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Modern Treatment Approaches for Lymphedema: A Comprehensive Literature Review

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Abstract

Background:

Lymphedema is a chronic disorder caused by impaired lymphatic drainage, leading to tissue changes, reduced limb function, and limitations in physical performance. Although conservative and surgical treatments are established, their effects on exercise capacity and return to sport remain insufficiently summarized.

Objective:
This narrative review evaluated current and emerging lymphedema treatments, focusing on improving limb function, physical activity, and quality of life in active individuals.

Methods:
A narrative review of studies published between 2015 and 2026 was conducted, supported by key earlier literature. Databases were searched using terms related to lymphedema, rehabilitation, exercise therapy, surgery, and lymphatic reconstruction, with emphasis on functional outcomes.

Results:
Complete decongestive therapy remains the standard conservative treatment, effectively reducing limb volume and maintaining function. Compression therapy and structured exercise are central to symptom control. Progressive resistance and aerobic training are safe and may improve strength, endurance, and physical performance without worsening edema.

Surgical procedures such as lymphovenous anastomosis, vascularized lymph node transfer, and liposuction may provide additional benefits in selected patients. Emerging approaches, including immediate lymphatic reconstruction and regenerative therapies, may improve lymphatic function and prevent progression. Modern imaging techniques support earlier diagnosis and individualized rehabilitation.

Conclusions:
Current lymphedema management increasingly emphasizes functional rehabilitation and preservation of physical capacity rather than only limb volume reduction. Exercise appears safe and beneficial, while surgical and regenerative approaches may further improve outcomes. Evidence regarding athletes and return-to-sport outcomes remains limited, highlighting the need for sport-specific research.

Key words: lymphedema, rehabilitation, exercise therapy, lymphatic surgery, complete decongestive therapy

1. Introduction

Lymphedema is a chronic, progressive condition characterized by impaired lymphatic transport and accumulation of protein-rich fluid in the interstitial space, leading to swelling, tissue remodeling, and functional impairment [1] Beyond its clinical manifestations, the condition has important implications for physical performance, as it may reduce muscle strength, limit range of motion, and impair exercise tolerance. These functional limitations are particularly relevant for physically active individuals, for whom even mild impairments can negatively affect training capacity, performance output, and return-to-sport outcomes.

Historically, management has been based primarily on conservative approaches, with complete decongestive therapy (CDT) considered the gold standard of care [9]. CDT integrates manual lymphatic drainage, compression therapy, exercise, and skin care, and is effective in reducing limb volume and preventing complications. However, its long-term success is highly dependent on adherence, and it may not fully restore functional capacity in individuals with higher physical demands [13]. This limitation is particularly important in athletic and active populations, where functional performance is a primary outcome.

In recent years, surgical interventions have significantly expanded treatment options for lymphedema. Physiologic procedures such as lymphovenous anastomosis (LVA) and vascularized lymph node transfer (VLNT) aim to restore lymphatic drainage, while reductive techniques such as liposuction target irreversible fibrofatty tissue changes in advanced disease [17,18,25]. Additionally, emerging strategies such as immediate lymphatic reconstruction

(ILR) and regenerative approaches, including stem cell-based therapies and lymphangiogenesis, suggest a potential shift toward biologically restorative treatments [24].

Advances in diagnostic imaging, including indocyanine green lymphography and magnetic resonance imaging, have improved early detection, staging, and surgical planning, enabling more individualized treatment strategies and better functional monitoring [14,15]. These developments support earlier intervention and more individualized rehabilitation focused not only on limb volume reduction but also on preservation of physical function. [9,11].

Despite these advances, there remains a lack of integrated evidence synthesizing conservative, surgical, and emerging therapies with a specific focus on functional outcomes in physically active populations. In particular, data on exercise performance, return-to-sport, and long-term physical capacity remain limited.

Therefore, this review aims to provide a comprehensive synthesis of current and emerging treatment strategies for lymphedema, with a particular focus on their effectiveness in restoring limb function, supporting physical activity, and optimizing quality of life in active individuals [11].

