Current Concepts in the Diagnosis and Management of Lymphedema

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GENERAL PURPOSE: To present a comprehensive review of lymphedema, including its pathophysiology, assessment, diagnosis, and treatment.

TARGET AUDIENCE: This continuing education activity is intended for physicians, physician assistants, nurse practitioners, and nurses with an interest in skin and wound care.

LEARNING OBJECTIVES/OUTCOMES: After participating in this educational activity, the participant will:

1. Summarize the etiology, pathophysiology, and clinical manifestations of lymphedema.
2. Describe the diagnostic and treatment approaches for patients who have lymphedema.

ABSTRACT

Lymphedema is a condition characterized by localized protein-rich swelling caused by damaged or malfunctioning lymphatics. Patients with lymphedema have an increased risk of infection because of the lymphostatic nature of the disease. Chronic ulceration of the skin can make individuals vulnerable to infection leading to serious, sometimes fatal, complications. Proper diagnosis and treatment modalities can aid in the prevention of these complications and ensure better outcomes for the patient.

KEYWORDS: complete decongestive therapy, compression, lipedema, lymphatic drainage, lymphedema, venous insufficiency

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CASE STUDY

A 70-year-old Hispanic man presented to the wound clinic with bilateral leg wounds of several weeks' duration. His medical history included coronary artery disease, congestive heart failure, diabetes mellitus type 2, hypertension, hyperlipidemia, and morbid obesity. His surgical history was significant for abdominal aortic aneurysm repair. The patient was a former smoker, and his family history was significant for stroke. The patient was recently hospitalized for heart failure exacerbation and acute atrial fibrillation. He currently resides in a rehabilitation facility.

The patient's bilateral lower extremities showed signs of significant nonpitting edema from the level of the knee distally (Figure 1). There were several areas with skin changes, notably over the bilateral calves and dorsal feet. The skin felt taut and thickened. The patient had several wounds over his dorsal foot as well as right anterior leg. The largest wound measured 15 cm^2. The wounds had exudate and the periwound area was moist.

The patient was diagnosed with stage 3 lymphedema. The wounds were debrided and cleaned, and foam was applied. Both legs were wrapped in a multilayer compression device. Nursing orders were placed to have dressings changed three times per week. The patient was encouraged to elevate the legs as much as possible

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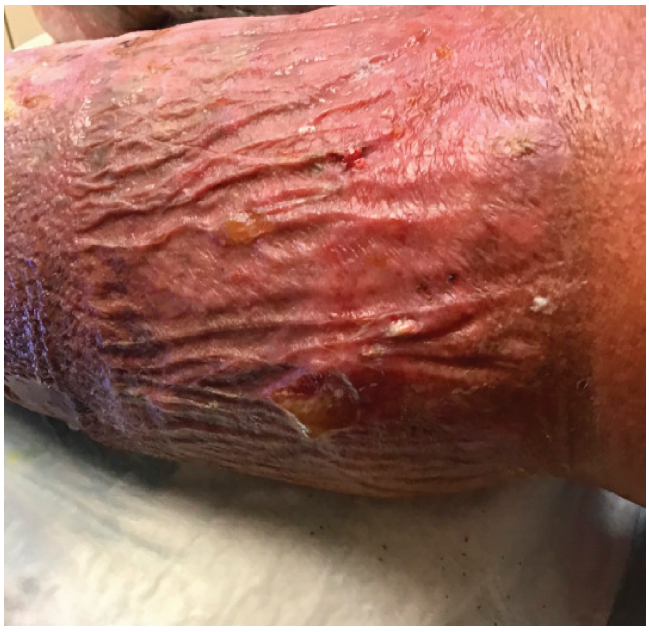
Figure 1. CASE STUDY DURING TREATMENT



and told to exercise as much as tolerable. A lymphedema pump was also ordered. The patient underwent decongestive therapy in subsequent weeks. He was followed weekly and rapidly began showing signs of improvement. His wounds had reduced in size by 50% within the first month of therapy.

INTRODUCTION

Lymphedema is an accumulation of fluid in the interstitial space as a result of a defect in the lymphatic system. The accumulation of protein-rich interstitial fluid results in edema, inflammation, fatty tissue proliferation, and eventual fibrosis.[1] Chronic stagnation of lymph in tissues results in consequent obliterative effects on the anatomy of the lymphatic system that can culminate in a difficult-to-treat, often incurable disease. Familiarity with the lymphatic system is important to understand its development.

