

Review

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Review

A Narrative Review of Lymphedema Following Head and Neck Cancer Treatment

Micah K. Harris, Joshua D. Smith, Jenny Kim, Wesley Cai, Kevin J. Contrera, Steven B. Chinn, Marci L. Nilsen, Shaum S. Sridharan[†] and Matthew E. Spector^{*†}

University of Pittsburgh Medical Center, Department of Otolaryngology–Head and Neck Surgery; Pittsburgh, PA, USA

* Correspondence: spectorme@upmc.edu; Tel.: +412-864-1300

[†] These authors contributed equally to this work.

Abstract

Head and neck lymphedema (HNL) is a common complication of head and neck cancer (HNC) treatment, with upwards of 70-90% of patients suffering from this condition. Surgery and radiation, the backbones of HNC treatment, disrupt lymphatic networks through direct injury and fibrosis, leading to accumulation of lymphatic fluid in interstitial spaces. This causes swelling of external and internal structures, leading to decreased quality of life, cosmetic distress, social withdrawal, and functional deficits such as dysphagia, dysphonia, and reduced cervical mobility. Having a reliable assessment tool is key to diagnosing and monitoring HNL; however, few tools specific to HNL exist. Currently, the cornerstone of HNL treatment is conservative management with complete decongestive therapy, which shows mixed efficacy. There is a lack of surgical options as well as prophylactic interventions. Imaging of lymphatic channels is a promising modality that can help providers guide and plan personalized therapies. This paper provides a narrative review of the pathophysiology, assessment, and prevention of HNL, highlighting future directions for improvement.

Keywords: lymphedema; head and neck; cancer; survivorship

1. Significance

Lymphedema is an increasingly recognized complication of head and neck cancer (HNC) treatment. Prevalence varies considerably depending on the definition of lymphedema used, the assessment tool utilized, as well as the tumor subsite, treatment modality, and radiation dose. Rates tend to be the highest among patients undergoing multimodal therapy (often surgery with adjuvant radiation or definitive chemoradiotherapy), with estimates as high as 70-90% in this group [17,57]. Conversely, single modality therapies tend to result in lower but still meaningful rates, ranging anywhere from 10-40% [15,34]. The sequelae of head and neck lymphedema (HNL) profoundly impacts quality of life (QOL).

HNL can be separated into internal and external. External HNL refers to fluid accumulation in the subcutaneous tissue that manifests as visible swelling and skin changes. External HNL can often result in noticeable cosmetic deformities that contribute to body image disturbance, psychological distress, and subsequent social withdrawal. Furthermore, chronic swelling and secondary fibrosis of the neck lead to reduced cervical range of motion, increased tissue stiffness, and pain during functional movement. Internal HNL, by contrast, involves edema of the mucosal surfaces of the aerodigestive tract (i.e., pharynx and larynx), which can result in significant dysphagia, dysphonia, and in severe cases, airway compromise. As novel therapies continue to extend the lives of HNC patients, survivorship has become a key priority. Given the widespread impact of lymphedema following HNC treatment, a thorough understanding of the disease and its management is of

importance. This narrative review provides an overview of the modern prevention, assessment, and management of HNL.

2. Anatomy and Pathophysiology

The lymphatic system is a unidirectional network that is essential for fluid balance and immune surveillance. Protein-rich fluid from the interstitial space is drawn into lymphatic capillaries, where it is transported through a hierarchy of lymphatic vessels and filtering lymph nodes before returning to the venous circulation. Lymphatic flow is driven by extrinsic compression from surrounding musculature and intrinsic compression from smooth muscles in the vessel walls, aided by one-way valves (Figure 1).

