Anatomy, pathophysiology and assessment of upper-body lymphoedema

Sandi Davis, Suzie Ehmann, Brandy McKeown, Neil Piller, Joseph Dayan, Hiroo Suami, Justine C Whitaker and Karen J Bock

Abstract

This article reviews the lymphatic system's anatomy and physiology, as well as the etiology of lymphoedema affecting the upper limbs, breast and trunk. It presents evidence-based strategies for assessment, including history-taking, physical exams and clinical tests to guide treatment planning. The importance of selecting personalised compression garments is emphasised. Legislative impacts—such as the US 2024 Lymphedema Treatment Act—and global variability in compression therapy funding are explored, along with nuanced approaches to assessment, staging and diagnostic criteria.

Keywords: Lymphoedema | Lymphatic anatomy | Compression therapy | STRIDE framework | ICG lymphography | Lymphatic drainage | Pathophysiology | Breast and trunk lymphoedema | Comorbidities | Assessment and diagnosis

Lymphoedema is a chronic condition resulting from the accumulation of lymphatic fluid. A nuanced understanding of lymphatic anatomy, physiology and pathophysiology is essential to advancing the care of people with primary and secondary lymphoedema, especially the targeting and sequencing of treatment. This makes the etiology and assessment of lymphoedema fundamental to the STRIDE algorithm for compression selection.

Anatomy

The lymphatic system is a delicate and ubiquitous network of vessels that efficiently transports lymph and its contents without a central pump, relying instead on intrinsic and extrinsic pumping mechanisms that revolve around the structural and functional unit called the lymphangion.[1]

Lymphatic physiology

The process of collecting extracellular fluid and its contents starts at the level of the initial lymphatic capillaries located in the skin (*Figure 1*). These initial lymphatics can accept large amounts of fluids, metabolic wastes, bacteria and a range of larger molecules, mainly proteins, that blood capillaries cannot.[1,2] Lymphatic vessels, referred to as pre-collectors, connect these initial lymph capillaries to the afferent lymphatic collectors, acting as a major highway in which lymph and its contents travel from the epi-fascial layers of the tissues to the lymph nodes.[2] Even when lymph crosses the deep fascia and drains into the deeper subfascial lymphatic system, it ends up in the lymph nodes, which are crucial for filtering and processing. The lymph nodes filter roughly 8 litres of lymph each day. Half of that lymph is drained through the thoracic duct, whereas the remaining lymph is absorbed by lymphovenous shunts, known as lymph node microvessels.[3] The efferent lymphatic vessels transport the residual lymph, which has undergone filtration and purification within the lymph nodes, onward to the larger lymphatic ducts, including the thoracic duct and right lymphatic duct.[4] These major ducts provide an essential connection to the venous system by emptying the lymph at or near the junction where the jugular vein meets the subclavian vein, commonly referred to as the jugular–subclavian junction.[2] At this juncture, the purified lymph is reintegrated into the circulatory system, becoming part of the bloodstream and contributing to overall fluid balance in the body (*Figure 2*).[4]

The physiology of filtration and purification involves the lymphatic tissue in lymph nodes filtering and recycling lymph fluid while supporting immune defence. When necessary, the cells within the lymph nodes will attack, destroy and remove waste.

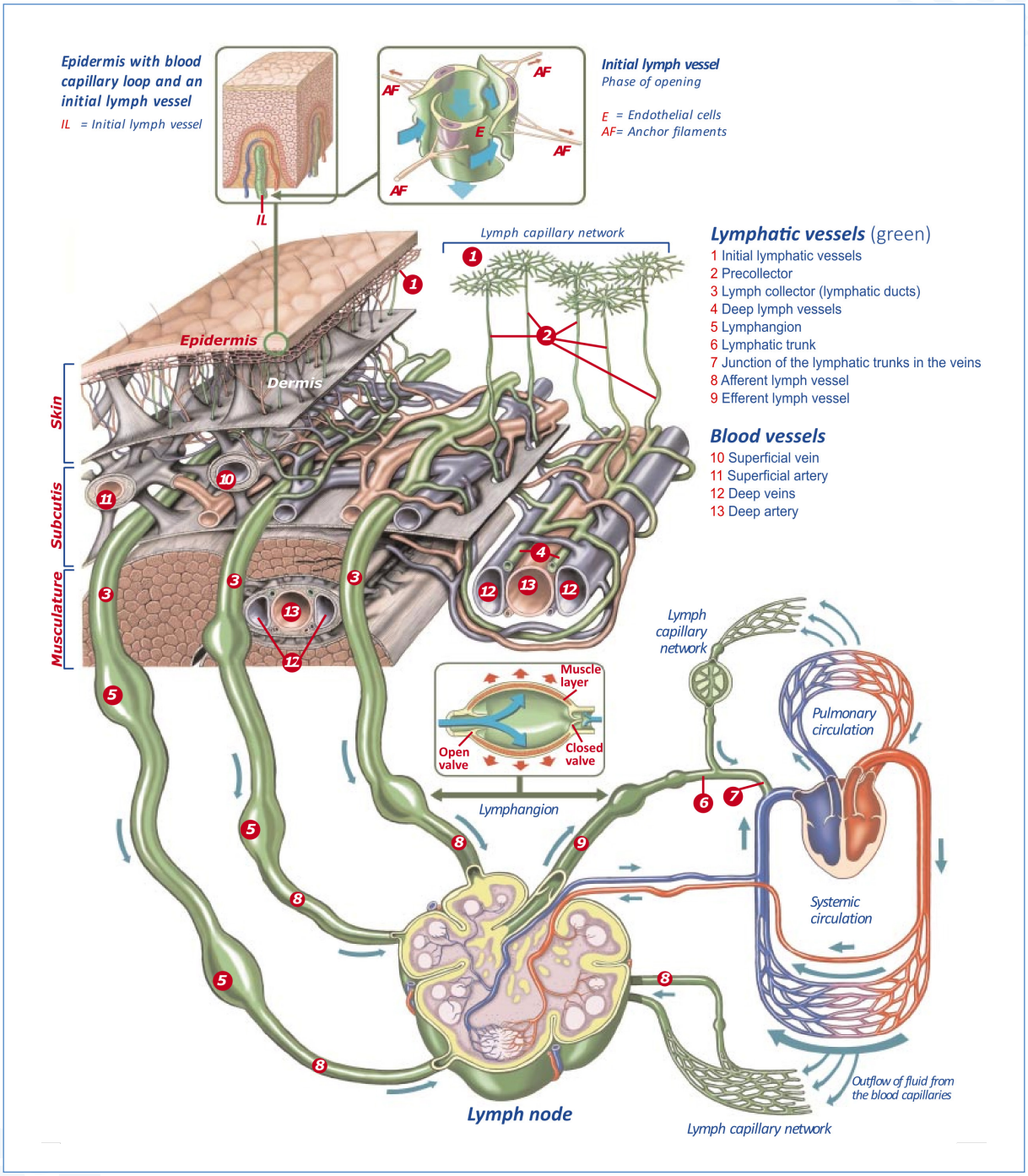
Drainage patterns

Much understanding of detailed lymphatic anatomy is historically based on the work of Mascagni and Sappey, later expanded by Leduc, using cadaver specimens, as described by Shinaoka et al..[5] The collective work of these pioneering lymphologists has afforded an expansive view of drainage pathways, describing anatomical division of the lymphatic

Sandi Davis, PT, DPT, CLT-LANA, CLWT, President, Davis Care Physical Therapy, New York City, NY, USA
Suzie Ehmann, DPT, PhD, CWS, CLT-LANA, CLWT, Lymphedema Therapist, McLeod Health Seacoast, Little River, SC, USA
Brandy McKeown, OTR/L, CLT-LANA, CLWT, Lymphedema Therapist, International Lymphedema and Wound Training Institute and the Lymphedema Center, USA
Neil Piller, MD, Lymphologist and Director, Flinders University, Adelaide, Australia
Joseph Dayan, MD, MBA, Plastic and Reconstructive Surgeon, Institute for Advanced Reconstruction, USA
Hiroo Suami, MD, PhD, Associate Professor, Macquarie University, Sydney, Australia
Justine C Whitaker, MSc, RN, PhD(c), Director & Nurse Consultant, Northern Lymphology, and Senior Lecturer, University of Central Lancashire, Preston, UK
Karen J Bock, PT, PhD, CWS, CLT-LANA, Assistant Professor, Rockhurst University, Kansas City, MO, USA

Figure 1. Lymphatic drainage system

The lymphatics are illustrated in green. The initial lymphatic vessels (1) drain through the fascial layer via the precollectors (2), which then lead to the lymph collectors (3) that run parallel to the deep veins (12) and deep arteries (13) and flow to the lymph nodes. Reprinted with permission from Jobst.

