National Lymphedema Network

Position Statement of the National Lymphedema Network

NLN Medical Advisory Committee

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Lymphedema Diagnosis and Treatment

General Considerations

Lymphedema is an abnormal accumulation of macromolecule-rich fluid (e.g., protein, cells, and cell fragments) in the interstitial environment, manifesting in the extremities, trunk, and the head and neck.[1,2] This chronic disease, also referred to as chronic edema,[3] results from dysfunction in the lymphatic system (mechanical insufficiency) due to malformations or extensive damage to lymphatic structures.[1,2,4] While the primary symptom is swelling, lymphedema is associated with other morbidities, either coexisting with or independent of swelling. Chronic inflammation caused by excessive macromolecules in the interstitial environment can lead to adiposity and fibrosis.[1,5] Additional morbidities include reduced health-related quality of life, lowered self-esteem, recurrent infections (cellulitis), altered clothing fit, musculoskeletal conditions (e.g., limited range of motion, weakness, pain), neurologic disturbances (e.g., sensation changes), skin changes, discomfort, heaviness, depression, diminished activities of daily living, difficulty returning to work, and[2,6,15,16,7-14][17]although rare, chronic lymphedema can progress to cutaneous malignancies or angiosarcomas, with mortality rates of 53.9% for Stewart-Treves syndrome and 10.5% for other malignancies.[18] Common comorbidities include obesity, diabetes, congestive heart failure, neurological disorders, and peripheral artery disease.[19]

Lymphedema is broadly categorized into two etiologies: primary and secondary. Estimating prevalence and incidence is challenging due to a lack of universal diagnostic criteria, limited global epidemiological studies and diagnostic underreporting by both patients and healthcare providers.[2021] Worldwide, lymphedema affects approximately 140–300 million individuals,[2,2022] with an estimated 3–10 million cases in the United States.[2]

Primary Lymphedema

Primary lymphedema is characterized by congenital malformations of the lymphatic system (e.g., vessel or nodal aplasia, hypoplasia, or fibrosis) that lead to lymphedematous swelling.

Classification is based on the age of onset:

1. **Congenital lymphedema** (birth to before 2 years old)
2. **Lymphedema praecox** (2 to 35 years old)
3. **Lymphedema tarda** (over 35 years old) [20]

Globally, primary lymphedema affects approximately 1 in 100,000 individuals, with a prevalence of 1.33 per 100,000 in the United States.[21,23] Most cases are diagnosed in pediatric or adolescent stages, with males more commonly affected in infancy (~68%) and females during adolescence (~55%).[24,25] Over 20 genes are associated with lymphatic malformations,[21,26] including those linked to hereditary conditions like Nonne-Milroy disease and Meige disease.[4,22] Other hereditary syndromes associated with vascular and lymphatic abnormalities include Klippel-Trenaunay syndrome, Turner syndrome, Noonan syndrome, Hennekam syndrome, and Parkes-Weber syndrome.[21] Swelling is typically observed in the lower limbs but can also affect the upper extremities, head, neck, and trunk.[27] Primary lymphedema may progress, stagnate, or regress over time.[21]

Secondary Lymphedema

Secondary lymphedema is an acquired condition resulting from injury to lymphatic structures.[22] It affects 1 in 1,000 individuals, accounting for 99% of adult and 3% of pediatric lymphedema cases.[23-25] This more common and often debilitating form is frequently associated with cancer treatments like surgery and radiation therapy. Prevalence is influenced by the cause of lymphatic injury and geographical location. In Canada, secondary lymphedema was considered to be caused by:

1. Venous disease (72%)
2. Obesity (54.4%)
3. Non-cancer causes (14.7%)
4. Cancer/metastatic disease (17.6%)
5. Treatment-related obstruction (8.8%) [19]

Globally, lymphatic filariasis (elephantiasis) is the leading cause of secondary lymphedema, affecting approximately 70 million individuals in 83 countries across Africa, Asia, and South America.[2,28] This condition arises from Wuchereria bancrofti parasite invasions. Podoconiosis, another cause, results from

the absorption of micro silica particles into the feet in endemic regions of Africa.[16] Obesity-induced lymphedema has become increasingly prevalent due to the global obesity epidemic, with over 650 million obese individuals worldwide.[29] Individuals with a BMI >50 are particularly at risk, especially for lower extremity lymphedema. Chronic venous disease can also contribute to secondary lymphedema (phlebolymphedema), with studies showing a prevalence of 10.4% and higher rates compared to cancer-related lymphedema (41.8% vs. 33.9%).[30,31] Certain medications, such as protein kinase inhibitors, antidepressants, antihypertensives, corticosteroids, and opioids, may exacerbate secondary lymphedema by promoting peripheral edema and lymphatic dysfunction.[32]

Secondary lymphedema research often focuses on breast cancer-related lymphedema (BCRL), which affects approximately 20% of breast cancer survivors in the U.S.[2,6,33] In lower-income countries, cancer-related lymphedema is also significant, with pooled prevalence rates for arm lymphedema reaching 27%.[34] Cervical cancer treatments may lead to lower extremity or genital lymphedema, with incidences up to 69%.[35] Prostate cancer treatments can result in genital lymphedema, with a prevalence of 29% for lower extremities and 22% for genitalia.[36] Head and neck lymphedema (HNL) associated with cancer treatments impacts both internal structures (larynx, pharynx) and external areas (face, neck), affecting 12–54% of cases.[37] Head and neck lymphedema limits activities such as chewing, swallowing, breathing, and social interactions.[37]

Purpose

Lymphedema is a significant global chronic disease that is progressive, debilitating, and impactful at multiple levels. Although it is not curable, lymphedema is manageable and progression is preventable with early diagnosis. Practitioners and researchers need comprehensive information on lymphedema's pathophysiology, assessment, diagnosis, classifications, and treatment options. Unfortunately, this awareness is not yet standardized.[38] The purpose of this National Lymphedema Network (NLN) Position Paper is to provide a foundation for understanding lymphedema diagnosis and treatment, paving the way for subsequent NLN position papers.

Diagnosis

Background and Universal Agreement

Since the NLN's 2011 position statement on lymphedema diagnosis and treatment, significant progress has been made in diagnostic criteria and measurement tools, particularly for BCRL. However, there remains no universally accepted gold standard for lymphedema diagnosis. Researchers aim to establish robust diagnostic thresholds, with an increasing focus on prospective surveillance for early diagnosis and improved patient outcomes.

Prospective Surveillance for Secondary Lymphedema

Prospective surveillance involves longitudinal monitoring of at-risk patients using objective and patient-reported outcome measures to facilitate early diagnosis and treatment.[39-43] Education on recognizing symptoms and self-referral is critical.[41] Compared to traditional treatment models, prospective surveillance is cost-effective,[44] improves early referrals, reduces the incidence and severity of clinical lymphedema[45] and has proven feasible in diverse healthcare settings.[41,43,46-49]

Secondary Lymphedema Risk Factors

Lymph node removal, particularly through dissection for staging cancers, is a major risk factor for lymphedema.[33,50] Risk factors for breast cancer-related lymphedema include axillary lymph node dissection (ALND), regional nodal irradiation, high BMI (>25 kg/m²), cellulitis, subclinical swelling, Black race, and Hispanic ethnicity.[50,51,60-62,52-59] Less clear factors include axillary web syndrome (AWS), taxane-based chemotherapy, and genetic predisposition.[63-68]

Elements of a Prospective Surveillance Program

An ideal prospective surveillance program includes preoperative baseline measurements, objective longitudinal assessments, patient education, and self-monitoring.[45,69] Preoperative baselines account for natural asymmetries and reduce misdiagnosis.[69-71] Screening should continue for at least five years, given the cumulative incidence during this period.[40,72] A risk-stratified approach is suggested for prospective surveillance, with close monitoring for high-risk individuals and less frequent screening for low-risk patients emphasizing self-monitoring.[56] As detailed in later sections, objective measurement tools and patient-reported outcomes play crucial roles.

Diagnostic Criteria for Lymphedema: The Call for Universal Agreement

Despite years of research, no consensus exists on the diagnostic tools or thresholds for lymphedema.[73-76] Some outdated and invalid methods persist. There is a pressing need for lymphatic organizations to align with evidence-based guidelines and discontinue outdated techniques in clinical and research settings.

