphatic drainage' above), and limb compression using repetitively applied, multilayered padding materials and short-stretch bandages (see 'Compression therapy' above). The patients receive daily therapy five days per week, with circumference and volume measurements weekly to see if improvement is continuing or the patient has plateaued [6]. The usual duration of the first stage is two to four weeks.

- The second phase (maintenance phase) is intended to conserve and optimize the benefit attained in the first phase. It consists of compression garments worn during waking hours and, if necessary, self-compression bandaging at night, skin care, continued exercises, and, as necessary, self-manual lymphatic drainage. Limb circumference and volume measurements should be monitored every six months or sooner if necessary [6]. (See "Clinical features and diagnosis of peripheral lymphedema".)

**Contraindications** — Experts have described several possible contraindications and/or precautions to complete decongestive therapy, and in particular, to manual lymphatic drainage [6,70]. Although commonly followed, these contraindications are predominantly based upon

theoretical concerns, and there are few clinical data to support them. As an example, the International Society of Lymphology consensus statement listed active neoplasia in the affected limb as a contraindication, but the theoretic concept that massage promotes metastases is debated [1]. A retrospective review found that patients with locoregional disease experienced similar benefit from complete decongestive therapy as did those without locoregional disease, and no study has ever demonstrated that massage therapy spreads cancer [45]. (See 'Palliative care modifications' below.)

The following conditions have been listed as possible contraindications to therapy. We suggest that decisions to pursue complete decongestive therapy or MLD in such patients should be made with the guidance of a trained lymphologist and clinician.

- Active cellulitis, neoplasm, or other inflammations of the infected limb (complete decongestive therapy may spread the infection or exacerbate symptoms).
- Moderate-to-severe heart failure (which may be exacerbated by the increase in central venous volume induced by mobilization of the lymphatic fluid).
- Acute deep vein thrombosis (since embolism may result from dislodging of clot).

Relative contraindications, such that patients may be treated but may warrant monitoring, include:

- Uncontrolled hypertension (which may be exacerbated by the increase in central venous blood volume caused by manual lymphatic drainage and compression bandaging). In this case, the patient's cardiac functions are monitored during the treatment phase.
- Diabetes mellitus (since associated vasculopathy or neuropathy may decrease the sensing of pain with improperly fitting compression garments, possibly leading to tissue injury and infection).
- Asthma (since parasympathetic activation can occur, possibly promoting an asthma attack). With these patients, the manual lymphatic drainage treatment time should begin at approximately 20 minutes, and if no negative reactions are noted, the treatment time should be increased 5 to 10 minutes until normal treatment times are reached [70].
- Limb paralysis (since a flaccid limb may offer insufficient resistance when compression bandages and garments are used, and any decrease in sensation may promote injury from improperly fitting compression garments).

**Palliative care modifications** — As many as 85 percent of patients at the end of life have edema, and it can severely affect comfort, mobility, and quality of life [71,72]. For these patients, the clinical context and goals of care must be carefully considered. (See "Approach to symptom assessment in palliative care", section on 'Swelling in the arms and legs'.)

While complete decongestive therapy is clearly beneficial for extremity lymphedema, its application may be associated with risk (eg, skin breakdown, fluid overload) when used in the context of metastatic cancer, liver and heart failure, neuropathy, and peripheral vascular disease, all of which are common in palliative care populations [73]. Further, complete decongestive therapy may reduce edema and it may also adversely affect well-being by being an overly burdensome treatment. However, one small review demonstrated improvements in limb volume, skin quality, and lymphedema-related quality of life for complex decongestive therapy in palliative cancer patients [74]. Therefore, the benefits and burdens of a full program of complete decongestive therapy need to be assessed to determine whether it may exceed patient needs or represent an unduly burdensome aspect of care at the end of life.

For patients in palliative care who are candidates for complete decongestive therapy, modifications may be necessary to reduce complications. Examples of this include [75,76]:

- Use of extra padding and skin protective materials for patients with impaired arterial circulation or sensation.
- Shortened bandaging durations between skin checks.
- Exercises to promote blood flow during bandaging (eg, repetition of ankle pumps or circles), especially in patients with arterial insufficiency.