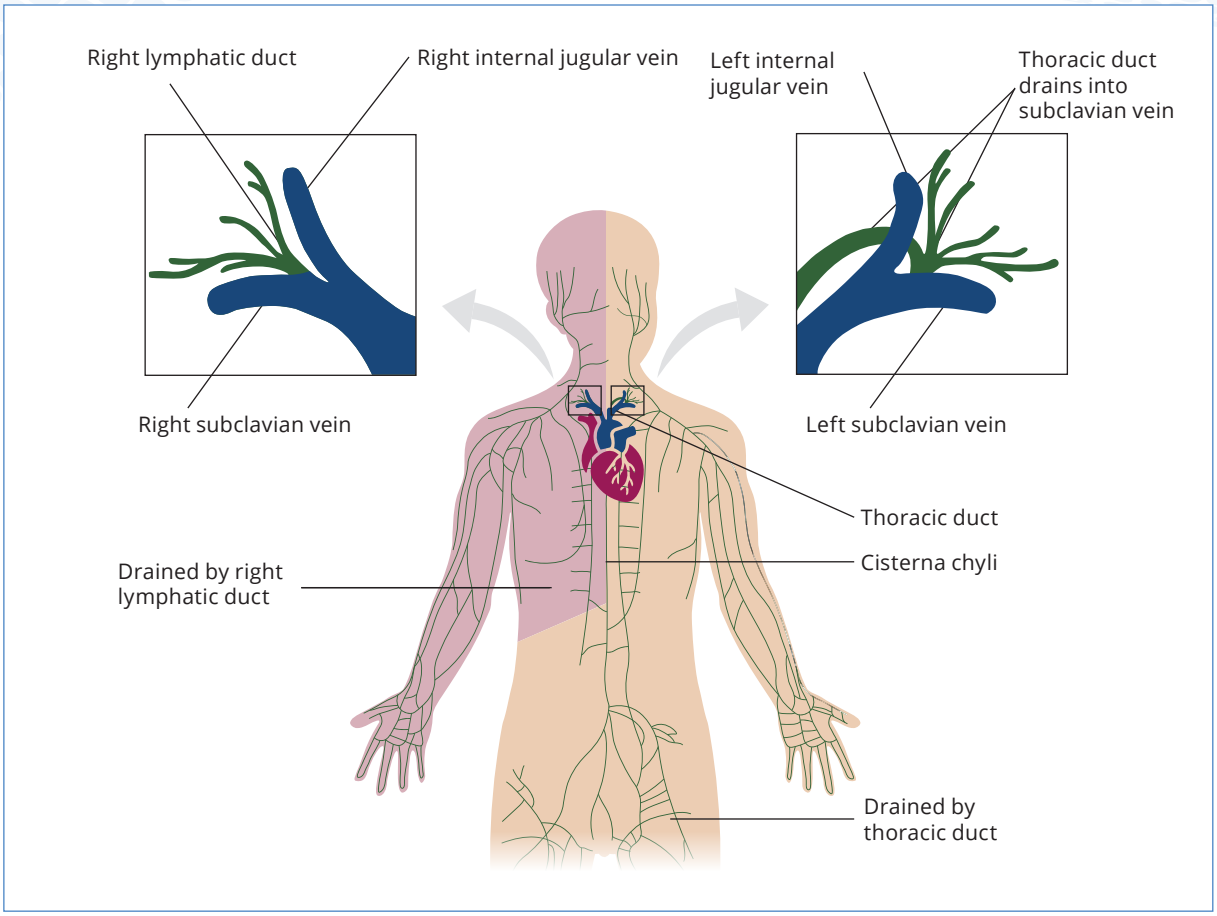


system into superficial lymphatic territories, serviced and drained by specific lymph collectors and separated by watersheds.[6]

Suami introduced the concept of 'lymphosomes', where specific areas of the limb are mapped out and drain into specific lymph nodes (*Figure 3*).[7] More recently, with the introduction of indocyanine green (ICG) lymphangiography, it is possible to observe the active function of the superficial lymphatic system, as opposed to static cadaver dissection.[8] This cutting-edge technology has unlocked a dynamic view of the upper limbs, trunk and breast, deepening understanding of lymphatic flow and drainage pathways.[9]

Figure 2. Asymmetric lymphatic drainage patterns of the right and left thoracic trunks

The right thoracic trunk collects lymph from the right upper limb, head and neck, draining into the right lymphatic duct. The left thoracic trunk, as part of the thoracic duct, drains lymph from the left upper limb, the left side of the trunk and both lower limbs.



Upper-limb drainage patterns

Granoff et al. observed three main lymph collectors in the normal upper limb: the median pathway along the volar forearm, the radial lymphatics and the ulnar lymphatics (*Figure 4*).[10] The researchers concluded that, although individual lymphatic channels appear as single pathways on ICG, they represent the convergence of numerous tributaries within a lymphosome.[10] Upper-arm connections vary; the median channel consistently connects to the medial upper arm, draining to the lateral axillary lymph nodes, whereas radial and ulnar connections depend on their forearm course, with dorsal pathways often linking to the lateral upper arm, draining to subclavicular lymph nodes.[10] On occasion, drainage occurs along a lymphatic collector traversing the deltopectoral groove, into the supraclavicular lymph nodes, avoiding the axillary lymph nodes entirely, particularly when these nodes are removed due to cancer treatments.[7]

Trunk and breast drainage patterns

As with other parts of the superficial lymphatic system, drainage from the trunk plays a crucial role in maintaining fluid balance and immune surveillance.[2] This region's drainage system has many variants, but some generalities can be applied.[2,8]

The drainage patterns of the trunk are as follows:[11,12]

- Anterior thoracic to external mammary (axillary) nodes
- Posterior thoracic to scapular (subscapular) nodes
- Lateral thoracic to axillary lymph nodes.

The drainage patterns of the breast quadrants are as follows:[11,12]

- Lateral to axillary nodes
- Medial to internal mammary (parasternal) nodes
- Upper quadrants to axillary and internal mammary lymph nodes
- Lower quadrants to axillary and parasternal nodes.

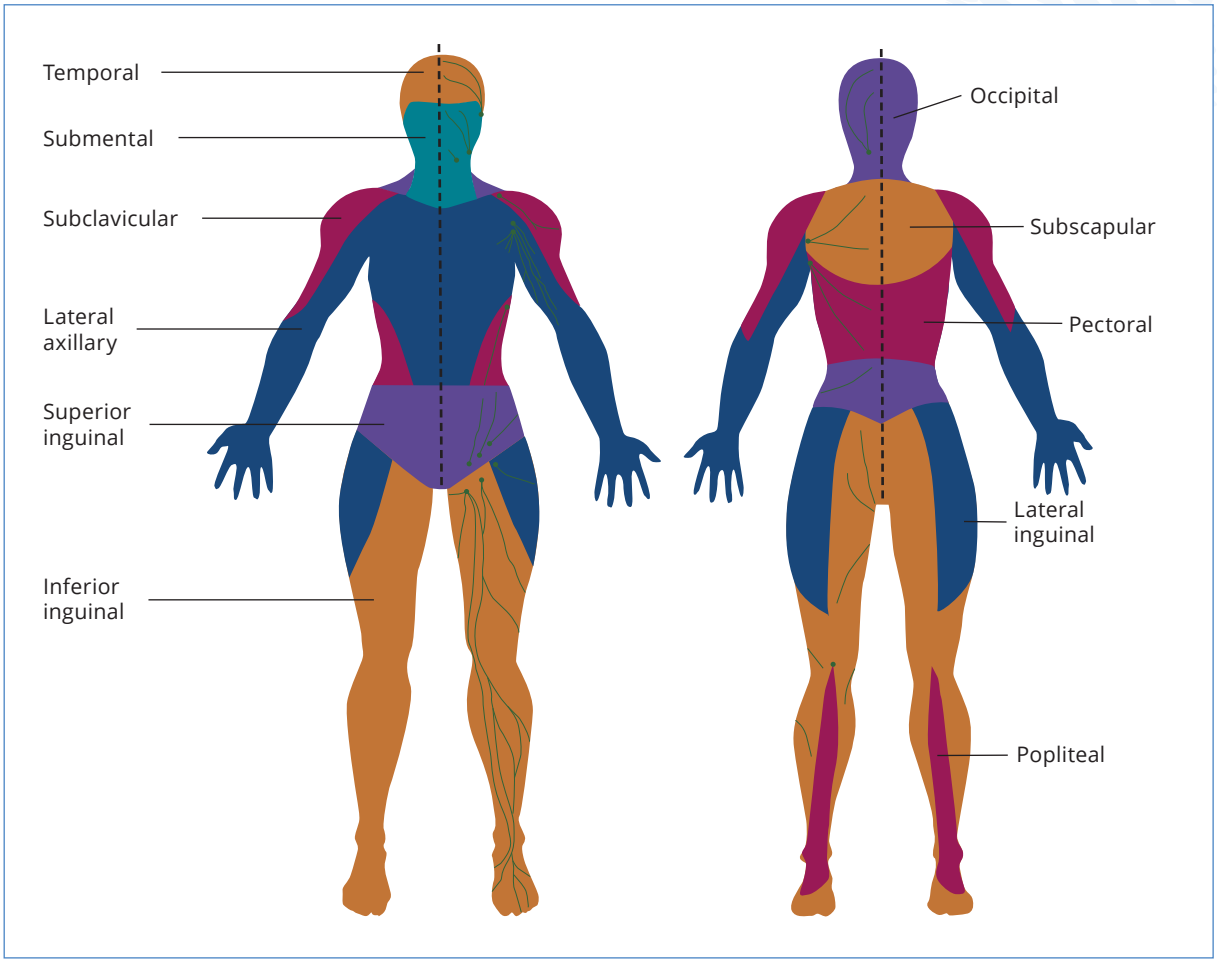
From these nodes, efferent lymph vessels converge into larger lymphatic trunks, ultimately reaching the right or left jugular/subclavian veins.

The lymphatic drainage patterns of the breast and trunk are structurally distinct from and more complex than those of the limbs. The breast and trunk pathways have a more intricate and interconnected architecture than previously appreciated, with each quadrant potentially draining to a distinct sentinel node.[13,14]

This structural complexity is compounded by regional variability in lymphatic drainage, as well as the fragile histological structure of lymphatic capillaries, characterised by thin walls

Figure 3. Lymphosomes of the body[7]

The lymphatic territories are demarcated according to their corresponding lymphatic basins.



and microporous structure. Therefore, lymphoedema of the breast and trunk demands tailored therapeutic strategies to ensure effective lymphatic flow while minimising unintended fluid congestion.[13-16]

Breast drainage patterns, surgery and compression

Breast drainage patterns have implications for surgical intervention and compression strategy. Superficial drainage of the breast flows laterally to the sentinel node in the lateral axilla.[11] This node serves as a primary drainage point for both the anterior trunk and the upper arm.[11]

Notably, superficial lymphatics lack direct connections to deep lymphatics in the anterior trunk, except through the lateral axilla.[11] This anatomy is particularly relevant when considering sentinel-node dissection. While the procedure is often viewed as lymphatic-sparing due to the removal of a single node, disruption of the sentinel node, which manages drainage for both the breast and upper limb, can significantly impair lymphatic flow.[11]

Recent findings underscore the complexity of breast lymphatic drainage. Giammarile et al. described it as multidirectional yet predominately routed to the ipsilateral axilla.[17] With a fraction of lymph (≈3%) draining to the intercostal, interpectoral, peri-clavicular, perimammary, contralateral breast or even abdominal nodes, there is a need to anticipate collateral flow disruptions.[17]