Core Outcome Set (COS)

Outcome measures (OMs) are essential for assessing lymphedema, its morbidities, and guiding care plans.[77] However, clinicians face barriers to their use, like an overwhelming number of options, knowledge gaps, and resource limitations.[77] A standardized COS has been proposed, comprising 12 core OMs domains for BCRL: volume, tissue consistency, pain, joint function, flexibility, sensation, strength, patient-reported function, quality of life, fatigue, activity, motor control, and mobility.[78-79] Other OMs domains that may be warranted for assessment include integumentary integrity (i.e. wounds, infections, and papillomas) and vascular assessment. These measures enhance interdisciplinary communication, improve documentation, and guide care across the disease continuum. Research is ongoing to develop COSs for lower extremity, truncal, and head and neck lymphedema.

Medical History

Collecting a thorough medical history and subjective data is essential for evaluating and treating lymphedema. Key areas of focus include:

1. Onset and Timeline
   - When did the swelling begin? Was the onset gradual or sudden?
   - Are there patterns of fluctuation? Specific times or activities that worsen it?
   - Does it improve overnight/with elevation?
2. Symptom Characteristics
   - Swelling Pattern: Unilateral or bilateral? Localized or generalized?
   - Sensations: Pain, heaviness, tightness, a sense of swelling or tingling?
   - Skin Changes: Erythema, skin thickening, texture changes, or peau d'orange?
   - Complications: History of infections (cellulitis/erysipelas), fluid leakage, hematoma or seroma?
   - Functional Impairment: Difficulties with daily activities or mobility?
3. Risk Factors and Triggers
   - Family History: Primary or hereditary lymphedema?
   - Surgical History: Cancer surgeries, lymph node dissections, radiation?
   - Chronic Conditions: Venous insufficiency, heart/kidney disease, obesity?
   - Infections: Recurrent infections or parasitic diseases like filariasis?
- Occupational and Lifestyle Factors
  - Sedentary behavior, comorbid local musculoskeletal conditions, or travel to filariasis-endemic areas?
  - Dietary patterns, especially sodium intake?
- Psychosocial and Quality of Life Impact
  - Emotional challenges such as body image issues or mental health concerns?
  - Availability of support for managing the condition?
- Prior Treatments
  - History of therapies like manual lymph drainage (MLD), compression therapy, or surgeries?
  - Medications that may impact lymphedema risk or fluid status?

Lymphedema Staging and Grading

The International Society of Lymphology (ISL) provides a widely accepted staging system for lymphedema:[80]

- **Stage 0 (Latent)**: Compromised lymphatic transport; no visible swelling.
- **Stage 1**: Reversible swelling that subsides with elevation; pitting may occur.
- **Stage 2**: Persistent swelling that does not subside with elevation; pitting present. Note: As this stage progresses pitting becomes more difficult due to fibrosis and adiposity proliferating.
- **Stage 3 (Elephantiasis)**: Severe fibrosis, adiposity, and trophic skin changes; no pitting.

Diagnostic tools like lymphoscintigraphy (LSG), magnetic resonance lymphography (MRL), and indocyanine green lymphography (ICG-L) complement ISL staging and lymphedema diagnosis. While volume differential guidelines (e.g., ≥200 mL for the upper extremity) exist for lymphedema diagnosis, lower differential volume values cannot rule out lymphedema, and its use is discouraged. Therefore, relative volume change (RVC) is recommended for use in supporting a lymphedema diagnosis and is detailed later in this document. Universal staging systems, despite limitations, remain critical for accurate classification, especially for lower extremity cases.[80,81-84]

Lymphatic Imaging

Advances in imaging have improved diagnosis, staging, and treatment planning:

Lymphoscintigraphy (LSG)

- A gold standard technique using technetium-99m tracers to evaluate lymphatic function.
- Key findings include lymphatic vessel count, node visibility, dermal backflow, transport delays, and collateral flow.
- LSG is highly sensitive (96%) and specific (100%), aiding in staging, differential diagnosis, and surgical planning.[85-91]
- LSG aids in surgical planning for lymphedema, including preventive procedures, and is increasingly used in clinical practice.[92,93] It differentiates lipedema and chronic venous insufficiency, both linked to lymphatic transport abnormalities. Patients with lipedema show delayed, asymmetric lymphatic flow on LSG.[94-100] As a widely available imaging test, LSG confirms lymphedema, guides therapy, and predicts treatment outcomes.[101,102]

Indocyanine Green Lymphography (ICG-L)

- Near-infrared fluorescence imaging maps superficial lymphatics in real time.
- Sensitivity (97%) and accuracy (82%) make it useful for diagnosis, surgical planning, and treatment monitoring.[103]
- MD Anderson classification stages lymphedema from 0 (normal) to 5 (no functional vessels, extensive backflow).[103-108]
- Applications include lymphaticovenular anastomosis (LVA), lymph node transfer, and tailored conservative treatments. ICG-L is minimally invasive but should be used cautiously in patients with liver/kidney disease, iodine sensitivity, or pregnancy. Combining ICG-L with other imaging modalities optimizes outcomes for individualized care.[109,110,119-123,111-118]

Objective Measurements for Lymphedema Assessment

Volume Measurement

Accurate and standardized volumetric methods have been pivotal in lymphedema screening and detection for decades.[47,48,51,56,74,124-126]

- **Water Displacement**: Once widely used, this method involves submerging a limb into a cylinder and measuring displaced water. Despite its accuracy, its use has declined due to equipment requirements, infection risks, and time inefficiencies.[74]
- **Girth Measures to Calculate Limb Volume**: Circumferential measurements using a flexible tape at regular intervals (e.g., 4 cm, 10 cm) or anatomical landmarks are common due to portability and cost-effectiveness. These are converted to volume using the truncated cone formula.[127] Interval-based protocols (e.g., 4 cm, 10 cm) are efficient but not interchangeable with other methods. Inter-rater reliability improves with standardized protocols and consistent testers.[127-130] Comparison of extremity volumes are common in clinical practice and is often used to make a lymphedema diagnosis. Using relative volume changes is recommended for comparisons of volume and is detailed later.
- **Infrared Optoelectronic Limb Volumetry (Perometry)**: Perometry provides reliable circumferential measures every 4 mm and automatically calculates limb volume.[127] It is sensitive to subclinical volume changes and efficient for screening but limited by cost, space, and portability.[41,51,75,131-134]
- **3D Imaging**: Using infrared cameras and custom software 3D imaging offers portable, efficient volume calculations. Early studies show strong correlation with girth measures, perometry, and water displacement.[135-137]

Bioimpedance Spectroscopy (BIS)

BIS uses a spectrum of electrical frequencies to differentiate fluid compartments, making it effective in detecting extracellular fluid changes, particularly in early-stage lymphedema.[138] In BCRL, BIS may aid in early detection and reduce progression to complex decongestive therapy (CDT).[126] Compared to excess volume-based methods, BIS lymphedema index (L-Dex) shows superior sensitivity (AUC = 0.832 vs. 0.649) in detecting BCRL.[139] Devices yield high positive predictive value (96.7%) but moderate sensitivity (72.5%) and specificity (87.5%), with limited accuracy in distinguishing fluid from fat.[140] False negatives are noted in early-stage cases (36%), necessitating combined use with clinical evaluations.[139,141,142] Variability among devices (e.g., platform vs. lead-based systems) highlights the importance of device-specific reference ranges.[139,143,144] Limitations may include space and cost restraints.

Measurement Protocol Considerations: Volume

1. Bilateral Limb Measurements: Arm volume on the side not affected by cancer has high variation, with a median within-patient change of 10.5% observed

in patients screened for BCRL across >6 measurements. Limb volume includes tissues prone to symmetrical fluctuation (e.g., adipose tissue changes), while lymphedema-related edema is asymmetrical and isolated to the at-risk limb. Bilateral measurements, regardless of method (e.g., water displacement, girth measures, perometry, 3D imaging), are recommended for accuracy.[125]

2. Differentiating Edema Types: Volumetric measures do not distinguish lymphedema from other edema types; combining risk factors, symptoms, and clinical exams improves differentiation.