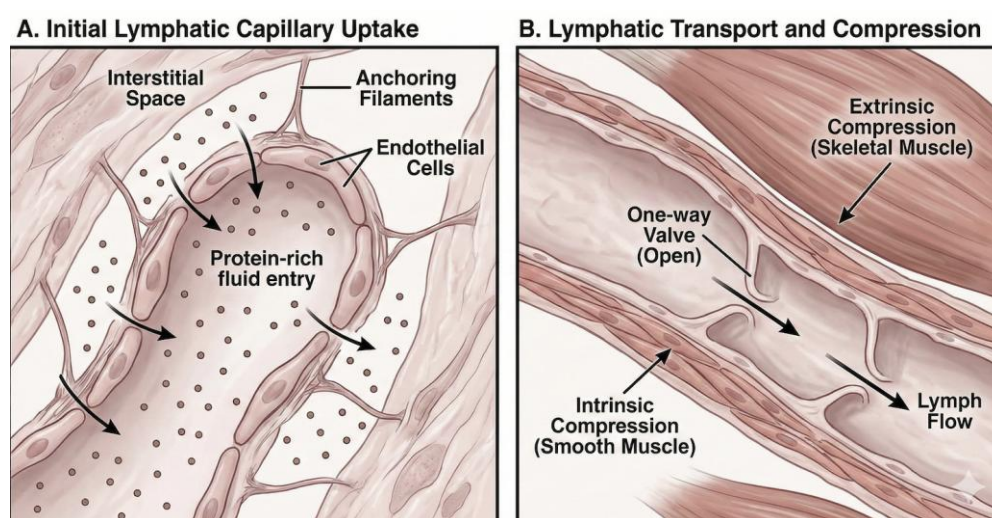


Figure 1. Mechanism of normal lymphatic uptake and transport Image created with Google Gemini. Generated on February 13, 2026.

The head and neck present unique anatomical considerations for the lymphatic system. Despite its relatively small area, the head and neck contain approximately one-third of the body's total nodal volume [1]. Broadly, these nodes can be anatomically divided by the deep cervical fascia: the superficial system drains the cutaneous skin and superficial musculature, while the deep system drains the mucosal linings of the upper aerodigestive tract [1]. On a granular level, the lymphatic network can be further subdivided into distinct territories, where specific subgroups are named according to the subsite they drain (i.e., submental). Lymphatic fluid eventually descends to the base of the neck, entering the systemic venous circulation via the thoracic duct on the left and the right lymphatic duct on the right prior to dumping into the venous circulation. A final distinction should be made for the facial and scalp lymphatic systems, which often lack one-way valves and thus permit retrograde flow [1].

Lymphedema can be defined as a pathological accumulation of fluid in interstitial tissues. In the setting of HNC treatment, secondary lymphedema often arises from a "two-hit" mechanism as a direct result of surgery and radiation (Figure 2). Surgical resection of tumors and diseased lymph nodes inevitably transects lymphatic vessels, physically severing drainage pathways. Surgical damage to surrounding musculature further reduces flow from extrinsic compression. Meanwhile, adjuvant radiation compounds this injury by causing fibrosis of surrounding tissue, constricting any remaining functional lymphatics, and simultaneously damaging the endothelial lining of the lymphatic vessels. The result of this damage is an accumulation of interstitial fluid, leading to the hallmark manifestation of swelling. Moreover, the stagnation of protein-rich lymph triggers a chronic inflammatory response characterized by dysregulation of CD4+ T cells, macrophages, and fibroblasts, leading to excess collagen deposition and adipose tissue remodeling [2,3]. These changes initiate a self-perpetuating cycle: increasing fibrosis from chronic inflammation prevents mechanical

compression necessary to shunt lymph to healthy vessels, while the failing lymphatic system remains unable to clear the accumulating fluid and inflammatory mediators [2].

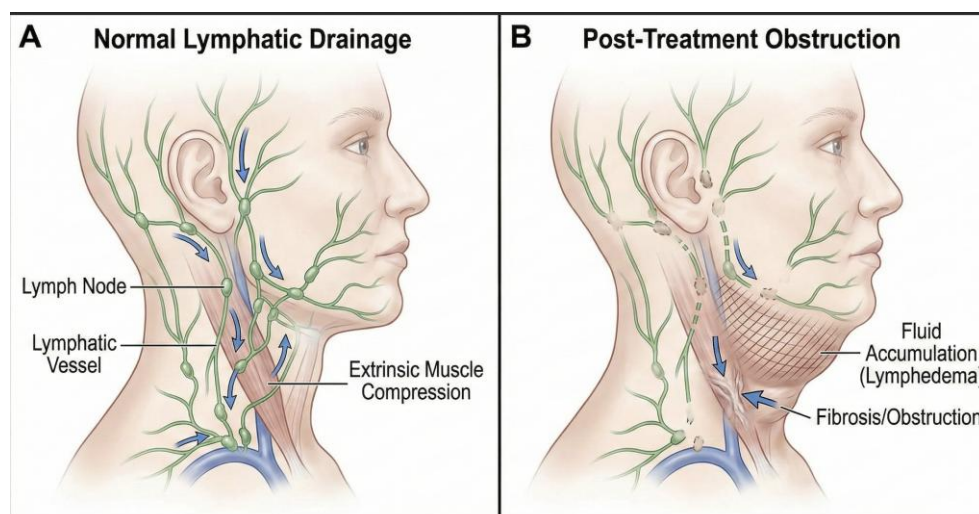


Figure 2. Patterns of normal lymphatic drainage are disrupted through surgical transection and radiation-induced fibrosis. Image created with Google Gemini. Generated on February 13, 2026.