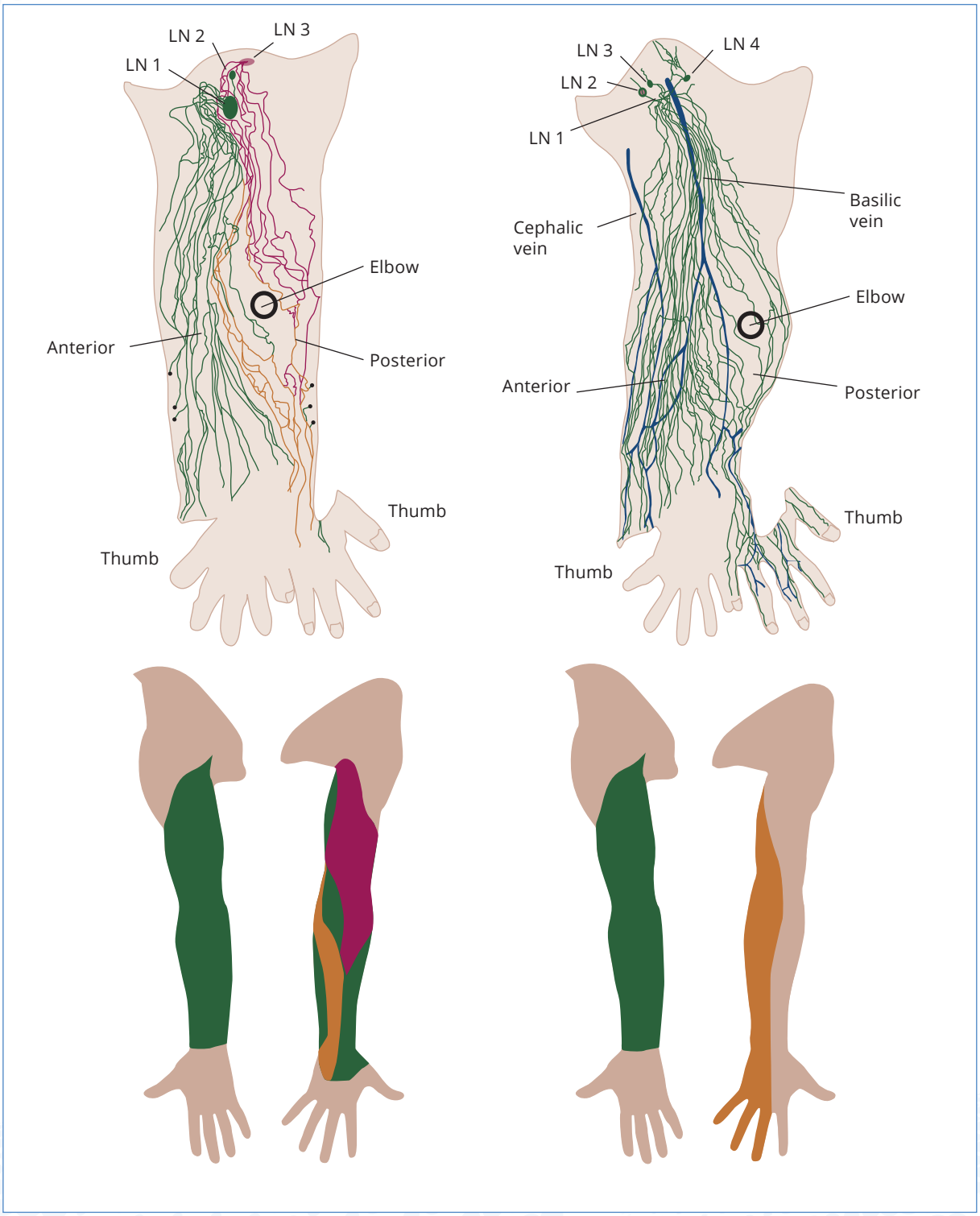
In a 2020 study by Aldrich et al., ICG lymphography was performed on 20 participants, 10 with breast lymphoedema, with the following findings:[12]

- All healthy controls exhibited linear ICG flow toward the ipsilateral axilla with no dermal backflow
- Among those with breast lymphoedema, only 40% maintained primary axillary drainage
- Importantly, 90% demonstrated compensatory pathways, including parasternal (6/10), contralateral axilla (4/10), intercostal (3/10) and clavicular (2/10) drainage routes.

These findings underscore the importance of early clinical assessment and individualised compression planning following breast surgery, particularly for patients at risk of breast or upper-limb lymphoedema. Pre- and post-operative evaluations allow for patient education and timely intervention. Understanding collateral lymphatic pathways can guide garment design and help avoid over-compression of newly recruited drainage routes.

Figure 4. Lymphatic drainage of the upper limb[6]

Side-by-side images of cadaver A (left) and cadaver B (right) illustrate the lymphatic territories of each sentinel node, colour-coded to match. In cadaver A, lymphatics were traced distally from each node, revealing distinct territories without overlap, interconnected pathways within each region and an orange territory capable of draining into either LN1 or LN3. In cadaver B, lymphatic drainage patterns were traced to align with radiographic findings. Sentinel nodes (LN1 and LN2) exhibit discrete territories, with LN1 forming a dominant pathway that connects proximally to LN3 and LN4. Veins were injected to highlight vascular structures within the mapped regions.



Breast and trunk lymphoedema pose assessment challenges due to anatomical variations and inconsistencies in lymphatic measuring and mapping techniques. Unlike limb lymphatics, breast drainage lacks direct connections to deeper lymphatic structures, making compression crucial for redirecting flow and mitigating fibrotic progression, especially after sentinel-node removal. Preventative compression is equally, if not more, important in these regions.[11,18]

Lymph transport

Lymph transport relies on two synergistic mechanisms: intrinsic and extrinsic pumping. Intrinsic pumping occurs in lymphatic collectors, which are segmented by one-way valves that prevent backflow and ensure unidirectional flow.[19,20] Contractions are triggered by myogenic responses when vessel-wall tension exceeds a threshold, and they are modulated by nitric oxide (NO), which reduces tone and enhances flow. Lymphatic pressure remains lower than venous pressure, unless active contraction is occurring.[20,21]

Extrinsic pumping supports intrinsic lymphatic transport through skeletal muscle movement, respiration and passive forces, such as arm elevation, trunk rotation, walking or manual lymphatic drainage.[20,21] These external compressions mobilise lymph within the non-contractile initial lymphatics and help overcome downstream resistance.[21] Lymphangions typically contract 6–10 times per minute at rest, with rates increasing up to tenfold during activity, positional changes or compression garment use.[21] Compression applications can enhance these external forces, optimising lymphatic flow and promoting oedema reduction.[22] However, if not appropriately selected, applied or worn, compression may obstruct flow or impair collateral drainage.[22] These considerations highlight the need for anatomically tailored compression strategies.

Together, the intrinsic and extrinsic pumping mechanisms maintain efficient lymphatic transport; ensure lymph moves unidirectionally and against gravity; and support essential physiological functions, such as fluid balance and immune response. This dynamic interplay illuminates the adaptability and robustness of the lymphatic system.

Pathophysiology

Etiology

Lymphoedema arises from two primary aetiologies: congenital (primary) and acquired (secondary). Primary lymphoedema involves structural abnormalities, such as aplasia, hyperplasia, hypoplasia or valvular defects, often linked to genetic mutations such as FOXC2 or SOX18.[23] Secondary lymphoedema results from external causes, including trauma, filariasis or cancer treatments (i.e., lymph node dissection and radiation), that damage lymphatic vessels.[24]

Clinical understanding of lymphoedema in the breast and upper limbs is largely shaped by cases involving axillary lymph-node dissection and/or radiation, most commonly in the context of breast-cancer treatment.[25-28] While lymphoedema is often attributed to disruption of afferent and efferent lymphatic pathways near excised nodes, immune activation also plays a critical role.[23] After tissue injury, axillary lymph nodes may initiate an amplified inflammatory response instead of a controlled immune reaction, leading to fluid buildup and tissue remodelling.

Nores et al. found that $CD4^+$ T cells exacerbate lymphatic dysfunction post-injury by increasing fibrosis and peri-lymphatic inflammation, while inhibiting collateral lymphatic formation.[25] This inflammatory shift leads to extracellular fat deposition, fibrosis, chronic inflammation, valvular insufficiency and lymphatic pump failure.[25] Ultimately, functional pathways diminish, and lymphatic load surpasses system capacity.[26]

Clinical presentation

Lymphoedema, whether primary or secondary, varies based on location of functional lymphatics, comorbidities and tissue changes such as post-radiation fibrosis. These fibrotic changes may hinder lymphatic regeneration and redirection of flow, complicating bypass of damaged regions. Beyond lymph-node removal, lymphoedema frequently follows radiation and taxane-based chemotherapy, both common in breast cancer treatment.[29-31] While radiation causes tissue and lymphatic scarring, the mechanism by which taxane-based therapy impairs lymphatic function remains unclear.

Increased breast cancer-related lymphoedema (BCRL) incidence has been reported in patients with taxane-induced peripheral neuropathy, suggesting a potential link.[31] ICG lymphangiography has shown abnormal lymphatic patterns and reduced contractility in patients after taxane therapy, even before axillary dissection or radiation.[30] These findings denote that lymphoedema is not merely a plumbing issue but also involves significant immunologic factors.

Though BCRL dominates research, lymphatic dysfunction can also stem from treatments for melanoma, lymphoma and osteosarcoma. Non-oncologic causes include orthopaedic injuries and surgical procedures, soft-tissue trauma, burns, neurological-dependent oedema (e.g., spinal cord injury, cerebrovascular incidents), vascular issues (e.g., dysfunctional dialysis ports, deep vein thrombosis), post implantation of cardiac devices, infections, vasculitis and intravenous drug use.

Ultimately, lymphatic dysfunction of the upper extremities, breast and/or trunk lymphatics signals impaired tissue health. Visible oedema often reflects lymphatic-system insufficiency, calling for timely and personalised interventions. Coexisting conditions may further complicate management, necessitating a comprehensive, multidisciplinary approach.

Effects of comorbidities

Lymphatic function is shaped by innate lymphatic sufficiency and compounded by coexisting comorbidities that increase lymphatic load. Factors such as a genetic predisposition, obesity, cancer therapies, infections and cardiovascular or metabolic conditions can accelerate lymphoedema onset and progression.

A range of coexisting conditions can compromise lymphatic function and tissue homeostasis, necessitating a comprehensive clinical approach. These include metabolic and structural factors that disrupt fluid balance, immune response and mechanical lymph transport.