For patients with heart failure or renal insufficiency, positioning adjustments might be needed (eg, not elevating the involved extremity, as it might reduce perfusion) [75]. In addition, initial bandaging should be done on a limited portion of the involved extremity to evaluate the impact more proximally, which can guide the extent of bandaging in future treatment. Patients and caregivers should be educated to identify dyspnea and/or abdominal bloating, which may reflect an adverse effect of fluid redistribution.

## EXPERIMENTAL AND UNPROVEN TREATMENTS

Pharmacologic treatments are not generally used, as no drug has definitively been shown to be beneficial. In particular, diuretics should **not** be given. Other treatments are considered experimental. A limited number of patients who fail conservative treatment options may be

candidates for surgical therapy, which may include lymphatic surgery, or soft tissue reduction. (See "Surgical treatment of primary and secondary lymphedema".)

**Pharmacotherapy** — There are no recommended pharmacologic agents for patients with lymphedema. Diuretics are of little benefit in the management of chronic lymphedema and may promote the development of volume depletion. When diuretics are given to treat the usual forms of peripheral edema, the initial fluid loss comes from the intravascular space. The ensuing reduction in venous, and thus intracapillary, pressure allows the edema fluid to be mobilized and the plasma volume to be maintained. However, this sequence does not occur with lymphatic obstruction, since the edema fluid cannot be easily mobilized into the vascular space. (See "Clinical manifestations and evaluation of edema in adults".)

Preclinical reports have suggested that anti-inflammatory therapies targeting the T cell-mediated inflammatory response may be beneficial in preventing lymphedema after lymphatic injury. In addition, these studies have shown promise in treating lymphedema once it has developed. One study demonstrated that topically applied tacrolimus, an inhibitor of T cell proliferation, significantly decreased the development of pathological changes of lymphedema in a mouse model of the disease [77]. Additional research is needed to translate these findings from the bench to the bedside.

An early report found that coumarin (a warfarin-like drug that might reduce high protein edema by stimulating proteolysis) was beneficial in patients with lymphedema [78]. However, a larger, carefully performed crossover study of 140 women found no difference between coumarin and placebo in reducing arm volume and relieving symptoms; coumarin was also associated with significant hepatotoxicity in 6 percent of patients [79]. A subsequent systematic review concluded that the poor quality of the trials prevented any conclusions from being made about the effectiveness of benzopyrones (including coumarin) in reducing limb volume, pain, or discomfort [80]. A later trial randomized 50 patients to a combination agent (coumarin/diosmin/arbutin) in addition to complete decongestive therapy or complete decongestive therapy alone [81]. Extremity volume and percent reductions in extremity volume were reduced with the combination agent.

**Low-level laser therapy** — Low-level laser therapy (also known as cold laser therapy) is a photochemical treatment used for soft tissue injury, chronic pain, and wound healing that has been used alone or in combination with other therapies for the treatment of peripheral lymphedema [82,83]. Among the hypotheses to explain the possible benefits of laser therapy are stimulation of macrophages and the immune system, a potential decrease in fibrosis, and a suggested role in encouraging lymphangiogenesis, which may stimulate available lymphatic pathways and encourage the formation of new pathways [84]. Some small randomized trials

have shown a reduction in limb volume [83,85,86]; others have shown minimal or no reduction [87-89]. In a systematic review evaluating low-level laser therapy for breast cancer-related lymphedema, outcomes were not significantly improved when compared with established active lymphedema interventions (eg, manual lymphatic drainage, complete decongestive therapy) [82].

## FOLLOW-UP AND OTHER CONCERNS

Clinical measurements of girth or estimates of lymphedema volume are necessary to track changes during treatment relative to baseline. Measurements of limb circumference and/or volume are the most common methods for monitoring the degree of lymphedema during and after therapy [1]. The schedule for follow-up depends upon the severity of lymphedema and treatment regimen. (See "Clinical features and diagnosis of peripheral lymphedema", section on 'Extremity measurements' and 'Extremity girth' above and 'Conservative treatment by severity' above.)

Patient compliance is important for achieving and maintaining a successful outcome. The patient must be made aware that failure to control lymphedema may lead to repeated infections, progressive skin changes, and possibly soft tissue cancer (ie, angiosarcoma) [1]. (See 'Complications' below.)