2. Materials and Methods

This study was conducted as a structured narrative review focused on current and emerging treatment strategies for lymphedema, with particular emphasis on functional outcomes, exercise capacity, and return-to-sport considerations.

A literature search was performed using PubMed, Scopus, and Web of Science databases. Studies published between 2015 and 2026 were prioritized to reflect contemporary clinical practice and recent advances in lymphedema management. Earlier landmark publications were included selectively to provide essential pathophysiological and historical background.

The search strategy combined Medical Subject Headings (MeSH) and free-text terms, including “lymphedema,” “complete decongestive therapy,” “compression therapy,” “exercise,” “rehabilitation,” “physical activity,” “lymphovenous anastomosis,” “vascularized lymph node transfer,” “liposuction,” “lymphatic reconstruction,” and “lymphangiogenesis.” Boolean operators (AND, OR) were applied to refine the search.

Priority was given to systematic reviews, meta-analyses, consensus guidelines, and clinical studies evaluating functional, rehabilitative, and surgical outcomes. Due to heterogeneity of study designs and outcome measures, a qualitative narrative synthesis was performed rather than quantitative meta-analysis.

The limitations of this review include the narrative design, potential selection bias, and the predominance of oncology-related populations within the available literature. In addition, limited evidence is available regarding athletic and high-performance populations.

3. Results

3.1. Pathophysiology of Lymphedema

Lymphedema is a chronic, progressive disorder resulting from impaired lymphatic transport, leading to the accumulation of protein-rich fluid in the interstitial space [1]. Unlike simple edema, lymphedema involves complex interactions among lymph stasis, immune activation, adipose tissue expansion, and fibrotic remodeling, creating a self-perpetuating cycle that progressively compromises limb function and tissue integrity [1,2].

3.1.1. Lymphatic Dysfunction and Initial Injury

The lymphatic system maintains interstitial fluid homeostasis, immune surveillance, and lipid transport. Primary lymphedema arises from congenital defects in lymphatic vessel development, including mutations in key regulators such as FOXC2 and dysregulation of lymphangiogenic factors such as VEGF-C, resulting in hypoplastic or dysfunctional lymphatic networks [3,4].

Secondary lymphedema develops following injury to previously normal lymphatics, such as surgical lymph node dissection, radiotherapy, or trauma, reducing transport capacity below the threshold required to clear interstitial fluid [1,2].

3.1.2. Inflammation and Immune Activation

Persistent lymph stasis triggers a local immune response that is central to disease progression. Experimental studies in murine models have demonstrated that $CD4^{+}$ T cells migrate to the skin and initiate local inflammation, promoting edema and tissue remodeling [6]. Moreover, Th2 cytokines, particularly IL-4 and IL-13, inhibit lymphangiogenesis and promote fibrosis [6,7]. Blocking these cytokines in animal models significantly reduces tissue swelling and improves lymphatic function, highlighting their critical role in lymphedema pathogenesis [6,7].

3.1.3. Adipose Tissue Deposition and Fibrosis

Chronic inflammation drives progressive tissue remodeling. In animal models, lymphedematous limbs demonstrate adipocyte proliferation and increased deposition of extracellular matrix proteins, particularly collagen, leading to fibrosis [5]. Transforming growth factor-beta 1 (TGF-β1), a key profibrotic cytokine, contributes to impaired lymphatic regeneration and further exacerbates tissue stiffness and functional limitation [6]

In addition to inflammation-driven fibrosis, clinical and translational studies have demonstrated that advanced lymphedema is characterized by substantial adipose tissue hypertrophy. Pioneering work by Brorson [8] showed that long-standing lymphatic dysfunction leads to progressive fat accumulation, which becomes a dominant component of limb enlargement and is not reversible with conservative therapy alone.

This adipose tissue expansion is thought to result from chronic lymph stasis, low-grade inflammation, and altered lipid metabolism within the interstitial environment. As the disease progresses, the relative contribution of fluid decreases, whereas fibrofatty tissue increasingly determines limb volume and mechanical properties. These structural changes explain the limited effectiveness of purely fluid-directed therapies in advanced stages and provide the pathophysiological rationale for reductive surgical approaches such as liposuction [8].