Pathophysiology

The lymphatic system is composed of a network of unidirectional, low-pressure vasculature that runs parallel to the blood circulatory system. There are three categories of lymphatic vessels (LVs) that are differentiated by their structural differences: lymphatic capillaries (LCs), precollecting LVs, and collecting LVs. The LCs are located in the superficial dermis. They are made up of a single layer of lymphatic endothelial cells that are joined by discontinuous "button-like" junctions that lack pericytes or smooth muscle cells.[1] These features ensure permeability to protein-rich interstitial fluid, solutes, and macromolecules. The "button-like" junctions are connected by alternating vascular endothelial cadherin and platelet endothelial cell adhesion molecule proteins that function as primary valves.[2] This prevents retrograde flow of fluid into the interstitial space. The LCs are anchored to the surrounding tissues by anchoring filaments that aid in increasing permeability by enabling expansion of the junctions when there is an increase in interstitial fluid. The LCs converge into the precollecting LVs in the deeper dermis. Precollecting LVs contain valves and are sparsely covered by lymphatic muscle cells. They are responsible for ensuring flow from the dermis into the subcutaneous tissue layer, therefore directing flow into the collecting LVs. The collecting LVs are differentiated as either superficial (epifascial) or deep (subfascial) vessels depending on their relationship to the fascia. Unlike the arterial or venous system, the epifascial and subfascial collecting LVs are independent of each other but may form valved connections in regional lymph nodes.[3]

The collecting LVs are subdivided into lymphangions, which are a functional unit of LVs that are bound between two luminal one-way valves and have muscular walls that have the ability to cause periodic contraction.[4] Collecting LVs additionally comprise a basement membrane that contains continuous "zipper-like" cell junctions covered by smooth muscle cells.[1] This allows contraction and the ability to propel lymph forward. In addition, the propulsion of lymph via the collecting LVs requires the aid of exogenous forces such as that of skeletal muscle contraction, inspiration, and arterial pulsation. Collecting LVs drain lymph into lymph node chains; the right side of the head and thorax subsequently empties out into the right lymphatic duct, and the rest of the body converges into the thoracic duct. The lymph ultimately flows into the low-pressure right or left subclavian vein.

In lymphedema, there is a backflow of fluid from the superficial collecting LVs to the precollecting LVs and LCs that eventually causes valvular inadequacy and leads to reflux into the skin. This causes dilation of the LCs and precollecting LVs, with complete disintegration of the superficial collecting LVs in advanced lymphedema. The impaired ability to propel lymph forward leads to the aggregation of proteins and increasing oncotic pressure, which consequently attracts water.[5] The excess water and proteins in the interstitial fluid cause edema. Lymphostasis stimulates the infiltration of immune cells that eventually die or propagate, activating an inflammatory response through the release of cytokines. Chronic lymphatic stagnation and protein accumulation eventually leads to fibrotic changes in the soft tissue because of collagen deposits by fibroblasts. This causes changes in the edema, transforming it from

an initial pitting edema to a more characteristic brawny, nonpitting edema.

The stagnation of lymph further compromises healing by inhibiting adaptive immunity. Immune cells cannot fight infection given their inability to make their way to detectable antigens because of impaired flow.[1] This results in an accumulation of antigens in the tissue that cannot be cleared, further increasing susceptibility to infection.

TYPES OF LYMPHEDEMA

Lymphedema is classified into two categories based on the underlying cause: primary and secondary. Primary lymphedema occurs when a developmental defect of the lymphatic system causes eventual failure of draining lymph from tissues. It occurs in 1 out of 6,000 people and is more common in women than men. Based on age at onset, it is classified into congenital (present at birth), praecox (appears before 35 years), and tarda (appears after 35 years). Milroy disease is one of the most common types of congenital primary lymphedemas. It is autosomal dominant and is caused by mutations in the vascular endothelial growth factor receptor 3 (VEGFR3) gene.[6] Patients usually present with symmetrical lower limb edema at birth. Meige disease is one of the most common types of primary lymphedemas, accounting for 65% to 80% of all cases of primary lymphedema. It is classified as lymphedema praecox, because of its manifestation during adolescence with lower limb edema.[7] Primary lymphedema tarda is the rarest form of the developmental lymphedemas and is thought to be attributable to faulty valves.

Secondary lymphedema is a condition that is acquired after an obstruction or disruption of lymphatic pathways. The most prevalent cause of secondary lymphedema globally is the parasitic disease filariasis. In developed countries, however, the most common causes of secondary lymphedema include tumors, trauma, or cancer treatments, such as lymph node removal and radiotherapy. Buruli ulcer is caused by *Mycobacterium ulcerans*. This neglected disease occurs in scattered foci around the world, with a higher concentration of cases in West Africa. The lesion often begins as edema before becoming an ulcer.[8]

Lymphedema can be transient or chronic. Transient lymphedema lasts less than 3 months and is characterized by pitting edema that ameliorates with compression and limb elevation. Chronic lymphedema is attributable to constant lymphostasis that eventually causes characteristic changes such as nonpitting edema, skin thickening, and fibrosis. Nonpitting edema is often a nonreversible stage of chronic lymphedema.

ASSESSMENT AND DIAGNOSIS

A complete medical history should be obtained that addresses the onset of symptoms; associated symptoms; medications; medical history (history of cancer, radiotherapy, infections, etc); and travel, surgical, and family history. Patients generally complain of a painless—sometimes aching—asymmetrical enlargement of an extremity. The limb's gradually increasing weight and size can cause discomfort and difficulty fitting into clothing and, if in the lower extremities, could begin to affect ambulation. Psychological morbidity accompanies embarrassment by appearance, difficulty with mobility, and a reduced quality of life.