**Refractory lymphedema** — Among patients with lymphedema following breast cancer surgery, a search for concomitant disorders should be pursued when there is massive lymphedema that is refractory to usual therapies or has an onset several years after the primary surgery without obvious trauma. In particular, recurrence of the breast cancer in the axillary area or the development of lymphangiosarcoma should be excluded by use of computed tomography (CT) or magnetic resonance imaging (MRI) [90-92]. (See 'Lymphangiosarcoma' below.)

**Air travel** — A common question among patients with lymphedema regards air travel. Although, in theory, lymphedema may be exacerbated at high altitude or during air travel, since the ambient atmosphere pressure is less than the relative outlet transcapillary pressure within the superficial tissues, studies suggest that the risk from air travel of precipitating or worsening lymphedema is very low [6,93-95]. Whether the use of compression sleeves during air flight in women with lymphedema is of benefit is debated. Some suggest that domestic air travel (<4.5 hours) is low risk and that compression devices may be counterproductive [96]. For longer duration air travel, compression garments, exercises, and self-massage may all be helpful.

## COMPLICATIONS

Lymphedema can result in multiple infectious complications and a rare form of sarcoma. It can also result in significant psychological comorbidity with a negative impact on quality of life. These complications are discussed below.

**Skin infection** — Lymphedematous skin is at risk for recurrent infections, including cellulitis, erysipelas, and lymphangitis [9,97-101]. Cellulitis is a well-described complication of lymphedema, particularly in patients who have undergone axillary or inguinal lymph node dissection [102,103]. Typical manifestations include erythema, pain, and tenderness. However, systemic signs, such as fever, may not be present. Although this is a complication, it is also a risk factor for both the onset and progression of lymphedema. (See "Clinical features and diagnosis of peripheral lymphedema", section on 'Infection'.)

**Lymphangiosarcoma** — A rare secondary malignant tumor, called lymphangiosarcoma, can occur in patients with chronic lymphedema. It is usually seen in patients with massive and protracted edema [104]. It is classically described as occurring in the postmastectomy patient (Stewart-Treves syndrome) [90-92]. It has also been described with primary lymphedema and chronic filarial lymphedema [105-107]. (See "Breast sarcoma: Epidemiology, risk factors, clinical presentation, diagnosis, and staging", section on 'Lymphedema'.)

The tumor originates in vascular endothelial cells of the affected arm with lymphedema, not the lymphatic vessels [91]. It may initially appear as blue-red or purple skin lesions with a macular or papular shape. Multiple lesions are common and subcutaneous nodules may appear. Such skin lesions should be carefully evaluated in patients with chronic lymphedema. (See "Pathogenetic factors in soft tissue and bone sarcomas" and "Breast sarcoma: Epidemiology, risk factors, clinical presentation, diagnosis, and staging".)

**Psychological morbidity** — Lymphedema results in psychological morbidity and a reduced quality of life, including aspects of emotional, functional, physical, and social well-being [108,109]. Psychological problems seen in women with chronic lymphedema after treatment for breast cancer include anxiety, depression, sexual dysfunction, social avoidance, and exacerbation of existing psychiatric illness.

## SURGICAL REFERRAL

Surgical referral is appropriate for any patient with lymphedema, particularly those in whom conservative management has failed or if the patient is motivated to pursue additional

treatments. Lymphedema may be surgically treated with physiologic interventions designed to restore lymphatic circulation including lymph node transplantation and lymphovenous bypass, which have shown promising results, particularly in patients with early-stage lymphedema. Reductive (excisional) procedures that aim to remove fibrofatty tissues deposited in lymphedematous limbs may be useful for patients with late-stage lymphedema. (See "Surgical treatment of primary and secondary lymphedema".)

## SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Lymphedema".)

## INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5$^{th}$ to 6$^{th}$ grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10$^{th}$ to 12$^{th}$ grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Peripheral lymphedema after cancer treatment (The Basics)")
- Beyond the Basics topics (see "Patient education: Lymphedema after cancer surgery (Beyond the Basics)")

## SUMMARY AND RECOMMENDATIONS

- **Staging** – Peripheral lymphedema is a chronic condition that is often difficult to treat, particularly if progression to later stages has already occurred. We suggest using the

staging system of the International Society of Lymphology (ISL) ( table 3) to characterize the severity of lymphedema. ISL staging involves two criteria: the "softness" or "firmness" of the limb (reflecting fibrotic soft tissue changes) and the outcome after elevation. Within each stage, severity based upon volume differences are assessed as mild (<20 percent increase), moderate (20 to 40 percent increase), or severe (>40 percent increase). (See 'Clinical stage' above.)

- **Conservative multimodal therapy** – Conservative multimodal therapy is the mainstay of treatment and is aimed at improving patient comfort and reducing limb volume. Multimodal therapy consists of general measures, physiotherapy, and compression therapy. For all patients with lymphedema, regardless of stage, and for those at risk for lymphedema following surgery, general measures are aimed at minimizing the degree of edema and slowing the rate of progression. We agree with the guidelines from the National Lymphedema Network and the International Society of Lymphology that suggest self-monitoring, limb elevation, maintenance of ideal body weight, avoidance of infection/injury, and avoidance of limb constriction [11]. (See 'Overview of management' above and 'General measures' above.)

- **Management by stage** – In addition to general measures, the type and level or intensity of physiotherapy (simple lymphatic drainage, manual lymphatic drainage, complete decongestive therapy) and compression therapy (compression bandaging, compression garments, intermittent pneumatic compression) vary depending upon the stage of disease.

  - **At risk for lymphedema** – For all patients at risk for lymphedema following surgery (ISL stage 0), we suggest physiotherapy to improve mobility. Other measures are commonly believed to be important, but there is little evidence to support efficacy or to compare the benefit of one modality with another.

  - **Mild lymphedema** – For patients with mild lymphedema (ISL stage I), we suggest physiotherapy (simple lymphatic drainage, a commonly taught self-help maneuver) and compression garments, rather than more intensive therapy (**Grade 2B**). (See 'Mild lymphedema' above.)

  - **Moderate-to-severe lymphedema** – For patients with moderate-to-severe lymphedema (ISL stage II to III) and no contraindications, we suggest intensive physiotherapy, usually in the form of complete decongestive therapy, rather than less intense therapy (**Grade 2B**). (See 'Moderate lymphedema' above and 'Severe lymphedema' above and 'Complete decongestive therapy' above.)

- **Severe lymphedema** – Patients with severe lymphedema (ISL stage III) may also benefit from intermittent pneumatic compression (IPC) in addition to complete decongestive therapy. (See 'Complete decongestive therapy' above and 'Intermittent pneumatic compression' above.)

- **Other treatments** – Pharmacologic or other treatments are not generally used. No drug has been shown to be beneficial. In particular, diuretics should not be given because edema fluid cannot be easily mobilized into the vascular space. (See 'Experimental and unproven treatments' above.)

- **Complications** – Complications of lymphedema include skin infections (cellulitis, erysipelas, and lymphangitis), lymphangiosarcoma, and reduced quality of life including aspects of emotional, functional, physical, and social well-being. Severe cellulitis, lymphangitis, or bacteremia requires intravenous antibiotics. If patients experience three or more episodes of cellulitis in a year, we suggest an extended period of oral antibiotic therapy. (See 'Complications' above.)

- **Surgical referral** – Any patient can be referred for surgical evaluation for either physiologic treatments (eg, lymph node transfer, lymphovenous bypass) or reductive procedures if they would like to pursue other avenues for treatment or if clinical goals have not been achieved with conservative management. (See 'Surgical referral' above and "Surgical treatment of primary and secondary lymphedema".)