3.1.4. Vicious Cycle of Pathology

The interplay among lymphatic stasis, immune activation, adipogenesis, and fibrosis establishes a self-reinforcing cycle that progressively deteriorates lymphatic function [2]. This cascade not only maintains fluid accumulation but also compromises local immunity, increases susceptibility to infections, and reduces functional capacity, which is particularly important in physically active patients [1,2]

Understanding these mechanisms underscores the importance of early intervention and targeted therapies that address both lymphatic drainage and tissue remodeling [1,6].

3.2. Conservative Treatment Approaches

3.2.1. Complete Decongestive Therapy

Complete decongestive therapy (CDT) is considered the gold standard in the conservative management of lymphedema [1,9]. CDT is a multimodal intervention consisting of manual lymphatic drainage (MLD), compression therapy, exercise, and meticulous skin care [1]. The combined approach targets both fluid reduction and long-term maintenance of lymphatic function by enhancing lymphatic transport and preventing complications such as infection and fibrosis.

Manual lymphatic drainage is a specialized massage technique designed to stimulate lymphatic flow and redirect fluid toward functional lymphatic pathways. Although widely used, evidence suggests that its additive benefit beyond compression therapy alone may be modest in some patient populations, particularly in chronic stages of the disease [10,11].

Compression therapy, delivered through multilayer bandaging or compression garments, is the cornerstone of CDT [10]. It increases interstitial pressure, reduces capillary filtration, and improves venous and lymphatic return. Sustained compression is essential for maintaining volume reduction achieved during the intensive treatment phase [9].

Exercise within CDT enhances the muscle pump mechanism, facilitating lymphatic drainage and improving functional outcomes [1]. Skin care is equally important because impaired local immunity increases susceptibility to infections such as cellulitis [1,2].

High-quality guidelines, including those from the International Society of Lymphology, recommend CDT as first-line therapy [9].

3.2.2. Compression Therapy Alone

Compression therapy as a standalone intervention remains highly effective, particularly for maintaining limb volume reduction after intensive CDT. Both compression garments and multilayer bandaging are widely used, although each approach has specific advantages and limitations [12].

Compression garments are more practical for long-term use and promote patient independence; however, their effectiveness depends heavily on proper fit and adherence [1,13]. In contrast, multilayer bandaging provides higher working pressure and may be more effective during the reduction phase but often requires professional application and may limit mobility [12].

Adherence remains a major clinical challenge. Discomfort, heat, cosmetic concerns, and difficulty in application frequently reduce compliance, ultimately affecting therapeutic outcomes. Long-term success in lymphedema management is strongly associated with consistent use of compression therapy [13].

3.2.3. Exercise Therapy and Functional Capacity

Exercise therapy is a central component of modern lymphedema management and plays a key role in preserving and improving physical function [1]. Current evidence indicates that both resistance and aerobic training are safe when appropriately prescribed and do not exacerbate limb volume in patients with lymphedema [11].

Progressive resistance training improves muscle strength, functional capacity, and quality of life, while supporting lymphatic flow through activation of the skeletal muscle pump [1,11]. Aerobic exercise enhances cardiovascular fitness, reduces fatigue, and contributes to overall physical conditioning in this population [11].

Systematic reviews and meta-analyses confirm that exercise interventions do not increase limb volume and may reduce symptom severity and perceived heaviness [11]. However, most evidence is derived from oncology-related populations, and data in athletic cohorts remain limited.

From a clinical perspective, exercise should be individualized according to disease stage, functional status, and patient tolerance, with gradual progression of intensity and volume [1]. High-intensity and sport-specific loading protocols remain under-investigated in lymphedema populations [14].

3.2.4 Pneumatic Compression Devices

Pneumatic compression devices (PCDs) are used as adjunctive therapy in lymphedema management. These devices deliver intermittent external pressure through inflatable sleeves, promoting lymphatic and venous return [1, 15].