Obesity

Obesity is a significant contributor to lymphoedema, with obesity-induced lymphoedema (OIL) common at body mass index (BMI) >40 and nearly universal at BMI >60.[32-34] In OIL, peri-lymphatic inflammation disrupts lymphatic endothelial cell

(LEC) gene expression, impairs pump efficiency and alters lipid metabolism—creating a feedback loop of fat deposition and lymphatic dysfunction.[33,35] Cytokine-driven inflammation and poor vessel remodelling worsen drainage.[33,36]

In patients with cancer, pre-operative BMI ≥30 triples the risk of lymphoedema compared with BMI ≤25.[36] Weight fluctuations post-treatment doubles this risk.[37] Obesity also complicates surgery and intensifies recovery, reinforcing the need for early monitoring, weight-loss strategies and anti-inflammatory interventions.[33,36,37]

Lipoedema

Lipoedema is a condition that involves symmetrical fat buildup in the arms and legs but sparing the hands and feet. It predominantly affects women, with an unclear etiology.[38] It worsens primarily with obesity rather than inherent progression.[39] Diagnosis requires a second cardinal symptom, often pain.[38,39] Proper diagnosis differentiates lipoedema from lipohypertrophy, idiopathic oedema or cellulite, each requiring distinct treatments.[38,39]

In stages 3 and 4, lymphatic impairment emerges, particularly in patients with high BMI.[38] Compression garments, lymphatic drainage and weight management are critical.[38]

Movement restriction and underlying medical disorders

Reduced motion, whether due to trauma, surgery, stroke or neurological impairment, limits intrinsic and extrinsic lymph transport.[40,41] Oedema creates a cycle of pain and inactivity, worsening fluid retention.[40,42,43] Poor positioning, compression misuse and cardiovascular dysfunction in patients who are critically ill can further strain drainage.[40,42,44]

Management includes elevation, light exercise and customised garments.[40-43] For stroke-related oedema, passive range of movement (ROM), compression and active contraction help preserve lymphatic and venous return.[41] Breast oedema benefits from compression bras and early mobilisation.[45]

Nutrition

Sodium promotes water retention and increases arterial pressure, impairing lymphatic flow.[46,47] Processed foods can amplify systemic inflammation.[46] Potassium, magnesium and vitamin B6 counter these effects by reducing retention, enhancing circulation and regulating inflammatory mediators.[46]

Weight loss is vital, although lipoedema adiposity often resists conventional methods.[47] Hypocaloric diets paired with supplements (e.g., green tea catechins, caffeine, whey protein) and exercise may improve fat metabolism and lymphatic function.[46] Tailored plans, such as Mediterranean or ketogenic diets, can complement compression and physiotherapy, although more research is needed.[46]

Metastatic disease

Cancer often spreads via lymphatics, disrupting node and vessel integrity.[48] Metastatic deposits create obstructions, while tumour-induced lymphangiogenesis further alters drainage.[48] Vascular endothelial growth factor (VEGF)-C/D signalling supports vessel proliferation but facilitates cancer dissemination.[48,49]

Lymphoedema incidence varies, with 6–70% in patients with breast cancer[50,51] and 4–15% in upper-limb melanoma.[52] High-burden axillary metastasis—seen in over one-third of patients post-neoadjuvant therapy—not only signals treatment resistance but also compounds the risk of lymphoedema by increasing nodal disruption and surgical morbidity.[53]

Diabetes

Diabetes exacerbates lymphoedema through chronic inflammation, vascular impairment and immune dysfunction. Persistent hyperglycaemia and insulin resistance damage LECs, triggering oxidative stress, disrupting lymphangiogenesis and increasing vessel permeability.[54] These effects impair lymph drainage and elevate infection risk.[54,55]

Individuals with type 2 diabetes are at increased risk for early-onset lymphoedema due to leaky lymphatics.[55] Patients with diabetes and breast cancer undergoing mastectomy or extensive dissection often experience delayed wound healing from tissue hypoxia and poor vascular supply, both linked to higher BCRL rates.[56] Chronic inflammation from both conditions amplifies lymphatic damage and worsens disease progression.[55,56]

Infections

In response to infection, lymph nodes recruit macrophages and neutrophils to capture bacteria and trigger an immune responses.[57] Fewer nodes or impaired transport reduce this response, increasing susceptibility to infections.[26,58] Bacterial invasion can scar lymphatic tissue and aggravate lymphoedema.[57] Symptoms include warmth, redness, swelling, pain, fever and chills.[59]

Timely antibiotic treatment is vital to control spread and prevent complications.[59] Patients with advanced arm lymphoedema are at heightened risk for cellulitis, making prevention of lymphoedema progression crucial.[58,60]

Radiation

Radiation impairs lymphatics by depleting lymphocytes and inducing fibrosis in lymph nodes.[61] This elevates intranodal pressure and disrupts filtration, fostering lymphoedema development.[61] Axillary lymph-node dissection increases the risk of BCRL by over threefold, and, when combined with regional lymph node radiation, the risk approaches fourfold compared with sentinel-node biopsy alone.[62] Radiation alone contributes modestly to this risk.[62] Tangential photon radiation poses a higher lymphoedema risk than electron beam therapy, with additional risks tied to total dose, overlapping fields and posterior axillary boost.[61]

Assessment

Lymphoedema is a clinical diagnosis, determined through systematic evaluation that differentiates it from other causes of oedema. A thorough understanding of the underlying etiology enables clinicians to conduct an in-depth examination, combining clinical tests, physical assessments and detailed patient history to confirm lymphoedema presence and stage.

Patient-reported symptoms are the first diagnostic clue in lymphoedema evaluation. Common complaints include arm, breast or trunk size changes, as well as heaviness, numbness,

redness and aching pain.[63] Family history can support diagnosis, especially in suspected primary lymphoedema. If hereditary patterns are evident, genetic testing and specialty referral may be warranted.

A comprehensive clinical evaluation of a patient with lymphoedema should follow the Subjective, Objective, Assessment and Plan (SOAP) format, ensuring a systematic approach to diagnosis and management. The history review serves as the foundation, including medical history, surgical history and clinical tests previously performed to assess lymphatic function, vascular status and comorbid conditions. Being part of a collaborative network of healthcare professionals can be helpful in pairing information obtained from these tests and measures to give a baseline as to why the lymph system may be failing, as well as to guide clinical assessment and treatment planning.

Lymphoedema impacts multiple systems, and so, to guide diagnosis and care, assessment must go beyond limb-volume measurements to encompass ROM, sensation, BMI, vascular health and genetics. Accurate diagnosis involves more than confirming lymphatic insufficiency, it requires assessment of concurrent pathology, such as increased capillary filtration. Often, ultrafiltration and lymphatic overload coexist, perpetuating chronic oedema.

Assessment of a patient's lifestyle, activity level, environmental context and ability to perform (potentially instrumental) activities of daily living are important for effective compression therapy. Likewise, body habitus and tissue response factors, including refill time, positional variation and oedema fluctuation, guide compression choices suited to the size, shape and severity of swelling. Compression therapy must also align with lymphatic, vascular, neural and metabolic status for safety and effectiveness. Likewise, comorbidities such as Raynaud's disease may require lower-pressure garments.

Lymphatic function

Several imaging modalities are used to evaluate lymphatic function, each method assessing distinct aspects of lymphatic health, including flow dynamics, vessel integrity and inflammation markers (*Table 1*).[27,64-67]

Tissue

Tissue-assessment tools can help confirm lymphatic insufficiency and characterise oedema. Further research is needed to validate these tools for truncal and breast lymphoedema, aiming to enhance diagnostic precision and management. Together, these findings inform compression strategies and diagnostic confidence when evaluating tissue integrity and fluid retention.

Stemmer's sign

Originally described in 1976 for lower limbs, Stemmer's sign is positive when skin over a toe cannot be pinched to determine skin lift, indicating fibrotic change.[68] It has also been adapted for the upper limb by assessing skin over the hand's metatarsophalangeal joint.[69] With 92% sensitivity compared to lymphoscintigraphy, this modified method is reliable for limb assessment but not applicable for truncal swelling, which lacks digit-based evaluation points.

Bjork bowtie test

The Bjork bowtie test can be performed anywhere on the body and is useful for assessing truncal or breast oedema. This tactile test involves pinching and rolling skin between the thumb and index finger, noting quality of tissue texture and thickness. Healthy tissue lifts easily, feels smooth and forms wrinkles resembling a bowtie.[70,71] A positive result reflects compressed, unyielding skin and absent wrinkling, suggesting fibrosis from chronic lymphatic inflammation (*Figure 5*).[70]

Pitting scale

The pitting scale is used to gauge tissue fluid dynamics. It is assessed via thumb sustained pressure applied with the thumb pad, noting how long the indentation takes to rebound. There are four severity grades, ranging from grade 1+ to grade 4+.[72,73] Rebound time helps determine lymphatic function and appropriate compression levels (*Table 2*).[70,74] Breast assessments may rely on visual cues (e.g., bra imprints) due to limited skin pinchability. Early-stage lymphoedema shows pronounced pitting, while advanced cases with fibrosis may require extended pressure of 10–60 seconds to elicit indentation.[73] Refill times exceeding 30 seconds indicate lymphatic compromise.[70]

Palpation

Evaluating tissue texture requires a hands-on approach, involving gently palpating the limb, breast or trunk to assess skin feel and pliability, alongside documentation of visual appearance. The subjective variability of this assessment can be minimised by using consistent terminology for tissue texture, such as that described in the STRIDE framework (*FIgure 6*).[70] A shared glossary supports standardised documentation and clearer communication within a clinical setting.

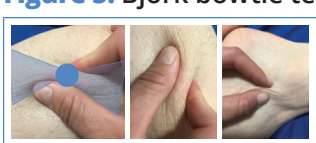
Volume and oedema

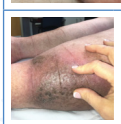
Volumetric tools can help quantify limb and trunk oedema, supporting consistent diagnosis, monitoring and treatment evaluation.

Circumferential measurement

Circumferential measurement is a cost-effective, accessible method to track limb size and shape. Lymphoedema is indicated when the affected limb exceeds 10% of the unaffected side.[75] Key metrics include limb volume, excess volume, percentage excess and proximal–distal ratios.[76] Breast and trunk measurements are challenging due to tissue variability and lack of a comparable side. Baseline measurement around the trunk and axilla help with monitoring changes.[77] Taking baseline circumferential measurements around the trunk and axilla are necessary to track fluid and volume fluctuations and reductions throughout care.