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Topic 738 Version 50.0

## GRAPHICS

### Causes of lymphedema

| **Primary lymphedema** |
| --- |
| Congenital |
| Precox (adolescence) |
| Tarda (adulthood) |
| **Secondary lymphedema** |
| Malignancy |
| Recurrent cellulitis |
| Connective tissue disease |
| Infection (filariasis) |
| Contact dermatitis |
| Lymphatic damage (surgery, radiation therapy, burns, etc) |

Graphic 64677 Version 1.0

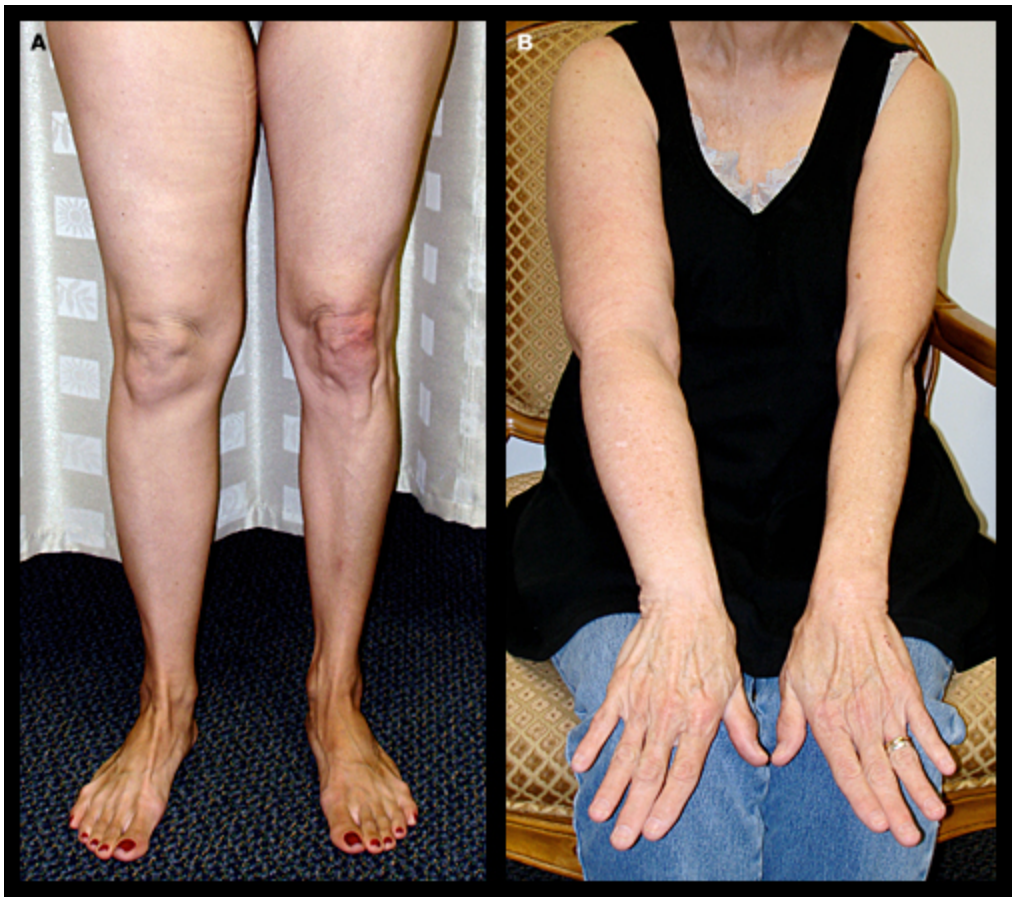
## Campisi staging system for lymphedema

| |
|---|
| **Stage 1** |
| 1A: No edema with presence of lymphatic dysfunctions (eg, after mastectomy and axillary lymphadenectomy, without any difference in volume and consistence between the arms) |
| 1B: Mild edema, reversible with declivous position and night rest |
| **Stage 2** |
| Persistent edema that regresses only partially with declivous position and night rest |
| **Stage 3** |
| Persistent and ingravescent edema (acute erysipeloid lymphangites) |
| **Stage 4** |
| Fibrotic lymphedema (with initial lymphstatic verrucosis) and column-shaped limb |
| **Stage 5** |
| Elephantiasis with severe limb deformation, scleroindurative pachidermitis, and marked and widespread lymphstatic verrucosis |

*From: Campisi C, Boccardo F, Zilli A, et al. Long-term results after lymphatic-venous anastomoses for the treatment of obstructive lymphedema. Microsurgery 2001; 21(4):135–139. https://onlinelibrary.wiley.com/doi/abs/10.1002/micr.1025.*