Intermittent pneumatic compression can be particularly beneficial in patients who do not respond adequately to CDT, have limited mobility, require additional home-based therapy [1,15]. Evidence suggests that PCDs may enhance volume reduction when combined with standard therapy, although they are generally not recommended as a standalone treatment. Their effectiveness depends on proper pressure settings, treatment duration, and patient adherence [1,15,16].

3.3 Surgical Treatment Options

Surgical interventions are considered in patients with lymphedema who do not achieve satisfactory outcomes with conservative management or present with advanced disease characterized by fibrosis and adipose tissue deposition. Modern surgical approaches can be broadly divided into physiological procedures, which aim to restore lymphatic drainage, and reductive procedures, which focus on removing excess tissue volume. The selection of technique depends on disease stage, lymphatic function, and patient-specific factors [17].

3.3.1 Lymphovenous Anastomosis (LVA)

Lymphovenous anastomosis (LVA), also known as lymphaticovenular anastomosis, is a supermicrosurgical technique that creates direct connections between lymphatic vessels and nearby venules, bypassing obstructed lymphatic pathways. This procedure reduces lymphatic pressure and facilitates the drainage of lymphatic fluid into the venous system.

LVA is most effective in early-stage lymphedema, when functional lymphatic vessels are still present. Systematic reviews and meta-analyses have demonstrated significant reductions in limb volume and improvements in quality of life following LVA, particularly in patients with breast cancer–related lymphedema [18,19]. However, its efficacy is limited in advanced stages, where lymphatic vessels are often fibrotic or obliterated.

Advances in imaging techniques, such as indocyanine green (ICG) lymphography, have improved patient selection and surgical precision, further enhancing clinical outcomes [15].

3.3.2 Vascularized Lymph Node Transfer (VLNT)

Vascularized lymph node transfer (VLNT) involves the transplantation of functional lymph nodes with their vascular supply to the affected region. This technique aims to restore lymphatic function through mechanisms such as lymphangiogenesis and the establishment of new lymphatic pathways.

VLNT is typically indicated in patients with moderate to advanced lymphedema, particularly when lymphatic vessels are severely damaged and unsuitable for LVA. Systematic reviews report significant reductions in limb volume, decreased frequency of infections, and improved quality of life following VLNT [20]

Despite its effectiveness, VLNT carries potential risks, including donor-site morbidity and the possibility of inducing lymphedema at the donor site. Careful patient selection and surgical expertise are therefore essential.

3.3.3. Liposuction for Advanced Fibrosis

Liposuction, also referred to as suction-assisted lipectomy, is a reductive surgical technique used primarily in advanced-stage lymphedema characterized by fibrofatty tissue deposition. Unlike physiologic procedures, liposuction does not restore lymphatic function but instead removes excess adipose and fibrotic tissue, leading to substantial reductions in limb volume [17,19].

Pioneering work by Brorson demonstrated that chronic lymphedema is associated with significant adipose tissue hypertrophy, which cannot be reversed by conservative or microsurgical treatments alone[8]. Liposuction directly targets this pathological fat accumulation, making it particularly effective in non-pitting, late-stage disease.

Clinical studies have shown that liposuction combined with controlled compression therapy can achieve near-complete and sustained volume reduction, with long-term follow-up demonstrating minimal recurrence when compression is maintained [21,22]. Importantly, this technique does not restore lymphatic transport but compensates for lymphatic impairment through volume reduction and lifelong compression therapy.

Liposuction is therefore considered the treatment of choice in advanced fibrotic lymphedema, particularly when physiologic surgical options such as LVA are no longer feasible because of lymphatic vessel destruction [8,17,21,22].

3.3.4. Clinical Decision-Making and Treatment Algorithm

The choice of surgical intervention should be guided by disease stage and underlying pathophysiology. Current evidence supports a stage-based approach:

- Early-stage lymphedema → LVA (functional lymphatics present)
- Moderate-stage lymphedema → VLNT (lymphatic damage with residual function)
- Advanced fibrotic lymphedema → Liposuction (irreversible tissue changes)

Recent comprehensive reviews emphasize the importance of combining surgical and conservative therapies to optimize long-term outcomes [17].