Diagnostic Considerations: Volume

1. Preoperative Baseline: Absence of preoperative baseline volume measurements can lead to misdiagnosis rates up to 60%, as arm volume asymmetry often exists preoperatively. Early postoperative measurements are unreliable as baselines, making preoperative baselines crucial for accurate diagnosis.[69,124,125]
2. Relative vs. Absolute Volume Changes: Absolute volume changes (e.g., 2 cm or 200 mL) are influenced by body weight and BMI fluctuations, while relative volume changes (RVC) (% change) are independent of these factors, making them the preferred metric.[56,124,125,145] Any volumetric method can use the RVC formula: RVC = $[(A_2U_1)/(U_2A_1) - 1] \times 100\%$, where A_1, A_2 are affected-side volumes and U_1, U_2 are unaffected-side volumes.[124]
3. Diagnostic Thresholds: Although no universal diagnostic threshold exists, RVC increases of 5–<10% (subclinical lymphedema) and ≥10% (clinical lymphedema) from baseline have demonstrated efficacy in early detection and intervention.[45,51,56]
4. Bilateral Risk: In cases of bilateral risk (e.g., bilateral lymph node dissection), unaffected limbs are unavailable as controls. For these patients, relative % volume changes, symptoms, clinical exams, or alternative methods like bioimpedance or tissue dielectric constant (TDC) may be utilized.

Electrical Conductive Testing

- Tissue Dielectric Constant (TDC): TDC measures tissue water by analyzing reflected electromagnetic waves. TDC values range from 1–80, with 80 indicating pure water. TDC is supported by normative thresholds for arm and breast lymphedema (1.28–1.40 affected: unaffected TDC ratio).[146-151] While primarily a research tool, TDC is useful for quantifying tissue water in areas less accessible to circumferential and volumetric methods such as the breast or trunk.

Measurement for Head, Neck, Breast, and Trunk Lymphedema

Traditional volumetric measures are unsuitable for body parts with variable sizes and shapes. Head and neck lymphedema, despite its prevalence, lacks reliable tools. Systematic reviews highlight promising tools like the Patterson scale for internal lymphedema and the LIDS-H&N for external lymphedema, though reliability across measurement points remains inconsistent.[152] For breast and trunk lymphedema, TDC is supported by published thresholds.[147-151] However, variations in protocols (e.g., resting time, position, measurement site) limit diagnostic accuracy. Emerging methods like 3D imaging show potential for future use.

Integument Assessment

Assessment of primary and secondary lymphedema includes documentation of soft tissue observations such as fibrosis, scar tissue, and radiation damage. Photographic evidence and descriptions of size and color are essential for monitoring intervention outcomes.

The presence of indurated tissue (fibrosis) is critical for staging lymphedema progression according to ISL criteria, as it reflects proliferative fibrosis rather than just volume changes.[80] However, clinically feasible tools to measure fibrosis remain limited, with CLTs often relying on subjective descriptors or semi-quantitative pitting edema tests, which have shown poor reliability.[153-155] Emerging tools such as pitting[154,156] edema trainers, edema testers, and rulers require further research to improve reliability and correlation with fibrosis and ISL staging.

More advanced tools like ultrasonography and tonometry provide precise fibrosis measurements. Ultrasonography, recommended for Stage III BCRL diagnosis,[155] assesses tissue thickness and assists with differential diagnoses like lipedema.[157-160] High-frequency ultrasound has demonstrated good intra-rater reliability in assessing skin and subcutis thickness.[161,162] Tonometry measures tissue stiffness, with tools such as the various tools showing strong reliability.[163-168] Despite these advances, the cost often limits access, emphasizing the need for affordable, standardized tools for fibrosis measurement.

Axillary web syndrome (AWS), common after ALND, presents as tight cords in the axilla extending to the arm and thumb.[169] Symptoms may appear weeks to years' post-surgery. Assessment includes medical history, diagnostic imaging, observation, palpation, and documentation of cord size, location, and

associated pain, with photographic evidence when possible.[169-171]

Dermal changes such as hyperkeratosis, papillomas, lymphatic cysts, or fistulas may require adjusted care. Clinicians should document these epidermal conditions with size, location, and photographs. Cysts may progress to lymphatic fistulas, promoting lymphorrhea.

Infections, especially cellulitis, pose significant risks in lymphedema, with 92% of lymphedema-related hospitalizations linked to cellulitis.[172] Non-purulent cellulitis presents as erythema, warmth, edema, and pain, often without fever. Diagnosis relies on clinical observation and patient history, as laboratory tests and blood cultures are unreliable.[173-174] Other conditions mimicking cellulitis include stasis dermatitis, DVT, and gout, with misdiagnosis contributing to unnecessary antibiotic use.[173]

Malignant lymphedema, indicated by red blotches, rapid progression, and possible open lesions, requires urgent referral.[27] Chronic lymphedema may result in Stewart-Treves syndrome, an angiosarcoma with poor prognosis, presenting as hematoma-like lesions or ulcerating papules.[175] Immediate biopsy and consultation are advised when such signs appear.

Genetic Testing
Genetic testing is a valuable tool for diagnosing lymphatic vascular malformations and primary lymphedema by identifying syndromes with lymphatic abnormalities associated with specific phenotypes, alleles, and loci mutations. It is also important to recognize that secondary lymphedema may have a genetic predisposition triggered by iatrogenic factors.[176,177] Targeted sequencing, followed by gene identification through the Online Mendelian Inheritance in Man (OMIM) database, is the evidence-based recommendation for molecular diagnosis of primary lymphedema.[176] Michelini et al. identified 382 genetic tests for hereditary lymphedema, most employing Sanger or next-generation sequencing.[176] However, the current molecular diagnostic system lacks efficiency and standardized guidelines,[176,178] prompting researchers to propose molecular diagnostic flowcharts[176] or pathways[178] for identifying underlying mechanisms. There may also be value in prenatal, early postnatal, or pre-operative genetic testing for primary or multifactorial lymphedema, particularly in cases where early intervention could improve management, surgical planning, or family counseling about familial inheritance patterns.

Objective Measurements for Lymphedema Burden Assessment
Outcome measures are critical in the assessment of impairment severity (e.g., volume, fibrosis, range of motion) and participation burdens (e.g., sports involvement, limitations in daily activities, pyschosocial influences) of lymphedema. While most research focuses on BCRL, recent studies have emphasized the need for standardized OMs across various types of lymphedema.[77-79] Clinicians commonly assess impairments by measuring active range of motion using goniometric measures, muscle strength via manual muscle testing, circumferential measures converted to volume, light touch sensation, tissue consistency through palpation, flexibility of pectoralis major and minor, grip strength using dynamometry, and pain via a visual analog scale.[77-79]

Patient-Reported Outcome Measures (PROMs)**:**
PROMs are vital for assessing health-related quality of life (HRQOL) in lymphedema patients, but many lack robust methodological and psychometric development.[179] The Lymphedema Life Impact Scale (LLIS) and the Lymphedema Quality of Life Questionnaire (LYMQOL) are helpful with assessing general HRQOL in individuals with lymphedema.[79] For lower extremity lymphedema, the Lymph-ICF-LL and LSIDS-L are appropriate.[180,181] Male genital lymphedema assessments include the lower limb lymphedema questionnaire and the male genital self-image scale.[182] For head and neck lymphedema, the EORTC QLQ-C30 and FACT-HN are frequently used.[183]

BCRL-specific PROMs include the Lymph-ICF-UL, which has strong psychometric properties,[184] and the Upper Limb Lymphedema-27 (ULL-27).[179] Functional impact tools include the Functional Assessment Screening Questionnaire (FAS-Q)[180]and the Lower Extremity Functional Scale (LEFS) for lower extremity lymphedema.[180] The DASH and QuickDASH may be used to assess upper quadrant function in BCRL.[79] The 9-hole peg test may be used to assess upper extremity activity and motor control.[79]

Mobility and Balance:
Lymphedema often affects mobility and balance.[185,186] Tools to assess lower extremity lymphedema include the Timed Up and Go (TUG),[79] Fullerton Advanced Balance (FAB) Scale,[187] and the 5x Sit-to-Stand test.[79]

Treatment

Early Intervention for Asymptomatic Lymphatic Deficits

Untreated lymphedema leads to tissue changes, including excess adipose tissue and fibrosis, making later stages more resistant to treatment.[188] Chronic tissue changes increase infection risks (e.g., cellulitis, erysipelas), initiating a cycle of recurrent infection and worsening edema.[188] Subclinical lymphedema, identified through prospective screening, poses a higher risk for progression to clinical lymphedema, particularly after invasive nodal surgeries (e.g., axillary dissection vs. sentinel node biopsy).[51] Studies report 39.7% of subclinical lymphedema cases after axillary dissection and 11.5% after sentinel biopsy progress to clinical lymphedema without treatment.[51]

Subclinical lymphedema, often detected via limb volume increases (3%-5%)[51,131] or bioimpedance changes (L-Dex increase ≥6.5),[126] may be present without visible swelling or symptoms. Early intervention strategies have been evaluated in ten prospective studies, including two randomized controlled trials (RCTs) which have shown that benefits of early intervention to reduce the incidence of lymphedema to a range of 7% - 11%.[126,131,189-194] Early intervention using compression, exercise, or manual techniques may reduce progression, especially in high-risk patients. Prospective screening allows for close monitoring of efficacy.[45,51,131] Further research is needed to establish evidence-based methodologies, study interventions across all etiologies, and evaluate compression dosing.