Graphic 81911 Version 4.0

## Lymphedema stage I

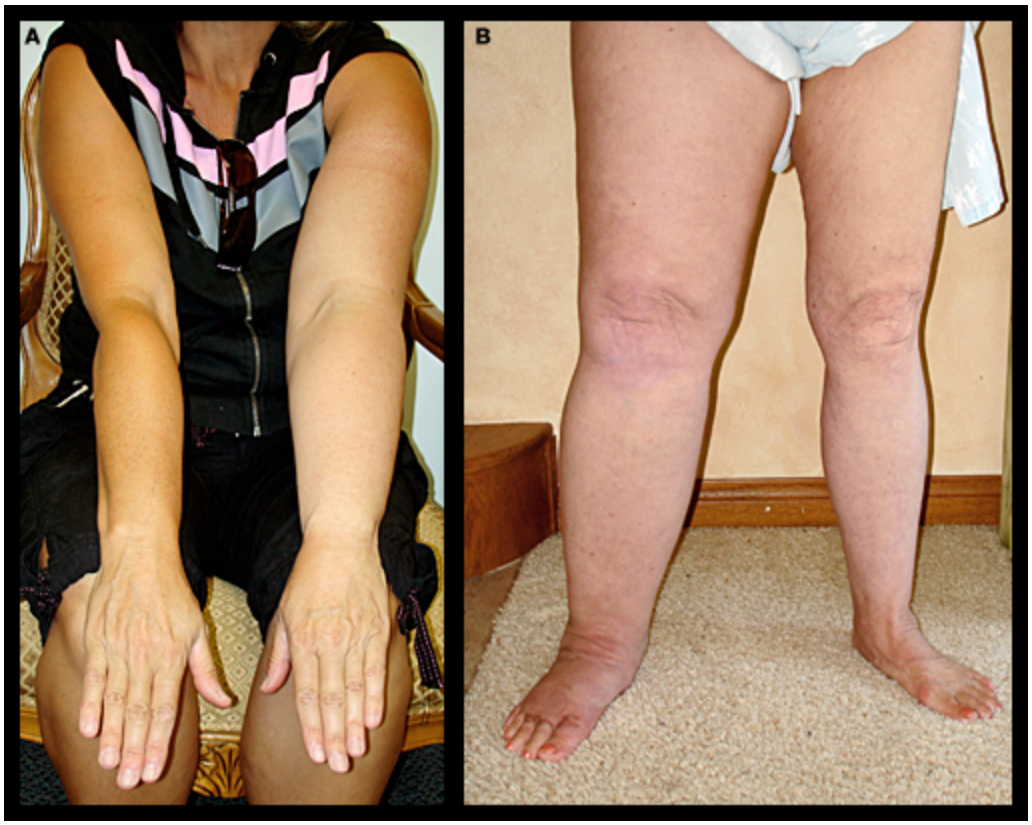



Stage I lymphedema. A) Right lower extremity. B) Right upper extremity.