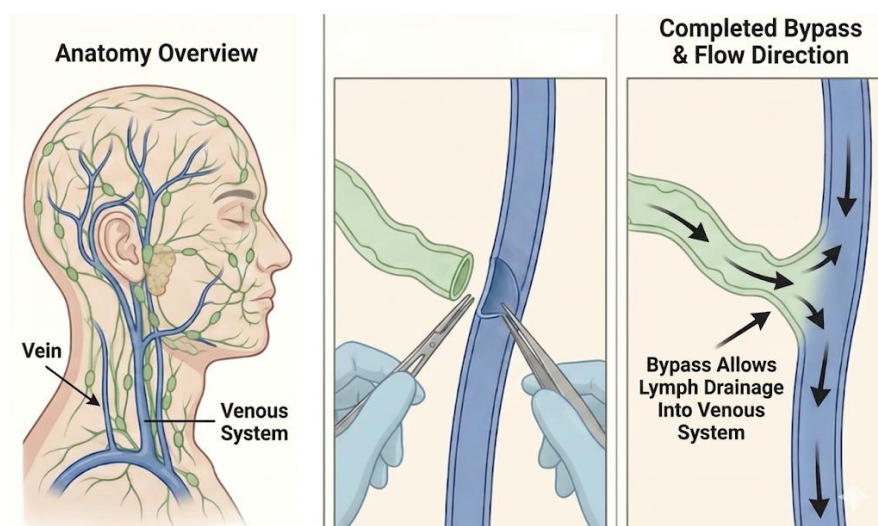


Figure 3. End-to-side anastomosis from lymphatic duct to vein for lymphovenous bypass. Image created with Google Gemini. Generated on February 13, 2026.

3. Methods of HNL Assessment and Patient-Reported Outcome Measures (PROMs)

Having a reliable assessment tool is key to diagnosing, quantifying, and monitoring HNL. However, no gold standard for assessing HNL currently exists. Broadly, assessment tools can be categorized into PROs, clinician-reported methods, and imaging-based methods.

3.1. PROMs

Patient-reported outcome measures are useful for quantifying and monitoring the impact of HNL on QOL [4]. While a variety of assessment methods exists, few are specific to HNL [5]. Generic lymphedema assessments have been applied to HNL, including the Visual Analog Scale, Wong-Baker Faces Pain Scale, Positive and Negative Affect Schedule, and Distress Thermometer [6–8]. However, these measures are not specific to the head and neck region, missing key components unique to this body site. Other PROMs that are specific to the head and neck such as the European

Organization for Research and Treatment of Cancer Quality of Life Questionnaire: Head and Neck, and the Vanderbilt Head and Neck Symptom Survey have been utilized [9,10]. While these capture symptoms unique to HNC patients, they are not specific to lymphedema. Only two PROMs have been designed specifically for HNL. The Lymphedema Symptom Intensity & Distress Survey - Head & Neck was first reported in 2012, followed by its abbreviated versions, the Head and Neck Lymphedema and Fibrosis Symptom Inventory, and the Lymphedema Symptom Intensity & Distress Survey - Head & Neck version 2.0 [11–13]. More recently, Starmer et al. published on The Comprehensive Assessment of Lymphoedema Impact in the Head and Neck (CALI-HaN) [14]. These measures address HNL-specific symptomatology including altered sensation, neck/shoulder musculoskeletal changes, head and neck function, psychosocial burden, systemic symptoms, and site-specific swelling.

3.2. Clinician-Reported Assessments

Assessments by trained clinicians hold the advantage of greater standardization than PROMs, allowing for more sensitive diagnosis and more consistent tracking of HNL. Broadly, these measurements can be categorized as being focused on external versus internal lymphedema. Popular measurements based on external appearance include the American Cancer Society Lymphedema of the Head and Neck Staging Criteria, the MD Anderson Cancer Centre Head and Neck Lymphedema Rating Scale, and the Head and Neck External Lymphedema and Fibrosis Grading Criteria [15–17]. The National Cancer Institute has also published a patient-reported outcomes version of the common terminology criteria for adverse events (PRO-CTCAE) that includes lymphedema, though this is not specific to HNL [18,19]. These scales require the clinician to take into account several standardized features rather than a general impression. For internal HNL, scales are based solely on appearance on laryngoscopy. The most widely recognized is the Revised Patterson Edema Scale, which requires the clinician to estimate the amount of edema at laryngeal subsites [20]. However, it should be noted that while these scales have been validated, they remain inherently subjective and variable due to their reliance on human observers. Future studies may benefit from integrating clinician-reported and PROMs to create a comprehensive score.