Prophylactic Intervention with Compression Garments for Lymphedema Progression

Two studies assessed postoperative compression sleeves in patients undergoing ALND for breast cancer. In the studies by Ochalek et al. and Paramanandam et al., subjects wore Class I compression sleeves on a daily basis. In addition to the compression sleeves, subjects were involved in a standardized exercise program in the study by Ochalek et al. The outcomes for Ochalek et al. and Paramanandam et al., studies that the control group had significantly greater edema ($P < 0.001$), and the compression group showed reduced arm swelling incidence (HR 0.61 for BIS; HR 0.56 for RAVI) and delayed swelling onset, respectively.[195-197] Follow-up measures revealed persistent benefits of the interventions for both studies. Prophylactic use of class I compression sleeves may reduce arm swelling in the postoperative period for BCRL, especially in those at high risk of BCRL after nodal dissection. However, data is limited to this population, and further studies are needed to determine effectiveness in other lymphedema etiologies.

Complete Decongestive Therapy

Overview

Effective lymphedema treatment relies on comprehensive approaches. Prior to the advent of Complete Decongestive Thearpy (CDT), interventions included diuretics, limb elevation, pneumatic compression, elastic garments, and invasive procedures such as debulking surgeries. CDT emerged from the foundational work of pioneers such as Winiwarter, Vodder, Asdonk, and Michael and Etelka Foeldi, whose contributions from the 19th century to the 1970s shaped its development.[27] Building on anatomical insights from Sappey and advancing manual lymphatic techniques, CDT became a standardized approach in the 1970s under the Foeldis' leadership in Hinterzarten, Germany.

CDT is a two-phase, non-invasive approach for managing lymphedema and other peripheral edemas. Recognized internationally as the conservative gold standard for lymphedema treatment, it is practiced by rehabilitation professionals, nurses, physicians, and licensed manual therapists.[80] The two phases include an intensive clinical phase followed by a self-management phase. Its effectiveness and utility are supported by extensive clinical experience and endorsed by International Society of Lymphology Consensus Documents.[80]

Components

CDT consists of the following components, tailored to the treatment phase, severity, and therapeutic goals:

- **Manual Lymph Drainage** (MLD): Increases lymphangion activity and reabsorption of protein rich fluid to promote lymphatic flow and reduce congestion.
- **Skin Care**: Prevents infection and maintains tissue integrity.
- **Multilayered Short-Stretch Bandaging**: Reduces filtration, improves the muscle and joint pump,

softens indurated tissue, and prevents re-accumulation of edema.
- **Elastic and Non-Elastic Compression Garments**: Allows for containment and maintains decongestion in the self-management phase.
- **Decongestive Exercises**: Promotes the muscle and joint pump to facilitate lymphatic and venous return.
- **Self-Care Education**: Empowers patients to manage their condition effectively.

Each component's role is adjusted to optimize therapeutic outcomes across the treatment continuum.

Phases of Therapy: Intensive/Clinical (Phase I) & Maintenance/Optimization (Phase II)

Phase I: Intensive/Clinical Phase
During Phase I, therapy involves daily (five days per week) sessions designed to significantly reduce systemic lymphatic and peripheral limb congestion. This is achieved through MLD, gradient compression, and exercises promoting lymphatic flow within a compression environment. Daily skin inspection follows bandage removal, accompanied by cleansing and moisturizing to restore suppleness and the skin's acid mantle, followed by manual lymphatic drainage and reapplication of multiple-layer bandaging or other reductive compression garments. Compression is left in place until the next treatment session, without disruption in care.[198]

The comprehensive nature of Phase I therapy allows for individualized interventions, focusing on:
- Limb volume reduction[199,200]
- Improvements in limb function, weight, contour, and skin integrity[201]
- Patient education for autonomous care.

Therapists use this phase to assess and adapt treatment based on patient-specific needs, maximizing therapeutic outcomes.

Frequency and Duration of Phase I Therapy
The duration of Phase I is guided by clinical factors such as disease severity, skin condition, infection risk, functional limitations, and other practical constraints. CDT is ideally performed 5 days per week until a volume reduction plateau is reached, typically over 3 to 8 weeks.[202,203]While daily sessions are optimal, modified schedules may also yield positive outcomes for some patients. However, in general, response to Phase I CDT will depend on lymphedema severity, with more treatment sessions rendered for advanced stages of lymphedema.[204]

Phase II: Maintenance/Optimization Phase
Once Phase I goals are achieved, patients transition immediately to Phase II care, without a gap in compression, to independent home management.

The objectives during Phase II include:
- Sustained improvements in limb volume, contour, skin integrity, weight, and function.
- Education concerning skin integrity, hygiene, and infection management.[205,206]
- Prescription of individualized maintenance compression garments for day and night use.[207] These may include off-the-shelf ready-to-wear or customized made-to-measure garments.
- Proficiency in using compression systems and self-administered MLD.
- Incorporation of activity, weight management, and specialized exercises.[208-212]
- Confidence in independent self-management and discharge from daily clinical care.

Monitoring and Support During Phase II
Periodic medical monitoring is critical for long-term success, including:
- Regular garment fittings and replacements every 4-6 months.[209,213-215]
- Addressing barriers to optimal limb maintenance and stability.
- Providing education and assessing adherence to CDT components.

Specialized equipment used in self-care should be maintained and replaced per manufacturer guidelines to ensure effectiveness.[209,213-215]

Frequency and Duration of Phase II Therapy
Phase II may last a lifetime, particularly for advanced lymphedema (Stages 2-3).[216]Early-stage lymphedema (Stages 0-1) may require minimal management focused on preventing exacerbation. When compression therapy alone is sufficient, Phase II can be simplified with basic skincare and general health practices.[27,216] Prospective surveillance, early identification, and targeted interventions play key roles in tailoring Phase II programs.[217]

Modifications and Individualization of Complete Decongestive Therapy
Lymphedema affects various body regions, requiring flexible application of CDT. Adjustments are often necessary for regions such as the head, neck,

genitals, and trunk, where safe compression or manual manipulation may be challenging. Pediatric lymphedema also requires adaptations to account for age, developmental stage, and caregiver involvement. Strategies focus on engaging intact and impaired lymphatic pathways, using MLD and compression to promote tissue decongestion, while emphasizing skin care, infection prevention, and self-care education.