3.4. Emerging and Innovative Therapies

3.4.1. Immediate Lymphatic Reconstruction

Immediate lymphatic reconstruction (ILR), also known as LYMPHA or prophylactic lymphovenous bypass, is an emerging surgical strategy aimed at preventing lymphedema at the time of lymph node dissection [7,20] This technique involves immediate anastomosis of transected lymphatic vessels to nearby venules, thereby preserving lymphatic drainage pathways.

Recent systematic reviews and clinical studies have demonstrated that ILR significantly reduces the incidence of secondary lymphedema following oncologic surgery, particularly in patients undergoing breast cancer treatment [7,20]. Preventive lymphatic surgery has gained increasing attention over the past decade, with growing evidence supporting its role in reducing long-term morbidity and improving quality of life.

However, long-term outcomes remain heterogeneous, and further randomized controlled trials are required to establish standardized protocols and confirm the durability of results.

3.4.2. Regenerative Medicine

3.4.2.1 Stem Cells

Regenerative approaches represent a promising frontier in lymphedema treatment. Stem cell-based therapies, including mesenchymal stem cells (MSCs) and lymphatic endothelial progenitor cells, have demonstrated the ability to reduce inflammation, promote tissue regeneration, and improve lymphatic function.

A systematic review and meta-analysis by Lafuente et al. [23] demonstrated that cell-based therapies significantly improve lymphatic flow, reduce edema, and enhance lymphatic vessel density in both preclinical and early clinical studies. These effects are mediated through anti-inflammatory, antifibrotic, and pro-angiogenic mechanisms.

Despite encouraging results, clinical translation remains limited because of heterogeneity in study design, cell types, and delivery methods.

3.4.2.2. Lymphangiogenesis

Therapeutic lymphangiogenesis aims to restore lymphatic function by promoting the formation of new lymphatic vessels. Key molecular pathways include VEGF-C/VEGFR-3 signaling, which regulates lymphatic endothelial cell proliferation, migration, and differentiation [3,4,24].

Emerging strategies include:

- growth factor delivery (e.g., VEGF-C),
- gene therapy,
- combined cell-based approaches.

Experimental studies indicate that enhancing lymphangiogenesis may improve lymphatic drainage and reduce fibrosis, thereby addressing the underlying pathophysiology of lymphedema rather than only its symptoms [3,24].

3.4.3. Biomaterials and Tissue Engineering

Biomaterials and tissue engineering approaches aim to reconstruct or regenerate functional lymphatic networks using bioengineered scaffolds, hydrogels, and extracellular matrix-based constructs.

Recent reviews have highlighted that combining biomaterials with stem cells and lymphangiogenic factors enables controlled regeneration of lymphatic tissue and restoration of lymphatic flow [23,24]. These strategies may overcome limitations of conventional surgery by promoting physiologic repair without donor-site morbidity.

Although still largely experimental, tissue-engineered lymphatic constructs represent one of the most promising future directions in lymphedema therapy.

3.5. Diagnostic Advances in Lymphedema

Advanced imaging techniques play an essential role in early diagnosis, staging, and treatment planning [1]. Indocyanine green lymphography enables real-time visualization of superficial lymphatic flow and allows early detection of functional abnormalities prior to clinical swelling [15].

Magnetic resonance lymphangiography provides complementary information by visualizing deeper lymphatic structures and differentiating between fluid accumulation, fibrosis, and adipose tissue deposition [14]. This is particularly relevant for surgical decision-making in procedures such as lymphovenous anastomosis and vascularized lymph node transfer [17].

Overall, modern imaging facilitates earlier intervention and more individualized treatment strategies, improving both clinical and functional outcomes[1,17]. A summary of the main conservative, surgical, and emerging therapeutic approaches discussed in this review is presented in Table 1.