The physical examination should emphasize the vascular system and skin, with palpation of the lymph nodes. A careful examination entails assessing for any signs of infection such as erythema, tenderness, increased swelling, warmth, lymphadenopathy (swollen lymph nodes with glandular fever), and lymphangitis (red streaks, abnormal size of inflammatory swelling in lymph nodes), in addition to checking the patient for fever or chills. Toe web spaces and skin folds should be assessed carefully for any signs of infection, particularly signs of fungal infection such as white scaling and itching. Determining the degree of pitting edema is imperative along with confirming the presence of positional fluctuation. A positive Stemmer sign is pathognomonic for chronic lymphedema and is characterized by the inability to lift the skin at the base of the second toe or second finger when pinched.[9] In addition, assessing the degree of ulceration, if present, is imperative in procuring an appropriate treatment (Figure 2).

The use of the International Society of Lymphology criteria can aid in deriving the stage of lymphedema (Table 1).[10]

Documentation of lymphedema requires noting the location, stage, type (pitting or nonpitting), and extent and duration of swelling. Presence of any thickening of the skin, papillomas, ulcers, and lymphorrhea should be recorded. Any tissue changes, such as if it is rubbery or hard, must be noted. Any changes to the shape of the limb, limitations in limb function (eg, sensation, motor changes, gait analysis, need for aids, etc), and any

Figure 2. STEMMER SIGN
Left negative, right positive for lymphedema.[31]

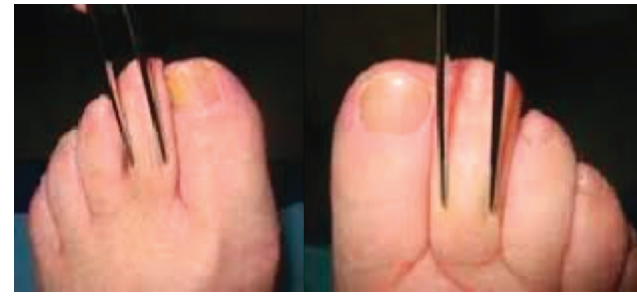


Table 1. LYMPHEDEMA STAGING WITH CLINICAL MANAGEMENT OPTIONS[10,32]

Grade	Clinical Exam	Edema	Management
Stage 0 (or Ia)	Asymptomatic or subclinical	Reversible	Conservative
Stage 1	Soft pitting edema	Reversible	Conservative
Stage 2	Inability to reduce swelling upon elevation; dermal fibrosis evident	Irreversible	Conservative or Surgical (VLN transfer, LVA)
Stage 3	Lymphostatic elephantiasis; pitting absent; trophic skin changes with fat deposits, acanthosis, and warty overgrowths	Irreversible	Conservative or Surgical (VLN transfer, LVA, Charles procedure)

Abbreviations: LVA, Lymphaticovenous anastomosis; VLN, Vascularized lymph node

psychosocial morbidities should be noted. In addition, the limb circumference should be measured and recorded.

- Upper limbs: Circumference of wrist 10 cm below olecranon process and 10 cm above olecranon process is measured; this is repeated with the other arm and compared. Dorsum of hand is measured if edematous.[11]
- Lower limbs: Limb is placed in relaxed position and measured 2 cm above medial malleolus, 10 cm above superior pole of patella, and 10 cm below inferior pole of patella. This is repeated with the other leg and compared. Circumference of foot is measured if edematous.[10]

In patients with coexisting arterial disease, documentation entails obtaining and recording the patient's ankle-brachial index to determine the severity of the peripheral artery disease and the degree of compressive therapy that should be used by the patient (compressive therapy is contraindicated in patients with an ankle-brachial index <0.5).[12] Further, peripheral pulses, capillary refill, and temperature changes in extremities should be noted. Complaints of claudication and numbness or tingling of limbs should also be recorded.

The diagnosis of lymphedema is generally clinical. Further evaluation with imaging can be conducted when the source of lymphedema is not clear based on clinical assessment or when there is suspicion of obstruction by tumor or parasites. Doppler ultrasonography, computed tomography scans, and MRIs are noninvasive techniques that can aid in the visualization of fluid accumulation in the soft tissue or masses causing obstruction. Lymphoscintigraphy is the imaging procedure of choice to assess the lymphatic system. It entails injecting radionuclide intradermally into the web spaces of the extremities with imaging 30 to 120 minutes later. Delayed transit of the radiotracer and dermal backflow are considered abnormal findings that can support lymphedema diagnosis.

Early stages of lymphedema may be difficult to differentiate from other causes of extremity edema. The following conditions should be ruled out prior to confirming lymphedema as the diagnosis:[8]

- Chronic venous insufficiency generally presents with bilateral pitting edema that may be associated with visible varicosities and hyperpigmentation.
- Lipedema presents with nonpitting, tender swelling of bilateral lower extremities that spares the feet. The affected area tends to bruise easily. Lipedema with secondary lymphedema may develop due to chronic lipedema, often combined with obesity. Differentiation between lymphedema and lipedema with secondary lymphedema can be difficult (Table 2).[13]
- Cardiac/renal failure usually presents with bilateral extremity pitting edema that improves with elevation.