Figure 5. Bjork bowtie test


Negative Bjork bowtie test


Positive Bjork bowtie test


Alternate method for the Bjork bowtie test

Table 1. Imaging modalities for assessing lymphatic dysfunction[27,64-66]

Modality	Function	Key findings	Advantages	Disadvantages
Ultrasound High-frequency sound waves to visualise lymphatic structures	Structural assessment of lymphatic vessels and surrounding tissues	• Impact of venous dysfunction • Lymphatic obstruction • Suitability of vessels for lymphovenous anastomosis • Tissue thickening or fibrosis	• Non-invasiveness • Wide accessibility	• Operator dependence • Limited ability to visualise deeper lymphatics (23.5 mm for 48 MHz; 10 mm for 70 MHz)
Magnetic resonance lymphangiography (MRL) Heavily T2-weighted sequences or contrast-enhanced techniques	Three-dimensional mapping of lymphatic pathways from head to toe	• Visualisation of altered flow dynamics of lymphatic vessels • Visualisation of tumours • Abnormalities • Adipose hypertrophy	• Excellent spatial resolution • Absence of radiation exposure	• High cost • Need for contrast injection for enhanced imaging
Dynamic contrast-enhanced MRL Contrast injected into lymph nodes, with scans tracking lymphatic flow	Functional and anatomical assessment	• Lymphatic leaks • Lymphatic congestion	• High resolution • Dynamic flow data	• Need for specialised setup • Need for contrast injection
Intranodal computed tomography (CT) lymphangiography Water-soluble contrast injected into lymph nodes and tracked via CT	High-resolution imaging of central lymphatics	• Mapping of the thoracic duct • Lymphatic leaks	• Ready availability • Excellent spatial resolution	• Radiation exposure • Timing challenges for imaging
Contrast-enhanced ultrasound lymphoscintigraphy Radioactive tracers injected and tracked via gamma serial images	Functional imaging of lymphatic flow	• Mapping of the sentinel lymph node • Lymphoedema diagnosis	• Minimal invasiveness • Wide availability	• Limited spatial resolution • Static image • Radiation exposure • Pain
Single-photon-emission CT with CT (SPECT-CT) More detailed visualisation for the lymphatic system and how the tracer moves	CT provides anatomic detail to help pinpoint lymph node and structural abnormalities	• Higher spatial resolution for lymph-node mapping • Improved differentiation of normal and abnormal lymphatic structures • Enhanced accuracy in complex anatomical regions, such as axilla	• Improved accuracy compared with lymphoscintigraphy alone	• High cost • Limited availability • Potential for false positives or misinterpretations leading to misdiagnosis • Inability to obtain serial images
Near-infrared fluorescent lymphatic imaging (NIRFLI) Protein-binding indocyanine dye injected and illuminated with near-infrared light	Real-time visualisation of functional superficial lymphatics	• Lymphatic function • Guide for surgical interventions	• High resolution • Dynamic imaging	• Limited penetration depth (<1 cm) • Need for specialised equipment • Lack of approval for all applications in US

Fluid displacement

Fluid displacement involves limb immersion in water to measure displaced volume. This method lacks localisation and poses hygiene concerns, limiting routine use.[27]

Bioelectrical impedance

Bioelectrical impedance, the movement of electrical currents through the body, can be measured to assess fluid and tissue composition. Bioelectrical impedance analysis measures tissue resistance using a single wavelength to assess extracellular fluid, expressed as a lymphoedema index (L-Dex). It is useful for early-stage lymphoedema (stages 0–1).[78] Without pre-operative data, BCRL is indicated by an L-Dex over 6.5,[79] while, when pre-operative data is available, BCRL is indicated by a 10-point rise from baseline.[75,80] Bioelectrical impedance spectroscopy, using multiple wavelengths, is a non-invasive measurement tool for oedema assessment that evaluates limb volume by measuring how easily a low-level electrical current passes through tissue—higher resistance suggests more extracellular fluid, which indicates oedema.

Table 2. Pitting scale[74]

Grade	Pit depth	Rebound time
Grade 1	2 mm (barely detectable)	Immediate
Grade 2	4 mm	≤20 seconds
Grade 3	6 mm	≤20 seconds
Grade 4	8 mm	>20 seconds

Figure 6. STRIDE descriptions of tissue texture[70]

	**Watery** Soft, pliable feeling, non-fibrotic, easily pitting, quickly rebounding, negative Stemmer sign and Bjork bowtie test
	**Doughy** Putty-like, somewhat fibrotic, deeply pitting, rebounding after 30 seconds, potentially positive Stemmer sign or Bjork bowtie test
	**Woody** Hard feeling, severely fibrotic, non-pitting, positive Stemmer sign and Bjork bow-tie test
	**Fatty** Spongy or squishy feeling, may indicate healthy or abnormal fat (i.e., lipoedema)
	**Fragile** Thin, delicate, inelastic skin, impaired, prone to breaks, fissures, lipomas, cysts, blebs or blisters (common in older adults)

Optoelectronic plethysmography

Optoelectronic plethysmography creates three-dimensional models of limb volume, visualising oedema patterns and tracking progression on both segmental and total levels.[81]

Tissue dielectric constant

The tissue dielectric constant (TDC) is a non-invasive tool that measures local water content in breast tissue to a depth of 2.5 mm via a 300 MHz probe.[82] TDC is cost-effective for early clinical detection of fluid retention.[83] This tool is used to assess site-specific swelling; it is effective for forearm lymphoedema at a 1:26 ratio,[83] and it has shown promise in assessing breast lymphoedema, with a threshold of 1.4, although further validation is needed.[83,84]

Tonometry

Tonometry assesses the skin's resistance to applied pressure, serving as an indirect measure of fibrosis and treatment response.[18,84] It is quick and portable, with a high interrater reliability,[85] and it can be used to guide compression resistance levels.[84,86] Normative data is limited, and tissue may soften or re-harden.[18,84,86] A digital tonometry device is known as an indurometer.[86]

Functional impact

Lymphoedema can impair ROM, alter sensation and disrupt movement patterns, as well as affect vascular and metabolic health, ultimately reducing mobility and quality of life. A comprehensive physical assessment is essential to establish a baseline, guide treatment and monitor progression.

Joint mobility

Swelling from lymphoedema can limit joint mobility, causing stiffness, discomfort and functional limitations. Contributing factors include fluid accumulation, fibrosis and reduced tissue elasticity. Goniometry quantifies joint angles and tracks ROM over time. Separate assessments of active and passive pain-free ROM can differentiate whether restriction is the result of swelling or a mechanical cause. Early use of stretching, manual therapy and movement-based interventions can help preserve joint function and prevent complications.

Sensory and neurological status

A thorough neurological evaluation, including sensation and deep-tendon reflexes, is crucial for ruling out nerve involvement and metabolic causes of sensory deficits. Chemotherapy-induced neuropathy increases the risk of complications in patients wearing compression garments on limbs with reduced sensation.[87] Light-touch and two-point discrimination testing along dermatomes can reveal sensory deficits. Nerve palsies, in either an oedematous or a non-oedematous limb, may hinder adherence and the ability to don and doff compression garments. Chemotherapy-induced neuropathy affects 28% of patients, with 67% reporting post-chemotherapy numbness and tingling.[88] Proper sensory assessment ensures safe and effective compression therapy.

Mobility and movement patterns

Assessing ROM, flexibility and activity levels helps guide lymphoedema treatment choices, as limits in movement can lead to reduced independence. Steady-state exercise boosts lymphatic flow over rest by two-to-three times.[89] Regular exercise reduces lymphoedema flare-ups, making movement essential.[90] Donning and doffing of compression garments requires upper-limb strength and coordination, highlighting the importance of rehabilitation focussed on early mobility.

Body-mass index and obesity

Obesity can cause or worsen lymphoedema. BMI and waist–height ratio are reliable indicators of healthy weight.[91] In a study of 138 patients, people with a BMI of 30 or more were 3.6 times more likely to develop upper-limb lymphoedema within 30 months of surgery.[92,93] Maintaining a healthy weight helps prevent and manage lymphoedema, reinforcing the importance of dietary and lifestyle modifications.

Vascular status

Upper-limb vascular assessment may be recommended in cases of lymphoedema affecting the arm, breast or trunk. Radiation therapy may alter arterial perfusion, occasionally causing brachial-artery narrowing.[61,62,94] Increased arterial flow has been reported after breast cancer treatment.[22,61] Angiography helps identify abnormal arterial flow. Venous outflow should also be assessed to rule out tumour compression or deep-vein thrombosis (DVT). DVT monitoring is critical, as vascular issues can worsen swelling and function.[95] Duplex ultrasound is key for diagnosis.[95] A multidisciplinary vascular team is advised.

Vascular status should inform tailored compression therapy. Compression, which supports circulation and lymphatic function, should enhance outflow without compromising arterial inflow.

Inflammatory and genetic factors

Emerging research highlights the role of inflammation and genetics in lymphoedema development. Laboratory tests can detect markers including CD8+ T-cells, macrophages and neutrophils, along with pro-inflammatory cytokines such as

Table 3. International Society of Lymphology lymphoedema staging system[24,70,99]

Stage	Description	Typical treatment
Stage 0 (subclinical)	Known or undiagnosed lymphatic dysfunction with no physical signs of oedema	Preventative therapy is critical at an early stage, especially after radiation or axillary lymph-node dissection
Stage 1 (reversible)	Oedema that reduces with elevation to a similar size to an unaffected limb (often confused with other causes of oedema)	Manual lymphatic drainage, compression garments, exercise and skin care potentially able to halt or revert progression
Stage 2 (spontaneously irreversible)	Pitting oedema with positive Stemmer's sign and that does not reduce with elevation	In advanced cases, multilayer bandaging, customised devices, pump therapy and manual lymphatic drainage can help maintain function
Stage 3 (elephantiasis)	Pitting and non-pitting oedema that shows notable skin changes and does not reduce with elevation	Severe disease may require high-grade compression, surgical options and intensive rehabilitation

TNF-a, VEGF-C, and LTB4.[96] Genetic mutations linked to primary lymphoedema include FLT4 (Milroy), GJC2 (Meige), FoxC2 (lymphoedema-distichiasis) and SOX18 (hypotrichosis-lymphoedema-telangiectasia).[97,98] ICG lymphography reveals stage 0 dysfunction in limbs that appear unaffected, showing disease progression.[98] Primary lymphoedema may be systemic, not limited to one limb, emphasising the need for early detection and comprehensive evaluation.[98]

Staging

Lymphoedema should be staged to guide treatment decisions. There are several staging systems for lymphoedema, the most widely accepted being from the International Society of Lymphology (*Table 3*).[24,99] Staging should guide selection of appropriate treatment:[24,70,99]

The severity of lymphoedema can also be assessed with a volumetric scale determined by the percentage difference in volume between an affected and an unaffected limb (*Table 4*).[24,100] While volumetric scales remain a common reference for lymphoedema severity, they reflect only one dimension of the condition. Current clinical understanding emphasises that tissue texture changes, such as fibrosis, induration and dermal thickening, may precede or occur independently of measurable volume differences. Therefore, there is a growing need for a multidimensional severity scale that incorporates both quantitative volume and qualitative tissue characteristics, including:

- Palpable fibrosis
- Pitting behaviour
- Skin integrity
- Responsiveness to compression
- Functional impact.