3.3. Imaging and Emerging Modalities

Though the use of medical devices and technology to diagnose and monitor lymphedema remains in experimental stages, they hold the potential to reduce the subjectivity inherent to clinician assessments. Digital photographs have been used to create a 3D profile of the head and neck, allowing for objective calculations of volumetric changes representative of external lymphedema [21]. The ability to quantify HNL using established imaging modalities such as ultrasound, CT scans [22], and MRI scans have also been examined, though these are limited by feasibility, cost, and radiation exposure [23]. The MoistureMeterD is a novel device that measures the tissue dielectric constant (an index for local tissue fluid content), and has been shown to discriminate between HNL and healthy controls [24]. Molecular markers of lymphedema such as microRNAs have been linked to lymphedema and may eventually evolve into more sensitive biomarkers [25].

Perhaps the most promising modality that has emerged is lymphatic imaging. Imaging of the lymphatic channels allows for both anatomic visualization and functional assessment of lymphatic drainage pathways [26]. By localizing lymphatic drainage pathways to target, providers may personalize therapies and enhance treatment efficacy. Lymphoscintigraphy requires intradermal and/or subcutaneous injection of radiolabeled tracer (typically ^{99m}Tc), which is then taken up by the lymphatic system and imaged by a gamma camera at several timepoints. While a functional “map” of lymphatic drainage pathways is possible, it is limited by poor spatial resolution [26]. Magnetic resonance lymphangiography provides higher spatial resolution and 3D imagery, but its reliance on MRI scanners results in high costs, long scan times, and limited availability [27]. Near-infrared fluorescence/indocyanine green (ICG) lymphography is a rapidly emerging modality that is accessible, minimally invasive, and radiation-free [28,29]. In this technique, ICG is injected

intradermally and a near-infrared laser is used to map the lymphatic system in real-time and with high resolution. Though limited by its depth penetration (typically 1-2 cm from the skin surface), providers have successfully used this map to guide conservative therapies and plan surgical interventions [30].

4. Risk Factors for HNL

Understanding the risk factors of HNL is essential for identifying and targeting modifiable variables. While surgery and radiation are often unavoidable, optimizing these treatments to ameliorate long-term morbidity, without sacrificing disease control, is very pertinent.

4.1. Surgical

Intraoperative transection of lymphatic drainage pathways is often the primary driver of HNL. While neck dissection is often necessary to remove lymph nodes harboring disease, it unavoidably damages the lymphatic architecture. The risk of HNL increases with the extent of neck dissection; more comprehensive and bilateral neck dissections carry a higher risk of HNL [31]. The removal of level Ib and II nodes are particularly impactful, as these serve as primary drainage pathways for the face and oral cavity [32]. Furthermore, failure to preserve venous structures – the terminal sites for lymphatic drainage – can exacerbate postoperative HNL. Interestingly, in a study by Raad et al., preserving the facial vein was associated with a significantly decreased risk of developing lymphedema (odds ratio 0.113), highlighting the potential of identifying modifiable surgical steps in order to reduce HNL [33].

4.2. Radiation

Radiation-induced tissue injury represents a second major insult that leads to late-onset, progressive lymphedema [34]. The underlying mechanism involves a complex cascade of proinflammatory cytokines, such as TGF-beta, which drive fibrosis and subsequent constriction of lymphatic channels [2]. Notably, radiation may have a greater impact on the development of lymphedema than surgery, with Nilsen et al. demonstrating a 3.46 times higher risk in those who received nonsurgical treatment versus surgery alone [35]. The dose of radiation is directly related to the risk of HNL, with specific dosimetric thresholds found to be predictive [36]. For example, Rogacki et al. demonstrated that a dose of V30 >50% strongly predicted external lymphedema, while a laryngeal dose of V45 >50% predicted internal lymphedema [37]. Along these lines, many studies have investigated the safety of response-adjusted adjuvant RT reduction [38]. However, HNL is rarely studied as an endpoint, despite the direct relationship with radiation. Finally, it is important to recall that the addition of concurrent chemotherapy as a radiosensitizer can further exacerbate damage to healthy lymphatic endothelium [39].