Table 2. COMPARISON OF LIPEDEMA AND LYMPHEDEMA

Lipedema With Secondary Lymphedema	Lymphedema
Affects mostly females; seen in males with endocrine pathologies that cause feminization	Affects females more than males
Bilateral symmetric lower extremity edema without foot involvement (ankle cutoff sign)	Edema often unilateral, generally asymmetric
Extent: iliac crest to ankle; can affect upper limbs	Can affect any part of body
Stemmer sign may be positive or negative	Positive Stemmer sign in chronic lymphedema
Painful	No pain
Bruising common with slightest trauma	Normal
Pitting edema in areas of lymphedema	Pitting at first but gradually becomes nonpitting
Positioning decreases edema	Positioning decreases edema in earlier stages
Other family members may have been diagnosed with lipedema	Family history of primary lymphedema
Normal lymphatic function in lipedema but abnormal lymphoscintigraphy if lymphedema present	Abnormal lymphatic function on lymphoscintigraphy

• Morbid obesity is considered a risk factor in developing lymphostasis, especially when body mass indices are greater than 60 kg/m^2 (Table 2).

TREATMENT

Conservative therapies are the preferred treatment for patients with lymphedema. Treatment requires an interprofessional approach including a wound specialist, dermatologist, podiatrist, infectious disease specialist, vascular surgeon, physical therapist, nutritionist, and/or a bariatric specialist.[11] Multimodal therapies including elevation, compression therapy with use of compression garments and intermittent pneumatic compression, manual lymphatic drainage (MLD), and self-care are recommended.

Compression Therapy

Determining the most appropriate compression therapy for the patient requires a full assessment that takes the site, stage, severity, arterial status, and any comorbidities into account. There are three management phases in compression therapy: initial management, transition management, and long-term management. Table 3 describes the management based on the stage of the lymphedema.[14,15]

The greatest loss of edema will occur during the initial management phase. Some patients may need a 1- to 3-month period in the transition management phase to optimize therapy before moving on to the long-term maintenance phase. Patients who would benefit from a transition phase are those who have had rebound swelling, difficulty maintaining the shape of the limb, or skin conditions that have proven difficult to manage.

Transition management is contingent on the presentation of lymphedema after the initial phase. It generally entails the use of MLD with a combination of compression garments and compression bandages. During the transition phase, patients should be evaluated weekly and then monthly if found to be stable. If improvement is noted, patients can proceed to long-term management. If a patient is not optimized for long-term management, consider another trial of intensive therapy.

Long-term management generally involves the use of compression garments. For patients who cannot tolerate compression hosiery, bandaging may be a better long-term option. In addition, some may benefit from using a combination of bandaging and compression garments. Measurement is required to ensure that the patient gets the appropriate compression garment size (small, medium, large). It is advisable that compression garments are used when the limb has returned to its normal shape and size. Custom-made hosiery may be necessary if constriction at the upper end of the limb is not tolerable.[15]

Table 3. LYMPHEDEMA STAGING WITH CONSERVATIVE AND ADJUNCTIVE THERAPY

Stage	Initial Treatment	Adjunctive Treatment	Follow-up
Stage I	Compression garments	Skin care, exercise, limb elevation, self-massage	Follow-up 4–6 wk after initial fitting and then every 3–6 mo (at each garment renewal)
Stage II	Modified multilayer inelastic lymphedema bandaging (MLLB) • MLLB entails using tubular bandage to absorb sweat and protect the skin, padding using orthopedic wool or soft foam, short stretch compression bandages, and cohesive bandages • Toes and fingers should be bandaged if swollen • Elastic bandages can be used in patients who are immobile or have venous insufficiency or ulcers	Skin care, exercise, limb elevation, self-massage, and psychosocial support	Type of bandaging used, frequency of bandage change, and degree of compression are contingent on patient's needs, whether contraindications exist, etc. Follow-up contingent on regimen • Usually daily bandaging for 1-4 wk • Inelastic bandages should be reapplied when they become loose to ensure appropriate compression
Stage III	• Standard intensive therapy uses lymphedema compression bandaging with short-stretch bandages that are changed daily • Modified intensive therapy uses inelastic bandages that are changed three times a week • Modified intensive therapy is for patients who can tolerate high pressures of compression but cannot commit to standard intensive therapy (daily visits) • Modified intensive therapy with reduced pressure should be used if ABI is between 0.5 and 0.8, patients with neurologic deficits and patients with lipedema	Skin care, exercise, limb elevation, MLLB. May require self-massage or intermittent pneumatic compression	Most intensive therapies are 2–4 wk in length; follow-up contingent on length

Complete Decongestive Therapy

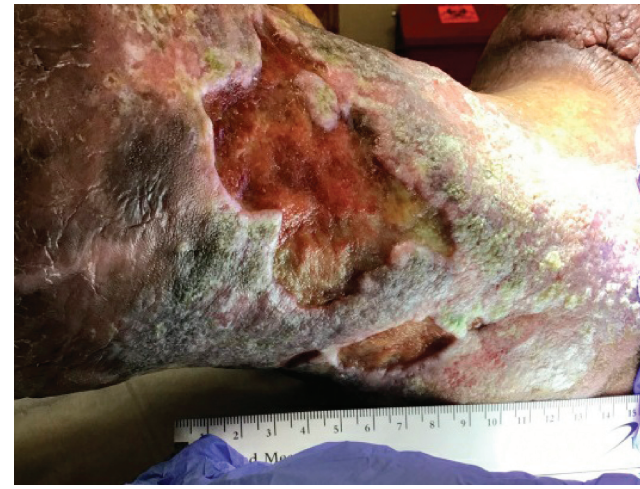
Complete decongestive therapy (CDT), also known as conservative therapy, is used to help move trapped lymph. Although surgery may be an option for certain patients with lymphedema, CDT is an important adjunct to treatment and helpful for most patients with lymphedema and some patients with lipedema.