Such a scale would better reflect the complexity of lymphatic dysfunction, especially in oncology-related presentations, and guide more tailored therapeutic strategies.

Table 4. Volumetric lymphoedema scale[24,100]

Severity	Volume difference
Mild	<20%
Moderate	20–40%
Severe	>40%

Discussion

Lymphatic dysfunction and Starling's revised equilibrium

Recent discoveries in lymphatic anatomy detailed in this article expand understanding of how the lymphatic system interacts with systemic health. Furthermore, Levick and Michel's 2010 revision of Starling's equilibrium reshaped the understanding of fluid dynamics.[101] Mortimer and Rockson noted that this updated model supports the assertion that chronic oedema exists along a continuum of lymphatic dysfunction.[102] Since the lymphatic system is solely responsible for clearing interstitial fluid, persistent swelling warrants a thorough evaluation of each individual clinical presentation.

Challenges in lymphoedema assessment and screening

Despite advancements in lymphatic research, clinical awareness and screening remain limited across medical education and practice. Rockson noted that most medical students receive minimal training on the lymphatic system.[103] In fact, a review of 110 US medical schools found an average of only 45 minutes devoted to lymphatic disease.[103] This inadequate exposure leads to patients being prescribed pumps or sleeves without referral to lymphoedema specialists—who are essential for targeted management.

A limited understanding of lymphatic anatomy and function often leads to a reactive approach, with intervention beginning only after signs and symptoms emerge. Preoperative lymphatic screening—across oncologic, vascular and orthopaedic procedures—remains uncommon, even though growing evidence suggests that identifying lymphatic vulnerability before insult could reduce post-surgical complications and support improved recovery.

Specialists ensure precise garment fitting based on refill rates and mobility limitations, optimising therapeutic outcomes. They also educate patients on proper pump use alongside complete decongestive therapy, which includes compression, exercise, manual lymphatic drainage and skin care. Strengthening lymphoedema education and screening protocols is vital for improving long-term outcomes. These specialists are often trained through accredited institutions, academic programmes or recognised certification pathways, ensuring they possess the clinical expertise needed to assess lymphatic function, tailor interventions and guide patients through complex care decisions.

Financial considerations and the importance of thorough documentation

Insurance coverage and funding disparities remain significant barriers to compression therapy access. In the US, the January 2024 Lymphedema Treatment Act has improved access by mandating Medicare coverage for compression garments. However, care is still restricted by gaps in affordability, coverage limits and prior-authorisation requirements.

Globally, access challenges persist, particularly in countries with socialised healthcare. For example, the NHS in the UK offers limited funding for compression therapy, often requiring restrictive criteria or extended wait times. Similar constraints are seen in Canada and parts of Europe, where formularies may not include advance compression products.

Thorough documentation of medical necessity, including objective findings, staging and previous interventions, is essential for clinicians to advocate effectively for coverage, reduce delays and improve equitable access to evidence-based treatment. When coverage is denied or delayed, patients are often unable to obtain medically necessary compression, resulting in unmanaged oedema, increased risk of complications and higher long-term healthcare costs. These gaps in access not only compromise clinical outcomes but also place significant financial and emotional strain on patients and care systems.[104-106]

Addressing disparities in insurance coverage and clinician availability

Disparities in insurance coverage continue to limit access to compression therapy, creating financial hurdles for patients. Although the US Lymphedema Treatment Act has expanded Medicare benefits, many private insurers and international systems still fall short. Broader policy reform is urgently needed to ensure equitable access to care.

The shortage of trained clinicians in compression fitting and lymphatic evaluation compounds the issue—leading to inappropriate garment use and ineffective therapy. Expanding training programmes and certification pathways are essential to equip providers with the skills needed for precision-based treatment.

Conclusion

Application of the STRIDE framework should be built on an understanding of the complexities of lymphatic anatomy and the pathophysiology of lymphoedema. Therefore, targeted clinician education initiatives will be critical in transforming care delivery. Awareness efforts should also underscore the role of comorbidities in lymphatic dysfunction, as well as the importance of timely referrals and multidisciplinary collaboration. Expanding clinical research into lymphatic anatomy should also drive innovation in compression science.

Thorough and accurate assessment is essential for the personalised, targeted and physiologically aligned compression therapy supported by the STRIDE framework. Lymphoedema diagnosis care continues to advance, with advanced imaging modalities such as ICG lymphography, lymphoscintigraphy and MRI lymphangiography providing critical information regarding lymphatic dysfunction. Emerging technologies such as TDC or BIA analysis offer promise for early detection by quantifying localised oedema and tissue change.[83] However, gaps persist in precision, and utility is often limited by referral delays, insurance constraint and cost barriers. Expanding research and standardising use across clinical settings will be crucial in making lymphatic evaluation more inclusive and actionable. Early-stage diagnostic tools, refined assessment models and enhancing diagnostic accessibility should improve outcomes and promote equity across healthcare systems, advancing lymphoedema management toward truly individualised, evidence-informed interventions. **JWC**

Declaration of interest: Sponsored by Haddenham Healthcare and the US Medical Compression Alliance (USMCA); Sandi Davis has been a paid consultant for Koya Medical; Suzie Ehmann has been a paid consultant or speaker for L&R, Urgo, OVIK, Compression Dynamics and Medline; Brandy McKeown has been a paid consultant or speaker for HMP global/Wound Source, L&R, LymphaPress, Juzo and Sigvaris; Justine C Whitaker has been a paid consultant or speaker for Medi and Jobst; Karen J Bock has been a paid consultant for Pure Medical

References

1. Brenner E. [Anatomy and physiology of the lymph system: what clinicians should know]. Radiologie (Heidelb). 2025; 65(5):301–306. https://doi.org/10.1007/s00117-025-01432-2
2. Földi M, Földi E, Strößenreuther C, Kubik S. Földi's textbook of lymphology: for physicians and lymphedema therapists. Amsterdam: Elsevier Health Sciences: 2012
3. Lampejo AO, Jo M, Murfee WL, Breslin JW. The microvascular-lymphatic interface and tissue homeostasis: critical questions that challenge current understanding. J Vasc Res. 2022; 59(6):327–342
4. Breslin JW, Yang Y, Scallan JP, Sweat RS, Adderley SP, Murfee WL. Lymphatic vessel network structure and physiology. Compr Physiol. 2018; 9(1):207–299. https://doi.org/10.1002/cphy.c180015
5. Shinaoka A, Koshimune S, Suami H et al. Lower-limb lymphatic drainage pathways and lymph nodes: a CT lymphangiography cadaver study. Radiology. 2020; 294(1):223–229
6. Suami H, Taylor GI, Pan WR. The lymphatic territories of the upper limb: anatomical study and clinical implications. Plast Reconstr Surg. 2007; 119(6):1813–1822. https://doi.org/10.1097/01.prs.0000246516.64780.61
7. Suami H, Scaglioni MF. Anatomy of the lymphatic system and the lymphosome concept with reference to lymphedema. Semin Plast Surg. 2018; 32(1):5–11. https://doi.org/10.1055/s-0038–1635118
8. Suami H, Kato S. Anatomy of the lymphatic system and its structural disorders in lymphoedema. In: Lee B-B, Rockson SG, Bergan J (eds). Lymphedema: a concise compendium of theory and practice. New York (NY): Springer; 2018: 57–78
9. Suami H, Pan W-R, Mann GB, Taylor GI. The lymphatic anatomy of the breast and its implications for sentinel lymph node biopsy: a human cadaver study. Ann Surg Oncol. 2008; 15(3):863–871. https://doi.org/10.1245/s10434-007-9709-9
10. Granoff MD, Pardo JA, Johnson AR et al. Superficial and functional lymphatic anatomy of the upper extremity. Plast Reconstr Surg. 2022; 150(4):900–907. https://doi.org/10.1097/prs.0000000000009555
11. Suami H, O'Neill JK, Pan WR, Taylor GI. Superficial lymphatic system of the upper torso: preliminary radiographic results in human cadavers. Plast Reconstr Surg. 2008; 121(4):1231–1239. https://doi.org/10.1097/01.prs.0000302511.21140.36
12. Aldrich MB, Rasmussen JC, Fife CE, Shaitelman SF, Sevick-Muraca EM. The development and treatment of lymphatic dysfunction in cancer patients and survivors. Cancers (Basel). 2020; 12(8). https://doi.org/10.3390/cancers12082280
13. Suami H, Pan WR, Mann GB, Taylor GI. The lymphatic anatomy of the breast and its implications for sentinel lymph node biopsy: a human cadaver study. Ann Surg Oncol. 2008; 15(3):863–871. https://doi.org/10.1245/s10434-007-9709-9
14. Carati C, Gannon B, Piller N. Anatomy and physiology in relation to compression of the upper limb and thorax. J Lymphoedema. 2010; 5:58–67
15. Hutton R. Developing new practices for managing breast and chest lymphoedema. Br J Community Nurs. 2024; 29(S10):S20–S24. https://doi.org/10.12968/bjcn.2024.0109