Head and Neck Lymphedema (HNL)

HNL is less common than lymphedema of the extremities but presents unique challenges. Certified Lymphedema Therapists (CLTs) often pursue advanced training to manage HNL, particularly internal swelling of the tongue, larynx, or pharynx. Intraoral MLD, facial exercises, and customized compression strategies—designed to avoid impairing breathing, swallowing, or daily functions—are effective tools.[27] Scars from surgery or radiation require techniques to soften tissue and improve lymphatic drainage, as raised or poorly healed scars reduce lymph flow.[218,219]

Compression for HNL must be carefully applied to avoid obstructing drainage or causing harm, especially in cases of carotid artery pathology, cerebrovascular disease, or tumor invasion. Low resting pressure and high working pressure are ideal. Elastic taping can complement MLD and compression, enhancing lymph transport through gentle lifting and stretching forces on the skin. However, caution is required in areas exposed to radiation, where skin integrity may be compromised.[216,218,220]

Breast and Trunk Lymphedema

Breast and chest wall lymphedema are often overlooked despite being common after breast cancer treatment, particularly in ipsilateral trunk quadrants. Symptoms such as heaviness, redness, and discomfort, along with localized swelling, require careful evaluation of lymphatic territories affected by surgery or radiation therapy.[148,221] Breast involvement often favors the lateral and inferior regions, with gravity contributing to fluid accumulation in pendulous breast tissue.[27,222]

Redundant skin folds ("dog ears") or tight bras can exacerbate fluid buildup, while sensory loss may delay reporting of symptoms. Clinical inspection is essential for developing treatment plans, which should prioritize the affected lymph node territories[223,224] and avoid deep techniques in irradiated fields to prevent rib fractures or other vascular or integument complications.[225]

Manual lymph drainage is key for addressing breast and trunk edema, focusing on superficial and deep lymphatic pathways, including intercostal, parasternal, and paravertebral nodes. Pretreatment should include the contralateral lymphatic system and superficial anastomoses. Compression therapy options may include wide short-stretch bandaging, compressive shapewear, or custom-fitted garments, ensuring proper fit to prevent fluid trapping. Padding can localize pressure, soften fibrotic tissues, and prevent garment edges from rolling. Additional modalities such as elastic taping and Low-Level Laser Therapy (LLLT) may support treatment, which are addressed in later sections.

Genital Lymphedema

The superficial lymphatic system of the lower abdomen, hips, buttocks, and genitals is highly susceptible to lymphedema when inguinal nodes are impaired. In females, swelling often respects the midsagittal watershed, leading to unilateral labial involvement, while males experience diffuse swelling without this boundary. Intrapelvic and abdominal cancer treatments which may include surgery, radiation therapy, and lymphadenectomy, can disrupt lymph flow, causing retrograde congestion in the genitals and lower limbs.[36]

Primary genital lymphedema is rare, usually resulting from lymphatic malformations, and may become evident during childhood. Chronic genital lymphedema often leads to skin changes (e.g., cysts, papillomas) and fluid leakage that heightens the risk of recurrent cellulitis, which is reported in 85% of cases.[226-228]

Treatment prioritizes the core components of CDT, including MLD to activate superficial and deep lymphatic pathways and compression to reduce swelling. Self-care education is critical, focusing on hygiene, infection management, and compression application. Diaphragmatic breathing exercises support thoracic duct drainage, while customized compression pads and garments ensure effective pressure without compromising function.

In cases involving severe complications, surgical excision of non-healing lesions, cysts, or papillomas has proven beneficial, significantly reducing

infections and antibiotic use.[226] Surgical intervention may also address gross enlargement, sexual dysfunction, or persistent pain, with patients reporting improved quality of life post-surgery.[27,227]

Upper and Lower Extremity Lymphedema

Complete decongestive therapy remains the gold standard for managing extremity lymphedema, combining intensive clinical care with long-term maintenance strategies. Compression therapy is a cornerstone, with duration and intensity tailored to disease severity and clinical outcomes.[229]

In early stages (Stage 0 or 1), interventions focus on self-care education, infection prevention, and compression garments, which may suffice to alleviate symptoms. Clinical sessions of MLD may be minimal while continuing prospective surveillance.

In Stage 2 and 3 lymphedema, protein accumulation, fibrosis, and abnormal fat deposition make intensive clinical care essential. Manual lymph drainage promotes lymph uptake and collateral drainage, while multi-layered short-stretch compression bandaging reduces filtration and fluid re-accumulation, facilitates the muscle joint pump, and remodels lymphostatic fibrosis. A plateau in clinical examination of symptoms and objective measurements signifies the transition to the maintenance phase, where compression garments and self-care sustain results. Multiple intensive phases may be necessary to achieve additional improvements.

Microsurgical techniques, such as lymphatic-venous anastomosis or lymph node transfers, can restore drainage following regional node impairment. CDT is utilized to maximize limb reduction prior to surgery, and as needed after surgery. Reductive or excisional surgeries may also be considered for patients with abnormal adipose deposition.[230] Further details about surgical treatments for lymphedema are expanded upon below. Pre- and post-operative consultations with a CLT are critical for optimizing surgical outcomes and managing complications.

Patient education is central to both conservative and surgical approaches, ensuring individualized feasibility of treatment, adherence and maintaining quality of life. Identifying specialized lymphatic surgeons with expertise in CDT and lymphology is essential for the best outcomes.

Therapist Training

Lymphedema treatment falls within the scope of rehabilitation professionals, but advanced education should be pursued due to the limited training in lymphatic system function and disease processes during professional licensure programs. This educational gap often leads to reduced confidence in providing safe and effective care, prompting therapists to seek the Certified Lymphedema Therapist (CLT) designation. [225]

Historically, lymphedema training in the U.S. was unregulated, with variations in program prerequisites and educator qualifications. Despite this, consensus emerged that the knowledge base was substantial enough to define the scope and duration of training programs. These programs, rooted in the German CDT system, included both theoretical and practical components.

The Lymphology Association of North America (LANA) was founded in 2000 to establish certification guidelines, assuring that lymphedema treatments meet state-of-the-art criteria. This association provides a standardized examination to assess the competency of graduates from established training programs. These programs require a minimum of 135 hours of education, divided between psychomotor and didactic training. LANA adopted this model as the baseline requirement for eligibility to sit for its certification exam. Successful candidates earn the CLT-LANA designation, signifying advanced competency.

Legislation introduced in 2010 sought to address lymphedema education and care standards, though it was not ratified. However, it catalyzed LANA's accreditation as a credentialing body. In 2017, LANA obtained recognition from the American National Standards Institute (ANSI) for the CLT-LANA designation, further ensuring minimum educational competencies for lymphedema treatment. Ideally, individuals seeking treatment for lymphedema should pursue a Certified Lymphedema Therapist.

Manual Lymph Drainage

Manual Lymph Drainage (MLD) is a hands-on technique designed to decongest tissues by promoting the movement of interstitial and lymph fluid. Its effects include reducing edema, increasing lymph pulsation and transport, and inducing relaxation via a parasympathetic response.[231,232] The technique comprises a working phase, where gentle

pressure and skin stretching increase lymph formation, and a relaxation phase, which allows lymph vessel refilling. Contraindications include acute infection, decompensated congestive heart failure, and acute deep venous thrombosis (DVT).

Manual lymph drainage is performed directly on the skin, with pressure adapted to tissue texture—firmer for fibrotic tissues and lighter for softer tissues.[233] Proper application softens fibrotic tissue while minimizing pain or erythema.[231,234,235] The treatment sequence begins proximally and progresses distally, promoting lymph flow from areas of stasis into viable lymphatic pathways. Near-infrared imaging has revealed MLD's ability to stimulate intrinsic lymphatic contractions and extrinsic mechanical pumping, increasing the normal lymphatic pumping rate from 6–10 times per minute to as much as 60–100 times per minute.[235-237]

Patient-specific MLD sequences are guided by individual medical and surgical histories. Imaging studies using indocyanine green (ICG) have identified region-specific drainage patterns, such as ipsilateral axillary drainage in 74.9% of upper-extremity lymphedema cases and ipsilateral inguinal drainage in 52.3% of lower-extremity cases.[233] In severe cases, fluid may cross into adjacent quadrants to reach viable drainage pathways.[233]

Evidence on MLD's efficacy is mixed. Systematic reviews and meta-analyses suggest it may not significantly enhance lymphedema management when used alone, citing inconsistent methodologies, variations in technique, and measurement limitations as factors.[231,232,238-240] Despite a lack of strong supportive evidence, MLD is considered safe and should not be withheld from patients.[231]

MLD has been shown to reduce volume and soften fibrotic tissue when intensively applied during Phase I of CDT.[234,241] It also benefits patients when combined with compression therapy, demonstrating decongestive effects and improved lymphatic contractile function in imaging studies.[234,242,243]Early MLD intervention during rehabilitation has proven particularly effective, such as in treating oral cancer-related lymphedema and improving neck range of motion.[244]Further research with larger populations is necessary to solidify its role and effectiveness.[241,245]

Bandaging

Compression bandaging is a key component of CDT and is worn 24 hours a day during the intensive treatment phase to accommodate daily changes in limb size. Its primary purposes are to increase venous and lymphatic return, reduce limb volume, and soften indurated tissues, making MLD more effective.[242,246,247] These effects are achieved by creating counterpressure to reduce fluid filtration, enhancing the muscle-joint pump, breaking up lymphostatic fibrosis, and preventing re-accumulation of fluid.