Although time-consuming, CDT can be highly effective and involves two phases: the reductive phase (phase I) and the maintenance phase (phase II). Phase I entails completing efforts to decrease the limb size to as close to normal as possible, whereas phase II requires maintenance after reaching the goal of a reduced limb.[5] Both phases comprise MLD, compression therapy, exercise, and skin care. Although it uses noninvasive techniques, compliance can be difficult to attain due to the time-consuming and expensive nature of the therapies.

Manual lymphatic drainage is a technique that is completed by a certified lymphedema therapist and involves gentle movements that are thought to stimulate lymphatic drainage. The skin is lightly stretched and massaged to help stimulate lymphatic drainage. The stretch technique is applied to subcutaneous tissues to manipulate filaments of lymph capillaries.[16] The therapist uses light pressure to orient lymph flow in the natural direction of lymph.[5] Light pressure also moves lymph fluid in the appropriate direction where it drains out to improve lymphatic flow. The effect of the MLD increases flow in lymph production and venous return while reversing the lymphatic flow where fluids accumulate in the limbs. General contraindication for MLD include medical conditions such as cardiac edema, renal failure, acute infection, acute bronchitis, and acute deep vein thrombosis (Figure 3).[17]

During the CDT session, MLD is performed and followed by the application of compression bandages. Patients should wear multilayer compression bandages until the follow-up treatment session to see significant reduction of swelling in the limbs. Multilayer compression bandaging of the limbs will move fluid out of the extremity and increase the pressure in the tissue itself and in the lymph vessels. It can also prevent the reaccumulation of evacuated lymph fluid and protect the beneficial results achieved during MLD. Multilayer bandaging technique is administered by using short stretching bandages allowing for 50% to 60% extensibility of the original length. In conjunction with various types of foam and padding materials, two different qualities of pressure (working and resting) are applied to decrease swelling down in the limbs.[18] Working pressure is active and temporary, applied only during muscle contraction and results in an increase of tissue pressure to return the fluids to the lymphatic system.[16] Resting pressure is permanent and depends on the amount of tension

Figure 3. A 63-YEAR-OLD MAN WITH CHRONIC BILATERAL LYMPHEDEMA, CHRONIC CELLULITIS, AND VERRUCOUS HYPERPLASIA

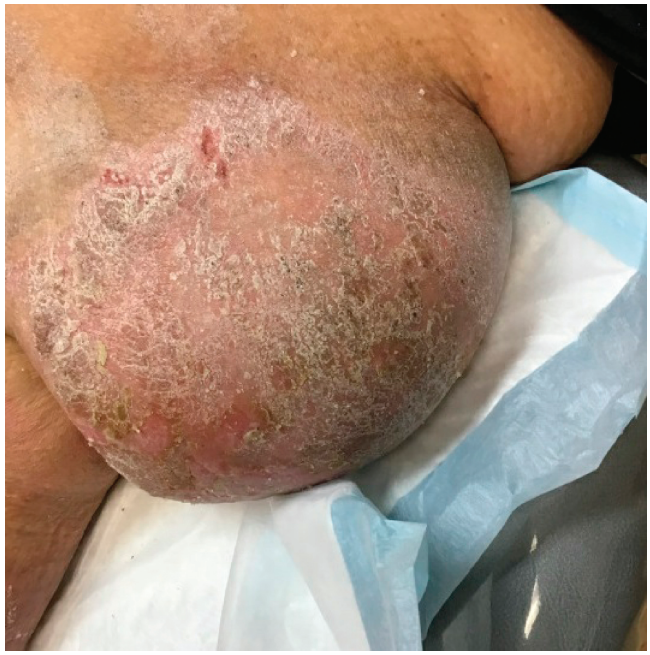


from the compression bandages.[16] Compression bandages should be applied in layers to avoid constriction of venous vessels and LVs and achieve a compression gradient (Figure 4).

Typically, CDT lasts 2 to 12 weeks depending on the severity of the condition. Sessions can be 1 hour long, with two to three sessions per week. After the intensive treatment phase is completed, wearing compression garments to prevent fluid from coming back into the limb is recommended. The objective of wearing compression garments is to preserve the treatment success achieved during CDT and resume prior functional levels with minimal restriction. It is important that patients be educated on the pathology of lymphedema, choice of compression selection, and compression garment care. Compression garments are available in various styles, compression levels, and materials, and can be ordered in standard or custom sizes (Table 4).