16. Mehta M, Sarrami S, Moroni E, Fishman J, De La Cruz C. Alternative lymphatic drainage pathways in the trunk following oncologic therapy. Ann Plast Surg. 2024; 92(4S2):S258–S261. https://doi.org/10.1097/sap.0000000000003861
17. Giammarile F, Vidal-Sicart S, Paez D et al. Sentinel lymph node methods in breast cancer. Semin Nucl Med. 2022; 52(5):551–560. https://doi.org/10.1053/j.semnuclmed.2022.01.006
18. Piller NB, Clodius L. The use of a tissue tonometer as a diagnostic aid in extremity lymphoedema: a determination of its conservative treatment with benzo-pyrones. Lymphology. 1976; 9(4):127–132
19. Moore JE, Bertram CD. Lymphatic system flows. Annu Rev Fluid Mech. 2018; 50:459–482. https://doi.org/10.1146/annurev-fluid-122316–045259
20. Bertram CD, Macaskill C, Davis MJ, Moore JE. Contraction of collecting lymphatics: organization of pressure-dependent rate for multiple lymphangions. Biomech Model Mechanobiol. 2018; 17(5):1513–1532. https://doi.org/10.1007/s10237-018-1042-7
21. Zawieja DC. Contractile physiology of lymphatics. Lymphat Res Biol. 2009; 7(2):87–96. https://doi.org/10.1089/lrb.2009.0007
22. Carati C, Gannon B, Piller N. Anatomy and physiology in relation to compression of the upper limb and thorax. J Lymphoedema. 2010; 5(1):58–67
23. Carson Sibley R, Crow-Petree D, Ferguson H. Primary lymphedema. 2024. https://rarediseases.org/rare-diseases/hereditary-lymphedema/ (accessed 20 August 2025)
24. International Society of Lymphology. The diagnosis and treatment of peripheral lymphedema: 2020 consensus document of the International Society of Lymphology (revised edition). Lymphology. 2023; 56(4):133–151
25. García Nores GD, Ly CL, Cuzzone DA et al. CD4+ T cells are activated in regional lymph nodes and migrate to skin to initiate lymphedema. Nat Com. 2018; 9(1):1970. https://doi.org/10.1038/s41467–018–04418-y
26. Yuan Y, Arcucci V, Levy SM, Achen MG. Modulation of immunity by lymphatic dysfunction in lymphedema. Front Immunol. 2019; 10:76. https://doi.org/10.3389/fimmu.2019.00076
27. Pappalardo M, Starnoni M, Franceschini G, Baccarani A, De Santis G. Breast cancer-related lymphedema: recent updates on diagnosis, severity and available treatments. J Pers Med. 2021; 11(5). https://doi.org/10.3390/jpm11050402
28. Hara Y, Otsubo R, Shinohara S et al. Lymphedema after axillary lymph node dissection in breast cancer: prevalence and risk factors-a single-center retrospective study. Lymphat Res Biol. 2022; 20(6):600–606. https://doi.org/10.1089/lrb.2021.0033
29. Swaroop MN, Ferguson CM, Horick NK et al. Impact of adjuvant taxane-based chemotherapy on development of breast cancer-related lymphedema: results from a large prospective cohort. Breast Cancer Res Treat. 2015; 151(2):393–403. https://doi.org/10.1007/s10549-015-3408-1
30. Johnson AR, Granoff MD, Lee BT, Padera TP, Bouta EM, Singhal D. The impact of taxane-based chemotherapy on the lymphatic system. Ann Plast Surg. 2019; 82(4S3):S173–S178. https://doi.org/10.1097/sap.0000000000001884
31. Tokumoto H, Akita S, Nakamura R, Yamamoto N, Kubota Y, Mitsukawa N. Investigation of the association between breast cancer-related lymphedema and the side effects of taxane-based chemotherapy using indocyanine green lymphography. Lymphat Res Biol. 2022; 20(6):612–617. https://doi.org/10.1089/lrb.2021.0065
32. Greene AK, Zurakowski D, Goss JA. Body mass index and lymphedema morbidity: comparison of obese versus normal-weight patients. Plast Reconstr Surg. 2020; 146(2):402–407. https://doi.org/10.1097/prs.0000000000007021
33. Sudduth CL, Greene AK. Lymphedema and obesity. Cold Spring Harb Perspect Med. 2022; 12(5). https://doi.org/10.1101/cshperspect.a041176
34. Williamson K, Nimegeer A, Lean M. Rising prevalence of BMI≥ 40 kg/m2: a high-demand epidemic needing better documentation. Obesi Rev. 2020; 21(4):e12986
35. Westcott GP, Rosen ED. Crosstalk between adipose and lymphatics in health and disease. Endocrinology. 2022; 163(1):bqab224
36. Mehrara BJ, Greene AK. Lymphedema and obesity: is there a link? Plast Reconstr Surg. 2014; 134(1):154e-160e. https://doi.org/10.1097/prs.0000000000000268
37. Jammallo LS, Miller CL, Singer M et al. Impact of body mass index and weight fluctuation on lymphedema risk in patients treated for breast cancer. Breast Cancer Res Treat. 2013; 142(1):59–67. https://doi.org/10.1007/s10549-013-2715-7
38. Faerber G, Cornely M, Daubert C et al. S2k guideline lipedema. Journal der Deutschen Dermatologischen Gesellschaft. 2024; 22(9):1303–1315. https://doi.org/https://doi.org/10.1111/ddg.15513
39. Herbst KL. Subcutaneous adipose tissue diseases: dercum disease, lipedema, familial multiple lipomatosis, and madelung disease. In: Feingold KR, Ahmed SF, Anawalt B et al (eds). Endotext. South Dartmouth (MA): MDText; 2000
40. Wickline A, Cole W, Melin M, Ehmann S, Aviles F, Bradt J. Mitigating the post-operative swelling tsunami in total knee arthroplasty: a call to action. J Orthopaed Exper Innov. 2023; 4(2). https://doi.org/10.60118/001c.77444
41. Todhunter-Brown A, Sellers CE, Baer GD et al. Physical rehabilitation approaches for the recovery of function and mobility following stroke. Cochrane Database Syst Rev. 2025; 2(2):Cd001920. https://doi.org/10.1002/14651858.CD001920.pub4
42. Peters SE, Jha B, Ross M. Rehabilitation following surgery for flexor tendon injuries of the hand. Cochrane Database Syst Rev. 2021; 1(1):Cd012479. https://doi.org/10.1002/14651858.CD012479.pub2
43. Saha S, Sur M, Ray Chaudhuri G, Agarwal S. Effects of mirror therapy on oedema, pain and functional activities in patients with poststroke shoulder-hand syndrome: a randomized controlled trial. Physiother Res Int. 2021; 26(3):e1902. https://doi.org/10.1002/pri.1902
44. Ahmadinejad M, Razban F, Jahani Y, Heravi F. Limb edema in critically ill patients: comparing intermittent compression and elevation. Int Wound J. 2022; 19(5):1085–1091. https://doi.org/10.1111/iwj.13704
45. Verbelen H, Tjalma W, Dombrecht D, Gebruers N. Breast edema, from diagnosis to treatment: state of the art. Arch Physiother. 2021; 11(1):1–10. https://doi.org/10.1186/s40945-021-00103-4
46. Cavezzi A, Ambrosini L, Campana F, Mosti G. Lymphedema and nutrition: a review. Vein Lymphat. 2019; 8:24–29
47. Bonetti G, Herbst KL, Dhuli K et al. Dietary supplements for lipedema. J Prev Med Hyg. 2022; 63(2S3):169–173. https://doi.org/10.15167/2421-4248/jpmh2022.63.2S3.2758
48. Padera TP, Meijer EF, Munn LL. The lymphatic system in disease processes and cancer progression. Annu Rev Biomed Eng. 2016; 18:125–158. https://doi.org/10.1146/annurev-bioeng-112315–031200
49. Lee C, Kim MJ, Kumar A, Lee HW, Yang Y, Kim Y. Vascular endothelial growth factor signaling in health and disease: from molecular mechanisms to therapeutic perspectives. Signal Transduct Target Ther. 2025; 10(1):170. https://doi.org/10.1038/s41392-025-02249-0
50. Armer JM. The problem of post-breast cancer lymphedema: impact and measurement issues. Cancer Invest. 2005; 23(1):76–83
51. Choi JE, Chang MC. Management of lymphedema is really a matter in patients with breast cancer. World J Clin Cases. 2024; 12(15):2482–2486. https://doi.org/10.12998/wjcc.v12.i15.2482
52. Arié A, Yamamoto T. Lymphedema secondary to melanoma treatments: diagnosis, evaluation, and treatments. Glob Health Med. 2020; 2(4):227–234. https://doi.org/10.35772/ghm.2020.01022
53. Gentile D, Canzian J, Barbieri E, Sagona A, Di Maria Grimaldi S, Tinterri C. Predictors of high-burden residual axillary disease after neoadjuvant therapy in breast cancer. Cancers (Basel). 2025; 17(10). https://doi.org/10.3390/cancers17101596
54. Jiang X, Tian W, Nicolls MR, Rockson SG. The lymphatic system in obesity, insulin resistance, and cardiovascular diseases. Front Physiol. 2019; 10:1402. https://doi.org/10.3389/fphys.2019.01402
55. Wang M, He Y, He Q, Di F, Zou K, Wang W, Sun X. Comparison of clinical characteristics and disease burden between early- and late-onset type 2 diabetes patients: a population-based cohort study. BMC Public Health. 2023; 23(1):2411. https://doi.org/10.1186/s12889-023-17280-5
56. Rifkin WJ, Kantar RS, Cammarata MJ et al. Impact of diabetes on 30-day complications in mastectomy and implant-based breast reconstruction. J Surg Res. 2019; 235:148–159. https://doi.org/10.1016/j.jss.2018.09.063
57. Burian EA, Franks PJ, Borman P et al. Factors associated with cellulitis in lymphoedema of the arm - an international cross-sectional study (LIMPRINT). BMC Infect Dis. 2024; 24(1):102. https://doi.org/10.1186/s12879-023-08839-z
58. Engin O, Sahin E, Saribay E, Dilek B, Akalin E. Risk factors for developing upper limb cellulitis after breast cancer treatment. Lymphology. 2022; 55(2):77–83
59. Vignes S, Poizeau F, Dupuy A. Cellulitis risk factors for patients with primary or secondary lymphedema. J Vasc Surg Venous Lymphat Disord. 2022; 10(1):179–185. https://doi.org/10.1016/j.jvsv.2021.04.009
60. Keeley V, Mortimer P, Gordon K. British Lymphology Society guidelines on the management of cellulitis in lymphoedema. 2022. https://www.thebls.com/public/uploads/documents/document-75091530863967.pdf (accessed 20 August 2025)
61. Allam O, Park KE, Chandler L, Mozaffari MA, Ahmad M, Lu X, Alperovich M. The impact of radiation on lymphedema: a review of the literature. Gland Surg. 2020; 9(2):596–602. https://doi.org/10.21037/gs.2020.03.20
62. Naoum GE, Roberts S, Brunelle CL et al. Quantifying the impact of axillary surgery and nodal irradiation on breast cancer-related lymphedema and local tumor control: long-term results from a prospective screening trial. J Clin Oncol. 2020; 38(29):3430–3438. https://doi.org/10.1200/jco.20.00459