*Courtesy of Tammy Mondry, DPT, MSRS, CLT-LANA.*

Graphic 56739 Version 2.0

## Lymphedema stage II

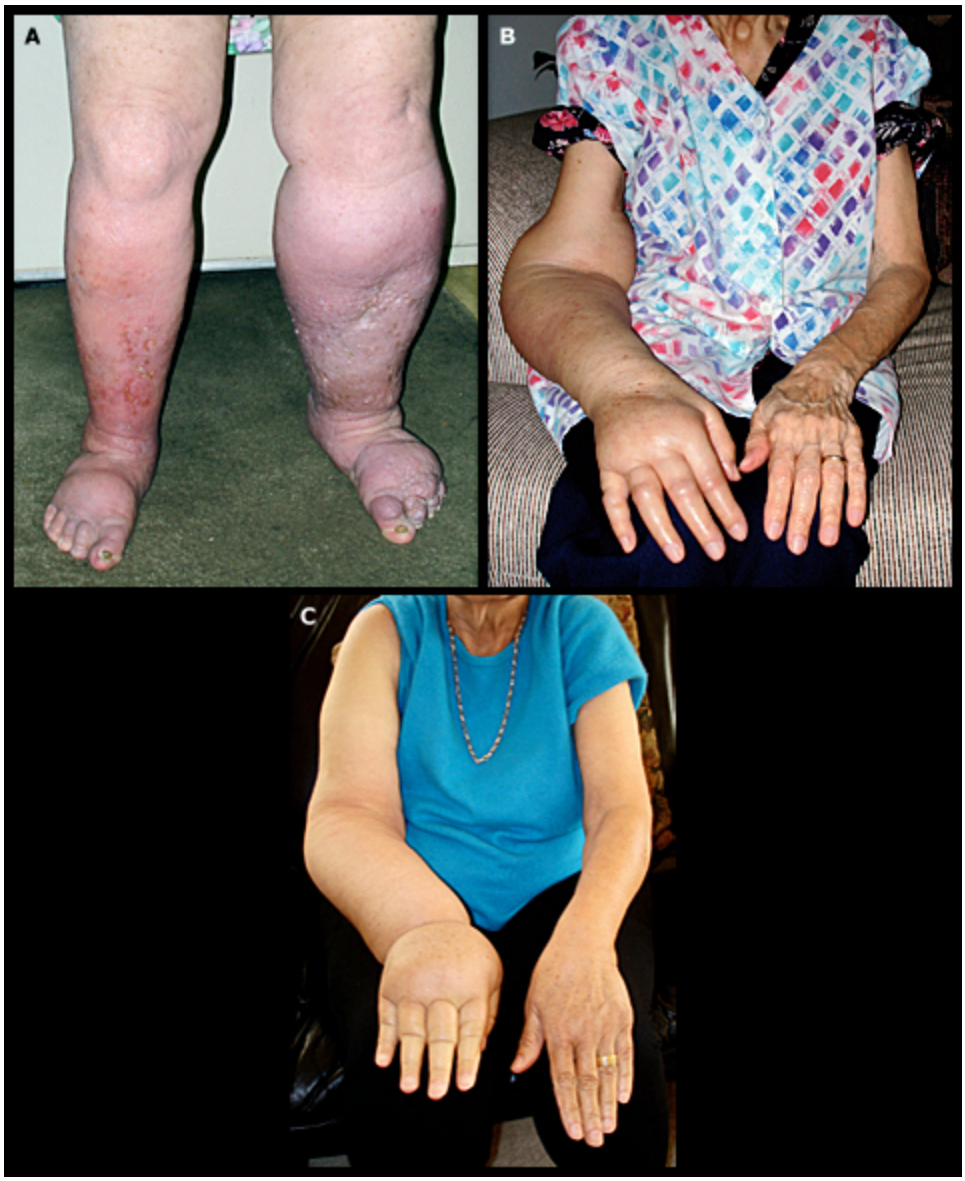



Stage II lymphedema. A) Left upper extremity. B) Right lower extremity.

*Courtesy of Tammy Mondry, DPT, MSRS, CLT-LANA.*

Graphic 76706 Version 2.0

## Lymphedema stage III




Stage III lymphedema. A) Left lower extremity. B) Right upper extremity. C) Right upper extremity.

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*Courtesy of Tammy Mondry, DPT, MSRS, CLT-LANA.*

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Graphic 63928 Version 2.0

## International Society for Lymphology lymphedema staging[1]

| ISL stage | Description |
|---|---|
| 0 | A latent or subclinical condition where swelling is not yet evident despite impaired lymph transport, subtle alterations in tissue fluid/composition, and changes in subjective symptoms. It may exist months or years before overt edema occurs (stages I to III). |
| I | An early accumulation of fluid relatively high in protein content (eg, in comparison with "venous" edema), which subsides with limb elevation. Pitting may occur. An increase in various types of proliferating cells may also be seen. |
| II | Limb elevation alone rarely reduces the tissue swelling and pitting is manifest. Later in stage II, the limb may not pit as excess subcutaneous fat and fibrosis develop. |
| III | Lymphostatic elephantiasis where pitting can be absent and trophic skin changes such as acanthosis, alterations in skin character and thickness, further deposition of fat and fibrosis, and warty overgrowths have developed. |

*Reference:*

1. *The diagnosis and treatment of peripheral lymphedema: 2016 Consensus Document of the International Society of Lymphology. Lymphology 2016; 49:170.*

Graphic 122830 Version 2.0

## Contributor Disclosures

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