Compression garments are designed to provide gradual distal to proximal compression; the distal end has the highest pressure. Patients with lower extremity lymphedema are usually recommended for compression higher than level II (from 30–40 mm Hg or higher) as long as they can tolerate the compression and can don/doff independently or with assistance from a caregiver.[16] Lately, adjustable compression garments using Velcro or slip-on styles have become available for patients with lymphedema. These compression garments provide gradient pressure via nonelastic adjustable bands or through built-in compression. Nonelastic compression garments are easier to don and doff and can be used as an alternate self-bandaging tool at nighttime to continue to reduce swelling around the clock.

Figure 4. A 70-YEAR-OLD WOMAN WITH UNILATERAL, RIGHT LOWER EXTREMITY LYMPHEDEMA WITH LICHENIFICATION



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Compression garments need to be worn all day, with the exception of bathing and showering. After completion of CDT sessions, compression garments are worn during the day. If capable, patients should be instructed to perform MLD for about 20 minutes each day to open up the lymphatic channel and help reduce the swelling. Special lymphedema garments and devices, such as pumps, may be used or worn at night to further decrease swelling. Exercise is recommended as an aid in reducing edema and to promote weight loss. Patients are encouraged to wear compression garments while exercising. A physical therapist may be involved in improving the range of motion of a patient.

Lipedema. Lipedema involves swelling in the lower extremity caused by excess fatty adipose tissue. Complete decongestive therapy including usage of compression garments may help to prevent further swelling and stimulate the venous, arterial, and lymphatic flows.[19] The CDT treatment protocol can be similar to primary lymphedema and shows slow results or sometimes none at all.[16] However, to avoid hypersensitivity and pain, light pressure and extra padding should be applied while performing MLD and multilayer bandage compression.[17] After finishing CDT, compression garments such as pantyhose or capri styles can be recommended to continually reduce the swelling.

Intermittent pneumatic compression, also known as a lymphatic pump, is a type of therapy that is used daily to promote the evacuation of excess tissue edema. Edema is reduced by the activation of a pump that fills an inflatable device enclosing the affected limb. The compression functions as an exogenous force that promotes the propulsion of lymph forward and out of the dermis. Pump pressures are usually adjusted between 20 and 60 mm Hg to prevent skin damage by the device.[20] Patients should use compression garments in periods between lymph pump treatments to promote lymph movement and prevent backflow.

Conservative therapy should be attempted before more invasive procedures. It is also sometimes used after surgery to encourage drainage and help alleviate postsurgical swelling. If conservative treatments are not effective in reducing symptoms and improving comfort, surgery or liposuction may be beneficial.

Skin Hygiene

Establishing a skin care routine is important to prevent infections that are common with this condition. Skin care that involves appropriate hygiene, protection of the area around the wound, moist wound care, and avoidance of contaminants has proven beneficial in encouraging wound care healing and decreasing the risk of infections. Ensuring proper nail and skin hygiene can aid in decreasing bacterial and fungal access points into the body that increase susceptibility to infections. A podiatrist and dermatologist may be helpful in difficult-to-treat cases.

In addition, it is recommended that patients use moisturizing soaps and apply fragrance-free emollients to decrease dermal lichenification from keratin overproduction. Lichenification occurs when skin is thickened as a function of lymphedema, perhaps exacerbated by chronic scratching and rubbing, dryness, and cracking.[20] In patients with hyperkeratotic skin, the use of humectant emollients such as lactic acid, urea, and ceramides concomitantly with skin care regimens is encouraged to promote penetration of products into the skin. In addition, humectants may cause burning or stinging that can prove to be unpleasant for the patient, and an allergy should be ruled out before use. Emollients with low water content are preferred because of their superseding hydrating properties. Patients with intact skin should apply emollients at night, and those with dry skin should apply emollients twice a day.[14] In addition, the use of topical pharmacologic agents such as topical

Table 4. COMPRESSION LEVEL[16]

Compression Level	Amount (mm Hg)
Level I	20–30
Level II	30–40
Level III	40–50
Level IV	>60

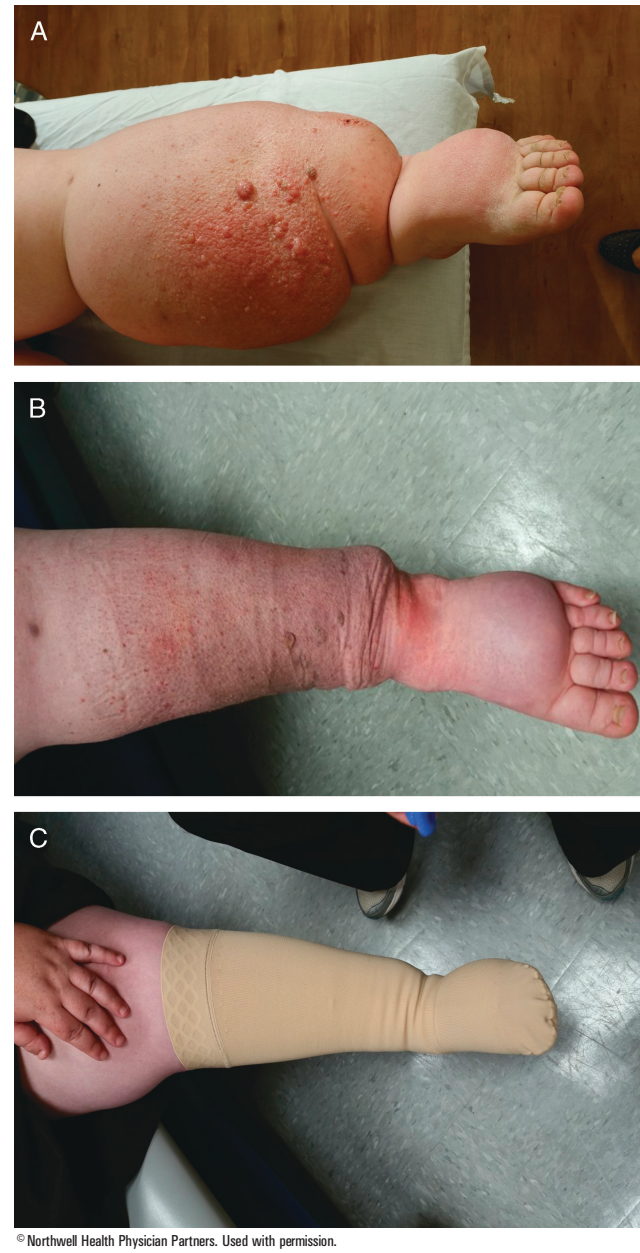
steroids for dermatitis or topical calcineurin inhibitors for off-label treatment of stasis dermatitis may prove beneficial in treating skin disorders that may be indirectly related to lymphedema and can further complicate its treatment (Figures 5 and 6).[21]