63. Armer JM, Ballman KV, McCall L et al. Lymphedema symptoms and limb measurement changes in breast cancer survivors treated with neoadjuvant chemotherapy and axillary dissection: results of American College of Surgeons Oncology Group (ACOSOG) Z1071 (Alliance) substudy. Support Care Cancer. 2019; 27(2):495–503. https://doi.org/10.1007/s00520-018-4334-7
64. Kitayama S, Maegawa J, Matsubara S, Kobayashi S, Mikami T, Hirotomi K, Kagimoto S. Real-time direct evidence of the superficial lymphatic drainage effect of intermittent pneumatic compression treatment for lower limb lymphedema. Lymphat Res Biol. 2017; 15(1):77–86. https://doi.org/10.1089/lrb.2016.0031
65. Polomska AK, Proulx ST. Imaging technology of the lymphatic system. Adv Drug Deliv Rev. 2021; 170:294–311. https://doi.org/10.1016/j.addr.2020.08.013
66. Nagy BI, Mohos B, Tzou CJ. Imaging modalities for evaluating lymphedema. Medicina (Kaunas). 2023; 59(11). https://doi.org/10.3390/medicina59112016
67. Kitayama S. Diagnosis and treatments of limb lymphedema: review. Ann Vasc Dis. 2024; 17(2):114–119. https://doi.org/10.3400/avd.ra.24-00011
68. Stemmer R. [A clinical symptom for the early and differential diagnosis of lymphedema]. Vasa. 1976; 5(3):261–262
69. Goss JA, Greene AK. Sensitivity and specificity of the Stemmer sign for lymphedema: a clinical lymphoscintigraphic study. Plast Reconstr Surg Glob Open. 2019; 7(6):e2295. https://doi.org/10.1097/gox.0000000000002295
70. Bjork R, Ehmann S. S.T.R.I.D.E. Professional guide to compression garment selection for the lower extremity. J Wound Care. 2019; 28(S6a):1–44. https://doi.org/10.12968/jowc.2019.28.Sup6a.S1
71. Bjork R, Hettrick H. Lymphedema: new concepts in diagnosis and treatment. Current Dermatology Reports. 2019; 8:190–198
72. Calzon ME, Blebea J, Pittman C. Quantitative measurement of pitting edema with a novel edema ruler. J Vasc Surg Case Innov Technique. 2024; 10(1). https://doi.org/10.1016/j.jvscit.2023.101373
73. Sanderson J, Tuttle N, Box R, Reul-Hirche H, Laakso EL. Pitting is not only a measure of oedema presence: using high-frequency ultrasound to guide pitting test standardisation for assessment of lymphoedema. Diagnostics (Basel). 2024; 14(15). https://doi.org/10.3390/diagnostics14151645
74. Hogan MA, Estridge S, Zygmont D, Davenport J. Prentice-Hall nursing reviews & rationales: medical-surgical nursing. London: Pearson; 2007
75. Kassamani YW, Brunelle CL, Gillespie TC, Bernstein MC, Bucci LK, Nassif T, Taghian AG. Diagnostic criteria for breast cancer-related lymphedema of the upper extremity: the need for universal agreement. Ann Surg Oncol. 2022; 29(2):989–1002. https://doi.org/10.1245/s10434-021-10645-3
76. Williams A. Measuring change in limb volume to evaluate lymphoedema treatment outcome. EWMA Journal. 2015; 15(1):27–32
77. Kassamani YW, Brunelle CL, Gillespie TC, Bernstein MC, Bucci LK, Nassif T, Taghian AG. Diagnostic criteria for breast cancer-related lymphedema of the upper extremity: the need for universal agreement. Annals of Surgical Oncology. 2022:1–14
78. Liu S, Zhao Q, Ren X et al. Determination of bioelectrical impedance thresholds for early detection of breast cancer-related lymphedema. Int J Med Sci. 2021; 18(13):2990–2996. https://doi.org/10.7150/ijms.53812
79. Borman P, Yaman A, Doğan L et al. The comparative frequency of breast cancer-related lymphedema determined by bioimpedance spectroscopy and circumferential measurements. Eur J Breast Health. 2022; 18(2):148–154. https://doi.org/10.4274/ejbh.galenos.2022.2021-9-2
80. Levenhagen K, Davies C, Perdomo M, Ryans K, Gilchrist L. Diagnosis of upper quadrant lymphedema secondary to cancer: clinical practice guideline from the oncology section of the american physical therapy association. Phys Ther. 2017; 97(7):729–745. https://doi.org/10.1093/ptj/pzx050
81. Farina G, Galli M, Borsari L, Aliverti A, Paraskevopoulos IT, LoMauro A. Limb volume measurements: a comparison of circumferential techniques and optoelectronic systems against water displacement. Bioengineering (Basel). 2024; 11(4). https://doi.org/10.3390/bioengineering11040382
82. Koehler LA, Mayrovitz HN. Tissue dielectric constant measures in women with and without clinical trunk lymphedema following breast cancer surgery: a 78-week longitudinal study. Phys Ther. 2020; 100(8):1384–1392. https://doi.org/10.1093/ptj/pzaa080
83. Riches K, Cheung KL, Keeley V. Improving the assessment and diagnosis of breast lymphedema after treatment for breast cancer. Cancers (Basel). 2023; 15(6). https://doi.org/10.3390/cancers15061758
84. Vargo M, Aldrich M, Donahue P, Iker E, Koelmeyer L, Crescenzi R, Cheville A. Current diagnostic and quantitative techniques in the field of lymphedema management: a critical review. Med Oncol. 2024; 41(10):241. https://doi.org/10.1007/s12032-024-02472-9
85. Pallotta O, McEwen M, Tilley S et al. A new way to assess superficial changs to lymphoedema. J Lymphoedema. 2011; 6(2):34–41
86. Vanderstelt S, Pallotta OJ, McEwen M, Ullah S, Burrow L, Piller N. Indurometer vs. tonometer: is the indurometer currently able to replace and improve upon the tonometer? Lymphat Res Biol. 2015; 13(2):131–136. https://doi.org/10.1089/lrb.2014.0016
87. Borman P. Lymphedema diagnosis, treatment, and follow-up from the view point of physical medicine and rehabilitation specialists. Turk J Phys Med Rehab. 2018; 64(3):179
88. Burgess J, Ferdousi M, Gosal D et al. Chemotherapy-induced peripheral neuropathy: epidemiology, pathomechanisms and treatment. Oncol Ther. 2021; 9(2):385–450. https://doi.org/10.1007/s40487-021-00168-y
89. Lane K, Worsley D, McKenzie D. Exercise and the lymphatic system: implications for breast-cancer survivors. Sport Med. 2005; 35(6):461–471. https://doi.org/10.2165/00007256–200535060–00001
90. Dittus KL, Lakoski SG, Savage PD et al. Exercise-based oncology rehabilitation: leveraging the cardiac rehabilitation model. J Cardiopulmon Rehabili Prev. 2015; 35(2):130–139
91. Tewari A, Kumar G, Maheshwari A, Tewari V, Tewari J. Comparative evaluation of waist-to-height ratio and BMI in predicting adverse cardiovascular outcome in people with diabetes: a systematic review. Cureus. 2023; 15(5):e38801. https://doi.org/10.7759/cureus.38801
92. Ridner SH, Dietrich MS, Stewart BR, Armer JM. Body mass index and breast cancer treatment-related lymphedema. Support Care Cancer. 2011; 19(6):853–857. https://doi.org/10.1007/s00520-011-1089-9
93. Mehrara BJ, Greene AK. Lymphedema and obesity: is there a link? Plastic and reconstructive surgery. 2014; 134(1):154e-160e
94. Zhang F, Wang Y, Xu W et al. Dosimetric evaluation of different intensity-modulated radiotherapy techniques for breast cancer after conservative surgery. Technol Cancer Res Treat. 2015; 14(5):515–523. https://doi.org/10.1177/1533034614551873
95. Koethe Y, Bochnakova T, Kaufman CS. Upper extremity deep venous thrombosis: etiologies, diagnosis, and updates in therapeutic strategies. Semin Intervent Radiol. 2022; 39(5):475–482. https://doi.org/10.1055/s-0042-1757937
96. Bowman C, Rockson SG. The role of inflammation in lymphedema: a narrative review of pathogenesis and opportunities for therapeutic intervention. Int J Mol Sci. 2024; 25(7). https://doi.org/10.3390/ijms25073907
97. Senger JB, Kadle RL, Skoracki RJ. Current concepts in the management of primary lymphedema. Medicina (Kaunas). 2023; 59(5). https://doi.org/10.3390/medicina59050894
98. Chen WF, Jou C, Pandey SK, Lo SL. Primary lymphedema: anatomically isolated or a pervasive systemic disorder? Plast Reconstr Surg Glob Open. 2024; 12(12):e6328. https://doi.org/10.1097/gox.0000000000006328
99. Douglass J, Kelly-Hope L. Comparison of staging systems to assess lymphedema caused by cancer therapies, lymphatic filariasis, and podoconiosis. Lymphatic Res Biol. 2019; 17(5):550–556
100. Greene AK, Goss JA. Diagnosis and staging of lymphedema. Sem Plast Surg. 2018; 32(01):12–16
101. Levick JR, Michel CC. Microvascular fluid exchange and the revised Starling principle. Cardiovasc Res. 2010; 87(2):198–210. https://doi.org/10.1093/cvr/cvq062
102. Mortimer PS, Rockson SG. New developments in clinical aspects of lymphatic disease. J Clin Invest. 2014; 124(3):915–921. https://doi.org/10.1172/jci71608
103. Rockson SG. Lymphatic medicine: paradoxically and unnecessarily ignored. Lymphat Res Biol. 2017; 15(4):315–316. https://doi.org/10.1089/lrb.2017.29033.sr
104. De PK. Impacts of insurance expansion on health cost, health access, and health behaviors: evidence from the medicaid expansion in the US. Int J Health Econ Manage. 2021; 21(4):495–510. https://doi.org/10.1007/s10754-021-09306-5
105. Weiss R. Cost of a lymphedema treatment mandate - 16 years of experience in the Commonwealth of Virginia. Health Econ Rev. 2022; 12(1):40. https://doi.org/10.1186/s13561-022-00388-6
106. Lynn JV, Hespe GE, Akhter MF, David CM, Kung TA, Myers PL. Cross-sectional analysis of insurance coverage for lymphedema treatments in the United States. JAMA Surg. 2023; 158(9):920–926. https://doi.org/10.1001/jamasurg.2023.2017