The bandages provide external compression to increase tissue pressure and facilitating passive lymphatic flow during muscle contraction.[247-249] This mechanical stimulation increases lymphatic vessel contractions, boosting the pumping rate from the normal 6–10 times per minute to 60–100 times per minute, aiding in tissue decongestion.[237,250] The efficacy of compression bandaging depends on the bandage type, properties, and the skill of the person applying it. Proper technique minimizes risks and ensures therapeutic benefit.[251-253]

Bandage Types and Application

Short-stretch bandages are most effective for lymphedema due to their low resting pressure and high working pressure.[254-259] Their rigidity provides the resistance needed to enhance the muscle-joint pump. Gradient pressure, achieved with greater compression distally, is created by applying short-stretch bandages in multiple overlapping layers with proper tension.[255,257,260]

The multilayer bandaging system includes stockinette, finger/toe bandages, padding (cotton, synthetic, or foam), and short-stretch bandages. Each component has a specific role: stockinette protects the skin, finger/toe bandages prevent localized swelling, padding distributes pressure and prevents skin breakdown, and foam softens fibrosis. Proper application ensures dynamic stiffness and structural support.258 Bandage pressure depends on tension, the number of layers, and limb circumference.[252,255]

Bandaging is applied after skin moisturizing to maintain integrity, covering the entire length of the limb (toes to knee/groin or fingers to axilla) with 50% overlap in layers. Gradient pressure and capillary refill should be assessed post-application, and patients should remain mobile to optimize the muscle-joint pump.

Maintenance and Limitations

Compression bandages can be safely worn for up to 72 hours, but pressure decreases over time due to limb size changes.[261] A 25% pressure loss can occur within 30–60 minutes, with only 56% of initial pressure remaining after 3 hours.[251,261] Frequent reapplication is essential to restore pressure, inspect the skin, and prevent tissue breakdown. There should not be a gap in compression bandaging during Phase I treatment; bandages should be maintained 24 hours per day unless they need to be removed in cases of discomfort, skin or sensation changes, or for skin inspection and daily hygiene needs. Skin should be cleaned and moisturized during rebandaging. Proper care and maintenance of short-stretch bandages also require regular washing, at least once per week (more frequently if soiled), to maintain compressive properties. Manufacturers recommend that bandages should be washed in lukewarm water with mild detergent, followed by air drying. Short stretch bandages are washable up to 10-50 times depending on the manufacturer of the bandage. Compression bandages should be replaced once they have met the manufacturer's quoted lifespan, averaging approximately every 6 months.

Contraindications

Compression bandaging is contraindicated in cases of acute infection, arterial insufficiency (ABI ≤ 0.8), arterial wounds, and decompensated congestive heart failure.

Skincare

Skin care education is a vital component of CDT, focusing on maintaining skin health and integrity to prevent infections. Lymphedema involves protein-rich stagnate fluid, which creates an ideal environment for bacteria, increasing the risk of infections like erysipelas and cellulitis.[242] Erysipelas affects superficial skin layers, while cellulitis involves subcutaneous tissue.[262] Persistent infections are common due to lymphedema-associated immune compromise.[263,264] The most significant risk factor for recurrent erysipelas and cellulitis is lymphedema.[262,265] Each cellulitis episode causes further lymphatic damage, increasing infection risk in a vicious cycle.[266]

The inflammatory response in lymphedema can lead to permanent skin changes.[263] Daily skin care and recognizing associated skin disorders are essential to prevent deterioration. Lymphedema-associated skin disorders can be classified into five categories: directly or indirectly related to lymphedema, caused by mixed venous and lymphatic disease, associated with diseases causing lymphedema, and linked to lymphedema treatment.[263] Disorders include lymphedema rubra, skin fissures, hyperkeratosis, papillomas, fibromas, fibrosis, lymphangitis, dermatitis, eczema, fungal infections, cellulitis, pressure injuries, and wounds.[263]

Observation and inspection of the skin are crucial for early intervention and wound prevention. Daily inspections should note cuts, scratches, chaffing, or signs of infection. Changes in skin color, texture, hair growth, fibrosis, hyperkeratosis, hyperpigmentation, papillomatosis, and lymphorrhea should be documented. Nail inspections should check for infection or fungal growth.

Patient education should emphasize cleansing and moisturizing the skin to prevent maceration and injury. Use of pH-neutral lotions and low-pH soaps is recommended to inhibit bacterial colonization while avoiding fragrances, parabens, paraffin, or waxes.[242,267] Moisturizing keeps skin supple and reduces the risk of breaks or tears that allow bacterial entry. Topical antibiotics can treat small skin breaks.[267]

Proper nail care is essential for limb integrity. Nails should be trimmed straight across to prevent ingrown nails, and cuticles gently pushed back rather than cut to reduce injury risk. Good nail hygiene minimizes bacterial and fungal infection pathways.[263]

Exercise

Exercise is an integral element of CDT and is utilized in both the decongestive and maintenance phases. Research confirms that exercise is safe and positively impacts lymphedema management by enhancing the muscle joint pump, improving venous and lymphatic return, increasing range of motion and strength, enhancing quality of life, and increasing bone mineral density. [241,242,268–272]

Remedial or decongestive exercises are specific movements designed to compress lymph vessels through rhythmic muscle contractions, and are a cornerstone of lymphedema exercise programs.[272] These exercises should be performed with compression in place to facilitate lymphatic flow and reduce limb volume.[241,242,271,272] The exercises should target all muscles of the affected limb and follow a sequence mimicking MLD, starting with the

neck and trunk to stimulate central lymph flow, incorporating diaphragmatic breathing, and progressing from proximal to distal muscles. Gentle arm exercises combined with deep breathing significantly reduce secondary arm lymphedema.[273,274] Diaphragmatic breathing enhances thoracic duct dilation, further promoting lymphatic flow.[275] Remedial exercises should be performed regularly to engage the pumping mechanism.

A comprehensive exercise program should address the whole person, not just the affected limb, and include aerobic, strengthening, and flexibility exercises.[271] Compression bandages or garments should be worn during exercise to increase effectiveness. Aerobic exercises should elevate heart rate to stimulate lymphangiomotoricity. Flexibility exercises maintain range of motion and improve posture. Strengthening exercises should begin with low weights and repetitions, progressing gradually.[271] Studies show that supervised weightlifting does not incite lymphedema in those at risk or exacerbate lymphedema in individuals already diagnosed.[268,269,271]Adhering to exercise guidelines decreases the frequency and severity of flares for individuals with lymphedema.[268,269] Progressive resistance exercises yield greater volume reductions in self-care routines.[276] Exercise equipment like resistance bands, weights, and gym machines can be tailored to individual needs and the severity of lymphedema.

Additional recommended exercises include Tai Chi, Pilates, yoga, walking, biking, and swimming. Aquatic exercises are particularly effective for lymphedema, especially truncal edema. The hydrostatic pressure of water creates a natural compression gradient (22.4 mmHg per 12 inches of immersion), while buoyancy alleviates limb heaviness.[277] Water's viscosity provides resistance, promoting strengthening and relaxation, and enhances lymphatic clearance through multidirectional movements.[277]

In brief, exercise, when performed in a supervised and mindfully progressive manner, should be incorporated for individuals at risk of or with lymphedema.

Compression Garments

Compression garments are a key component of the maintenance phase of CDT, helping to sustain volume reduction achieved during treatment.[278,279] These garments are essential tools for promoting self-care, reducing swelling caused by lymph fluid accumulation, and minimizing infection and hospitalization risks.[278]Patients should be educated on the importance of wearing compression garments, proper use, care, and the recommended replacement schedule of every six months.[278]

Designed to provide graduated compression, these garments apply the highest pressure distally, gradually decreasing proximally to cover the entire edematous area. The garment style and compression strength should align with the patient's ability to don and doff them, ensure optimal edema control, and maintain skin health. Proper fit is crucial for long-term lymphedema management.