Wound Care

If concomitant wounds are present, the percent wound area is measured based on validated measure of longest wound length multiplied by longest perpendicular wound

Figure 5. A, B, AND C, PRETREATMENT. D AND E, POSTTREATMENT.

Figure 6. A, PRETREATMENT. B, POSTTREATMENT. C, POSTTREATMENT WITH COMPRESSION STOCKING.



width and depth. A wound specialist may be helpful in tracking the progress of wound healing demonstrated by reduction of wound square surface area.[12,22] Wound healing centers have demonstrated improved outcomes in patients with wounds.[11]

Lymphorrhea, external lymph drainage onto the skin, can cause pruritus, further tissue breakdown, and worsening maceration. Maceration caused by the copious draining of lymphedematous limbs can cause wounds as well as prevent epithelialization of wounds. Adequate levels of compression will decrease drainage. Increased capillary

leakage may be seen when compression becomes suboptimal. For this reason, establishing a balance between absorbance and moisture is imperative in promoting wound healing and maintaining an appropriate skin barrier to decrease susceptibility to infections. Super absorbent dressings should be used under compression to absorb exudate and prevent maceration. Absorptive dressings and barrier films may help with the reduction of periwound maceration and decrease in wound size.[21]

Chlorhexidine and povidone-iodine may be used as cleansing agents that reduce skin flora and may aid in curbing infections such as cellulitis. Combination chlorhexidine and benzalkonium washes have been used to treat folliculitis.[15] These products are recommended for short-term purposes only because they may inhibit wound healing. Polyhexamethylene biguanide has not been shown to inhibit wound healing in low concentrations; in addition, it has been shown to reduce skin flora and biofilm.[23] There is insufficient evidence on which agent is superior for its cleansing and antiseptic properties. Patients who experience recurrent bouts of lymphangitis, however, may benefit from prophylactic long-term antibiotic treatment.[21] There is insufficient evidence as to a superior agent for significant clinical effects of wound cleansing or antiseptic agents on wound infection outcomes.[20] However, treating the underlying cause and providing proper treatment has proven to be critical in managing and/or preventing wounds.

Pain Management

Pain can be evaluated using the Visual Analog Scale. Randomized controlled trial evidence has reported standardized pain outcome measures for chronic wounds with lymphedema. To alleviate pain, local anesthetic may be applied to the wound in the forms of topical lidocaine, a combination of lidocaine-prilocaine, or an ibuprofen-releasing foam dressing.[24–27]

Surgical Intervention

Patients with severe lymphedema with failed conservative management may be candidates for surgery by either physiologic or reductive techniques. Physiologic techniques entail creating new conduits to increase lymph drainage and include lymphatic venous anastomosis or bypass, lymphatic-lymphatic bypass, and lymph node transfer, which may involve a vascular or plastic surgeon.

Lymphatic venous anastomosis is completed by creating a connection between the lymphatic and venous systems in the affected extremity. Fluorescence is used to identify the lymphatic system, and subsequently, superficial or deep lymphatics are anastomosed to proximal veins. Lymphatic-lymphatic bypass entails transferring healthy lymphatic-vessel-containing soft tissue to an affected area, such as a graft. Lymph node transfer includes transferring healthy lymph nodes to the site of obstruction. This entails using microsurgery with venous and arterial anastomosis at the affected site. Studies have indicated variability in the effectiveness of these procedures.[10]

Reductive techniques entail the removal of affected tissue to assist in counterbalancing the lymphedema-related load from sustained lymphostasis. For secondary lymphedema, this type of treatment is palliative and not curative, whereas it can be curative for patients with primary lymphedema. Direct excision and liposuction are the types of reductive techniques that are used. Direct excision entails removal of lymphedematous tissue either by the Charles procedure, which includes removal of all subcutaneous tissue by grafting, or by staged excision, which involves removal of a portion of skin and subcutaneous tissue with primary closure. A subsequent staged excision occurs 3 months later at a different location in the affected extremity. Staged excision is the preferred type of reductive therapy because it is not as disfiguring as the Charles procedure and is associated with fewer complications.