Intervention	**Main mechanism**	**Clinical effects**	**Functional effects**	**Limitations**
CDT	Fluid mobilization	Volume reduction	Improved mobility	Adherence-dependent
Compression	External pressure	Volume maintenance	Symptom control	Poor long-term adherence
Resistance training	Muscle pump activation	Safe volume control	Strength improvement	Limited athlete data
LVA	Restores drainage	Reduced edema	QoL improvement	Early-stage only
VLNT	Lymphangiogenesis	Reduced infections	Functional improvement	Donor-site morbidity
Liposuction	Removes fibrofatty tissue	Major volume reduction	Improved limb mechanics	Requires lifelong compression
ILR	Preventive bypass	Reduced lymphedema incidence	Preserved function	Limited long-term evidence
Regenerative therapy	Biological restoration	Experimental	Potential future role	Lack of clinical trials

Table 1. Summary of Current and Emerging Treatment Strategies for Lymphedema

4. Discussion

4.1. Principal Findings and Interpretation

This review highlights a shift in contemporary lymphedema management from exclusive focus on limb volume reduction toward preservation of physical function and long-term functional capacity. Although complete decongestive therapy remains the cornerstone of treatment, its effectiveness may be limited in physically active individuals with higher functional demands [1,9,13].

4.2. From Volume Reduction to Functional Restoration

A key implication of the reviewed literature is the progressive shift from purely morphological outcomes (e.g., limb volume reduction) toward functional recovery. Surgical approaches such as lymphovenous anastomosis (LVA) and vascularized lymph node transfer (VLNT) improve lymphatic drainage and symptom burden, particularly in early- and mid-stage disease [17,18,25].

In advanced disease, liposuction effectively addresses fibrofatty tissue accumulation that cannot be reversed by conservative or physiologic surgical techniques alone [17,21,22].

4.3. Exercise Therapy as a Functional and Performance Modulator

Exercise therapy is one of the most clinically relevant interventions for physically active individuals with lymphedema. Current evidence demonstrates that resistance and aerobic training improve strength, functional capacity, and quality of life without exacerbating limb volume [10,11]. These effects are likely mediated through improved skeletal muscle pump activity and overall physical conditioning [1,11].

4.4. Return-to-Sport and High-Performance Considerations

Return-to-sport remains insufficiently investigated in lymphedema populations. Most available evidence derives from oncology-related cohorts rather than competitive athletes, limiting applicability to high-performance sport settings [11,14]. Main limitations include the lack of sport-specific rehabilitation protocols and performance-based outcome measures.

4.5. Integration of Surgical and Exercise-Based Rehabilitation

Optimal management likely requires integration of surgical procedures with exercise-based rehabilitation to improve both lymphatic drainage and long-term functional recovery [11,17,18].

4.6. Limitations of the Evidence Base

Despite substantial progress, several limitations remain relevant for sport-oriented interpretation of the literature. The majority of studies focus on cancer-related lymphedema, limiting applicability to athletic populations [11].

Additional limitations include:

- heterogeneity in outcome measures and study design [1]
- limited reporting of functional and performance-based endpoints
- lack of standardized assessment tools for exercise capacity and return-to-sport outcomes

These factors significantly restrict translation into evidence-based sports rehabilitation protocols.

4.7. Future Directions: Toward Performance-Oriented Lymphedema Care

Future research should prioritize functional and performance-based outcomes in lymphedema rehabilitation. Important directions include development of return-to-sport protocols, inclusion of objective performance metrics, and longitudinal studies in physically active populations [11,14]. Emerging regenerative therapies may further expand future treatment options [3,23,24].

4.8. Practical Implications for Sport Practice and Rehabilitation

Rehabilitation in physically active individuals should include gradual progression of aerobic and resistance exercise with regular monitoring of symptoms and limb volume. Progressive loading appears safe and may improve neuromuscular function and lymphatic return [11]. However, standardized return-to-sport protocols remain unavailable, highlighting the need for future sport-specific rehabilitation research.

Disclosure

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During the preparation of this work, the authors used Jenni AI for the purpose of literature synthesis, content structuring, and initial writing. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the substantive content of the publication.

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