Compression garments assist venous and lymphatic return by exerting external pressure. Made of knitted elastic fibers, the garments provide positive pressure on the limb when worn. They reduce interstitial fluid formation, prevent lymphatic reflux, and support muscle pumping by offering an inelastic barrier.[280] This facilitates lymphatic fluid transport, enhances oxygen and nutrient delivery to the skin, and prevents swelling recurrence.[235]

Garments are available for both daytime and nighttime use. Daytime garments, designed for high activity, offer high containment, while nighttime garments, intended for low activity, provide mid-containment. Both types come in ready-to-wear and custom-made options. Daytime garments can be circular knit or flat knit. Circular knit garments, tubular and seamless, are typically used for mild lymphedema. Flat knit garments, custom-made and more robust, are recommended for most lymphedema patients due to their superior containment and adaptability to various limb shapes.

Flat knit garments, with their strong wall stability and minimal stretch, avoid settling into skin folds and accommodate shape disproportions. This ensures comfort and effective treatment, particularly for higher compression classes or unique body shapes. Patients should consult specialists for expert measurement and fitting to achieve optimal management of lymphedema.

Compression levels are measured in millimeters of mercury (mmHg). Circular knit garments are available in Compression Class (CCL) 1 (20-30

mmHg), CCL 2 (30-40 mmHg), and CCL 3 (40-50 mmHg), while flat knit garments range from CCL 1 to CCL 4 (>50 mmHg). Compression class selection depends on lymphedema severity, limb shape, and the patient's ability to manage the garment safely. Patients should demonstrate sufficient range of motion and strength for garment use.

Inelastic garments, such as adjustable Velcro wraps, are another option for daytime wear. Made of soft, non-elastic material with Velcro straps, these garments are easy to apply, adjust, and remove.[281] They offer comfortable resting compression and higher working compression during activity, replicating short-stretch bandaging. A fabric liner protects the skin underneath.

Nighttime compression garments provide gentle, gradient pressure through foam-lined garments or adjustable straps. These non-elastic garments are safe for overnight wear and include foam chips that gently massage the limb, encouraging lymphatic reabsorption and reducing fibrosis.[282] They prevent fluid re-accumulation during sleep, offering a time-saving alternative to compression bandaging. Custom-made and ready-to-wear options are available, with mild lymphedema patients benefiting most from their use.[207]

Maintenance compression garments should only be fitted after sufficient limb volume reduction. Patients should be instructed in proper garment care, including washing methods and frequency, to maintain effectiveness. Adherence to garment use and exercise during the maintenance phase is strongly associated with successful long-term lymphedema control.[281] Long-term care requires consistent compression garment use to prevent fluid re-accumulation.[283]

Intermittent Pneumatic Compression

Intermittent pneumatic compression (IPC) for lymphedema has advanced since the 2011 NLN consensus on lymphedema diagnosis and treatment. Available options for pneumatic compression include units that are single chamber, segmented multi-chamber, and advanced pneumatic compression devices (APCDs) which have truncal and proximal chambers for the purpose of proximal lymphatic pathway clearance. Devices may be controlled manually or preprogrammed for proper calibrations and sequencing of chamber inflation.

Several studies have compared CDT with and without IPC in managing BCRL. One study found no significant differences in volume reduction, pain, or heaviness between the groups, though IPC with CDT improved shoulder external rotation mobility.[284] Similarly, other studies support these findings, showing no significant advantage of IPC addition in routine BCRL management.[285,286] Regarding lower extremity lymphedema, research focusing on IPC and MLD in maintenance therapy found no significant differences in objective outcomes but noted improved quality of life (QoL) when IPC was included.[287] However, large-scale studies have examined the impact of APCD on lower extremity lymphedema. One study reported consistent volume reductions and improved patient-reported outcomes, including reduced pain and better function.[288]Another longitudinal study confirmed significant QoL improvements and reductions in limb girth, cellulitis episodes, and skin discoloration over 52 weeks, with high patient compliance.[289] Studies evaluating IPC in head and neck lymphedema (HNL) show promise. One study demonstrated that APCD use improved lymphatic drainage and reduced dermal backflow in head and neck cancer survivors. Improvements in facial swelling and patient-reported symptoms further supported its utility in HNL management, though longer-term studies are needed.[290]

Robust randomized controlled trials on specific dosage and compression parameter protocols are lacking for IPC, especially in upper extremity lymphedema, yet there is preliminary evidence for clinical application for lower extremity lymphedema. One study validated the long-term use of an 8-chamber IPC device with high pressure (100–120 mmHg) for a 50-sec (total 400 sec) sequential inflation, reporting sustained decreases in limb circumference and improved tissue elasticity in stage II to IV lower extremity lymphedema.[119] High-pressure IPC for stage II or III lower extremity lymphedema was also recommended as it was evidenced to produce a larger flow volume, decrease skin stiffness, and effectively move subcutaneous extracellular water from distal to proximal regions.[119] Another study used various IPC pressures on menopausal women who had lower extremity venous insufficiency. Although this study did not specifically investigate IPC on subjects with lymphedema, the results demonstrated that higher-pressure IPC (120 mmHg) was significantly more effective than lower-pressure IPC (60 mmHg) or CDT

alone in reducing edema in menopausal patients with venous insufficiency.[291] A systematic review of IPC dosage parameters in both children and adults identified a trend in IPC for adults toward the use of multichambered sleeves with lower pressures (30–60 mmHg) and shorter durations (45–60 minutes).[292] There was scant evidence for specific dosage recommendations of IPC for children. Another study explored different APCD dosing protocols, finding that daily 1-hour treatments over 12 days significantly reduced limb volume and extracellular fluid, while longer sessions (2 hours twice daily) yielded inconsistent results. Notably, it was found that adding padding under IPC sleeves significantly enhanced volume reduction in subjects being treated for lower extremity lymphedema.[293] Considering that dosage and pressure parameters are critical in IPC treatment, the synthesis of these studies emphasizes the need for further trials to define and refine dosing protocols and include metrics such as limb volume, bioimpedance, tissue dielectric constant, and patient-reported outcomes.

In summary, intermittent pneumatic compression (IPC) in its various forms plays a role in lymphedema management, as an adjunct to the CDT management phase, rather than a stand-alone treatment. IPC and APCD interventions show efficacy in reducing edema, enhancing lymphatic drainage, and improving patient quality of life across various lymphedema presentations. Programmable IPC devices can even reduce healthcare utilization.[294] While advancements in technology and individualized treatment protocols offer promising results, further high-quality, long-term studies are needed to establish standardized guidelines for dosage, duration, and device selection. Furthermore, the effectiveness of IPC and APCD depends on individual patient factors which should be considered in clinical practice and prescription.

Surgical Interventions

Lymphedema can be managed both conservatively and surgically, with conservative methods often serving as the first-line treatment due to their noninvasive nature and accessibility. However, advanced disease or cases unresponsive to conservative treatments necessitate surgical intervention. Surgical options are categorized into preventive procedures for subclinical lymphedema, physiologic procedures for fluid-predominant cases, and debulking procedures for solid-predominant lymphedema. A strategic combination of physiologic and debulking procedures often yields optimal outcomes.

Physiologic surgeries enhance the lymphatic system's ability to drain fluid, using techniques such as lymphatic tissue transfer or reconnection of lymphatic vessels. These technically complex procedures require specialized training and equipment. Lymph nodes or vessels, along with surrounding tissues, are transferred from donor sites like the groin, lateral torso, neck, or abdomen to recipient areas such as the groin, thigh, axilla, or distal locations like the ankle or wrist. Supermicrosurgery, which connects lymphatic vessels to veins with diameters under 1mm, is a common approach. Direct lymph node-to-vein connections have also been described as effective.[295]

The choice of physiologic surgery depends on the patient's clinical presentation and the surgeon's expertise. These procedures can result in significant improvements, including reduced infection risk, decreased reliance on compression garments and therapy, enhanced physiologic function, and an overall better quality of life than what nonsurgical treatments alone can achieve.[296-302] Lymph node or vessel transfers have a low risk of causing lymphedema at the donor site, but reverse lymphatic mapping significantly reduces this risk. This technique is well-documented and not experimental.[303] Physiologic procedures are also indicated for patients with early-stage lymphatic disease, where damage is only detectable through imaging and symptoms have not yet appeared. ILR/ELR procedures, which repair lymphatic damage during or shortly after cancer surgery, have been well-documented in the medical literature.[304-307] These procedures involve connecting lymphatic vessels to veins to preserve drainage in affected areas. Surgeons must carefully assess the risk of lymphedema development and provide appropriate recommendations to both the patient and cancer physician for informed decision-making.