Liposuction is effective in debulking the affected area and leads to a reduction in extremity girth. Liposuction can be effective in reducing both upper and lower extremity size and improving the patient's quality of life.[10] However, limitations of these reported studies include the paucity of randomized controlled trials. Meta-analysis studies mentioned are drawn from independent small sample size studies (Table 5).

COMPLICATIONS

Patients with lymphedema are susceptible to developing soft-tissue infections because the lymphostatic nature of the disease prevents lymph clearance and impairs macrophage response. Patients may experience recurrent bouts of cellulitis, most commonly caused by *Streptococcus pyogenes*.[6] Each infection further promotes fibrotic changes and damage to the LVs. Infections further complicate the disease process and can become life-threatening (Figures 2 and 3). An infectious disease physician may aid in addressing the complexity of the infection that can result.

Patients with chronic lymphedema may develop lymphangiosarcoma, a rare secondary malignancy that affects the vascular endothelial cells of the affected limb. It is also known as Stewart-Treves syndrome and generally occurs in patients after mastectomy; however, it has also been found in patients with primary lymphedema and lymphedema induced by filariasis infection. Lymphangiosarcoma may appear 5 to 11 years after surgery as a purplish patch or multiple bluish-red nodules. It has a poor prognosis; therefore, all skin lesions in patients with chronic lymphedema should be carefully evaluated.[30]

Table 5. SURGICAL OPTIONS FOR PATIENTS WITH LYMPHEDEMA

Procedure	Indications	Study Design	Results	Benefits	Risks
Direct excision	Advanced lymphedema with persistent swelling and fibrosis	Prospective study[4]	Upper extremity: a 21% and 118% reduction in volume[20] Lower extremity: a 16% and 52% volume reduction[28]	May be curative in primary lymphedema	Infection, wound healing complications, lymphatic fistulas, disfigurement, amputation, sensory loss
Lymphatic-venous anastomosis (LVA)	Effective in early stages of lymphedema	Meta-analysis[29]	• 89.2% of patients noted subjective improvement • 87.8% showed quantitative improvement • 56.3% no longer needed compressive therapy	• Reduced rates of infection • Prevents lymphedema when completed as a prophylactic measure in women who underwent axillary lymph node dissection	Infection, lymphorrhea, further operations
Lymph node transfer	Stage 2–4 lymphedema Presence of fibrosis that prevents LVA Patient with history of chronic cellulitis with stage II lymphedema Patient has few or no functioning lymphatic vessels in appendage	Meta-analysis[29]	• 100% noted subjective improvement • 90.7% showed quantitative improvement • 78% no longer needed compressive therapy	• Decrease in limb circumference • Reduction in limb volume • Improvement in lymph flow • Quality-of-life improvement	Infection, lymphorrhea, reexporation surgery, complications at donor site
Liposuction	Late-stage lymphedema Failed measures with conservative treatment	Prospective trial[29]	• Improved quality of life • 73% of patients noted a reduction in limb volume	When used as adjunct with compression therapy, long-term benefits noted	Infection, reduced skin sensation, asymmetric contours, persistent swelling

PREVENTION

Patient Education

Patient education is imperative in the prevention and management of lymphedema. Ensuring that patients are knowledgeable about their condition can encourage patient adherence to treatment, self-care, and monitoring for any complications. There is increasing evidence of significant benefits of patient feedback about progress.[27]

The following are topics providers should review with patients diagnosed with lymphedema:

- Keep limb elevated whenever possible.
- Avoid limb-constricting garments.
- Self-monitor for changes in size, sensation, color, temperature, and skin condition that could signify an infection.
- Apply cream to skin daily. Compression stockings should not be worn immediately after application of cream.
- Maintain ideal body weight through exercise and proper diet.
- Avoid trauma to the affected limb.
- Comply with using compression garments and lymphatic pumps.

CONCLUSIONS

Patients with lymphedema are at increased risk of developing chronic ulceration. These wounds are recalcitrant to most treatment because of their underlying pathophysiology. They also leave an individual vulnerable to infection that can lead to serious, sometimes fatal, complications. Ensuring proper treatment modalities are employed at the earliest possible time offers the patient the greatest chance of healing.

PRACTICE PEARLS

- Chronic lymphostasis leads to eventual destruction of the lymphatic vessels, complicating treatment and increasing susceptibility to infection.
- A positive Stemmer sign is pathognomonic for chronic lymphedema.
- Complete decongestive therapy is the criterion-standard treatment method for patients with lymphedema. It is characterized by manual lymph drainage, compression therapy, exercise, and skin care.
- Silver dressings decrease the risk of infection. Prophylactic oral antibiotic treatment is recommended for patients with chronic infections in lymphedematous limbs.
- The use of lymph pumps and compression stockings is crucial in preventing backflow and improving lymphostasis.
- An interprofessional team is necessary to address the various etiologies, management, and treatment of lymphedema.

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