In advanced lymphedema, where solid material accumulates in the affected tissues, conservative [119] and physiologic surgeries are inadequate. These solids must be surgically removed through reductive procedures, also known as excisional surgeries. Aspiration of solids has consistently been an effective treatment for over 25 years when performed by experienced teams, leading to substantial reductions in excess limb volume and

significant patient outcome improvements. Reductive surgery, involving the aspiration of solids, is far more complex than cosmetic liposuction (suction-assisted lipectomy, or SAL). These intense procedures often involve the removal of large volumes of solids and typically require overnight stays. Comprehensive postoperative care, including bandaging and custom-fitted compression garments, is essential for success, as standard SAL protocols are inadequate for patients with severely compromised lymphatic drainage systems.[230,308-313]

In conclusion, while conservative management remains the cornerstone of lymphedema treatment, surgical interventions play a vital role in advanced or refractory cases. Physiologic surgeries restore lymphatic function and address fluid-predominant lymphedema, while reductive procedures effectively manage solid-predominant lymphedema. When performed appropriately, these interventions can significantly improve limb volume, reduce complications such as infections, and enhance overall quality of life. Multidisciplinary collaboration, careful patient selection, and adherence to postoperative care protocols are essential to achieving optimal outcomes. As surgical intervention is not a cure for lymphedema, individuals should return to prospective surveillance postoperatively.

Pharmaceuticals and Natural Supplements

Currently, there are no medications that cure primary or secondary lymphedema.[314] Some pharmaceuticals, such as antidiabetics, calcium channel blockers, and antidepressants, may cause or worsen edema as a side effect.[315] Research into medications for lymphedema management has expanded but primarily focuses on treating morbidities like infections. Medications include anti-inflammatories, benzopyrones, antibiotics, topical retinoids, antimicrobials, and emollients. Anti-inflammatory drugs may provide temporary swelling reduction, especially during infections.

Coumarin, a benzopyrone found in plants and spices, has been studied for its potential to reduce edema by binding proteins, decreasing skin temperature, and reducing secondary infections. However, it is not FDA-approved due to liver toxicity risks at high doses.[80,316,317] Diosmin, marketed as Daflon, has been used for filarial lymphedema and BCRL but lacks sufficient evidence for its effectiveness.[316] Doxycycline, an antibiotic, has shown potential in reducing inflammation and lymphedema severity, though study results are mixed.[318,319]

Emollients containing ammonium lactate, salicylic acid, or urea can address hyperkeratosis and other secondary epidermal changes. Antimicrobials like penicillin and erythromycin treat cellulitis and lymphangitis.[80]Ketoprofen, an anti-inflammatory, may reduce tissue inflammation and skin thickness, but evidence remains limited.[320]

Obesity is a significant risk factor for lymphedema, with a BMI > 30 kg/m2 predictive of BCRL.[72] While weight loss may reduce lymphedema volume, evidence is insufficient to confirm its impact on disease progression.[55,321-323] However, establishing and/or maintaining a physician-recommended BMI is advisable with both exercise and nutrition playing key roles in achieving these goals. For individuals with lymphedema, dietary recommendations typically focus on reducing inflammation and fluid retention by avoiding high-salt foods, added sugars, and refined grains while promoting a balanced diet rich in whole grains, vegetables, fruits, and lean proteins.[324] Recent studies suggest specific diets and dietary supplements may improve lymphatic function in early-stage secondary lymphedema.[325,326] However, more research is needed to establish specific dietary guidelines.

Supplements, including synbiotics (probiotics and prebiotics), may benefit lymphedema patients. Preliminary evidence suggests synbiotics, combined with a calorie-restricted diet, can maintain levels of vascular endothelial growth factors and anti-inflammatory markers like interleukin-10 in BCRL patients.[327-329]

In summary, there is insufficient evidence to recommend specific pharmacologic therapies, dietary modifications, or supplements as primary treatments for lymphedema. Current recommendations focus on general health measures, with further research needed to develop targeted interventions.

Complementary, Integrative, and Alternative Treatments

Various complementary and alternative treatments may supplement standard care for lymphedema, particularly for those with severe cases or limited response to conventional therapies.

- **Vibration/Oscillatory Devices**: This electrostatic vibration therapy may reduce pain, swelling, and subcutis thickness but has limited supporting research.[330,331]
- **Negative Pressure Devices**: Negative pressure massage and endermology may help individuals by enhancing lymphatic drainage and improving circulation. Although studied for BCRL, there is a lack robust evidence and are not strongly recommended.[332,333]
- **Acupuncture and Moxibustion**: Acupuncture is safe during the maintenance phase of CDT but lacks sufficient evidence for significant lymphedema improvement.[334-336] Moxibustion, often combined with acupuncture, may reduce pain and arm circumference but requires further randomized studies due to moderate bias risks.[337-339]
- **Elastic Taping**: Elastic taping has shown mixed results in secondary lymphedema management. While not strongly advised for volume reduction, it may benefit areas difficult to bandage (e.g., head, neck, or trunk) by facilitating lymph drainage and improving quality of life.[340-343]
- **Photobiomodulation**: Low-level laser therapy stimulates lymphangiogenesis and lymphatic motility. While studies indicate reduced volume and improved quality of life in BCRL patients, its effectiveness is not superior to other interventions and lacks a standardized protocol.[344-349]
- **Stellate Ganglion Blocks**: This intervention may reduce volume and circumference in severe BCRL cases but has limited longitudinal effects and insufficient high-quality evidence. Patients must consult providers about contraindications and potential side effects.[350-356]
- **Extracorporeal Shock Wave Therapy** (ESWT): By promoting lymphangiogenesis, ESWT has shown favorable outcomes for advanced BCRL, such as reduced fibrosis and improved quality of life. However, limited data and lack of standardized protocols restrict its recommendation.[357-361]

Other modalities, including myofascial release, ultrasound, electrical stimulation, and Fluidotherapy, show some benefits when combined with CDT but lack robust evidence.[362-366]

For lymphatic filariasis-related lymphedema, integrative medicine (e.g., compression therapy, yoga, Ayurveda, and topical creams) has demonstrated success in reducing volume, improving quality of life, and decreasing cellulitis episodes.[367–370]

In summary, complementary treatments may enhance standard care for lymphedema, particularly in severe or refractory cases, but require further research to establish efficacy and protocols.

Summary and Recommendations

A comprehensive medical history and diagnostic evaluation by qualified healthcare professionals is essential before initiating lymphedema treatment. Prospective surveillance and early intervention, especially in cancer-related lymphedema, have been shown to prevent its manifestation or progression. Proper education and adherence to behavioral changes addressing risk factors are critical for both practitioners and patients.

The primary goals of lymphedema treatment are to reduce and maintain volume reduction, prevent functional complications, improve skin health, reduce infection risk, support patient adherence, and enhance overall quality of life. Complete Decongestive Therapy (CDT) remains the gold standard for conservative management, with proven benefits in reducing limb volume, improving symptoms, and preventing infections. Patient engagement during Phase II of CDT is crucial for sustaining these improvements. Intermittent pneumatic compression may be used as an adjunct to CDT.

Over the last decade, surgical approaches have achieved promising results in reducing limb volume. Although not a cure, microsurgical interventions, such as lymphovenous bypass or vascularized lymph node transfer, may be appropriate for qualified patients. Research into complementary therapies, including oscillatory devices, elastic taping, photobiomodulation, and others, suggests potential benefits but remains inconclusive due to limited evidence. Medications and genetic therapies for lymphedema are still in developmental stages.

Treatment plans should be tailored to individual needs and overseen by healthcare providers experienced in lymphedema care. Continued research is imperative to refine existing interventions and develop novel approaches. The integration of patient education, evidence-based practices, and multidisciplinary care will ensure optimal outcomes for those living with lymphedema.

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