4.3. Other

Other risk factors include obesity, in which excess adipose tissue promotes chronic inflammation and exerts mechanical pressure that impairs contractility of lymphatic capillaries [40]. Recurrent skin infections such as cellulitis may also lead to a vicious cycle through which lymphedema predisposes patients to infection, and each subsequent infection causes worsening scarring of lymphatic endothelium [41]. Other co-morbidities include advanced age, chronic venous insufficiency, and smoking, all of which impair microvascular healing capabilities [41].

5. Treatments for HNL

Treatments options for HNL are limited and vary in their efficacy. Broadly, these can be categorized into conservative, medical, and surgical. Notably, current therapies are reactive, occurring after the development of lymphedema, whereas there is a noticeable lack of preventative

interventions. A second major consideration is that while current interventions have demonstrated efficacy for treating external lymphedema, options of internal lymphedema remain limited.

5.1. Conservative Interventions

Conservative interventions represent the most widely used treatment for HNL. Historically, manual lymphatic drainage was the first-line therapy for lymphedema, in which guided, light-pressure massage redirects stagnant lymph from congested areas toward functioning drainage basins [42]. More recently, complete decongestive therapy (CDT) has become the cornerstone of conservative management. CDT builds on manual lymphatic drainage, adding the use of compression garments, skin and nail care, and decongestive exercises (e.g., neck rotations, shoulder shrugs to encourage muscle-driven lymphatic flow) to optimize results [42,43]. More recent studies have sought to enhance CDT with technologies such as advanced pneumatic compression devices [44]. As many as 60% of patients will see measurable improvement with CDT, though this leaves a significant number of poor responders [45]. Moreover, CDT does not address the deep lymphatic system responsible for internal lymphedema, which often has the greatest impact on dysphagia, speech, and breathing [46]. Nevertheless, CDT remains the most evidence-based conservative intervention for HNL and should be pursued when feasible.

5.2. Pharmacological Interventions

No FDA-approved medications currently exist for lymphedema. The use of orally administered sodium selenite has been investigated, though the only RCT by Zimmermann et al. found no difference in neck lymphedema compared to placebo at two weeks post-treatment [47]. Leukotriene B4 has been targeted for its role in chronic inflammation, with small scale trials showing moderate success [48,49]. However, the evidence for pharmacologic therapy remains weak overall, with no medications currently being used in clinical practice.

5.3. Surgical

Surgical interventions to improve lymphedema represent a promising and exciting avenue. Current interventions include lymphovenous anastomosis, vascularized lymph node transfer, and liposuction. Liposuction addresses the adipose tissue remodeling and accumulation characteristic of lymphedema [50,51]. While it provides volume reduction, the change is temporary and does not address the underlying pathology. Lymphovenous anastomosis is achieved by performing supermicrosurgery to anastomose submillimeter lymphatic vessels to neighboring veins, creating a bypass for lymphatic drainage [30]. In vascularized lymph node transfer, healthy lymph nodes are harvested along with their own artery and vein, and transferred to the affected area. Case reports within head and neck have shown impressive reductions in lymphedema following lymphovenous bypass as well as free vascularized lymph node transfer [52–54]. Additionally, depending on where in the neck the surgery is performed, lymphovenous bypass can address internal lymphatic systems, a major limitation of conservative therapy [55,56].

However, these techniques are highly complex and limited to surgeons with extensive microvascular reconstruction experience. They rely heavily on preoperative imaging to identify and address the correct pathway(s), which may benefit from further investigation within head and neck. Given the rarity of these cases, standardization of patient selection, planning, and surgical technique have much room to grow [56]. It is notable that current surgical approaches for HNL are reactive, only occurring once lymphedema has manifested. Despite the extent of surgery being directly related to lymphedema development, intraoperative decision-making has rarely been investigated. Immediate lymphatic reconstruction, performed at the time of initial surgery, has been heavily investigated within breast surgery and has shown benefit, though the same has not been applied to head and neck cancer. Raad et al. provided the only investigation into the relationship of intraoperative vein preservation and HNL, demonstrating value in facial vein preservation [33].

Future studies should continue to investigate methods of intraoperative lymphatic pathway preservation that may prevent the development of HNL without sacrificing disease control. Until the benefits of these emerging surgical methods are more thoroughly investigated, surgeons may consider preserving lymphatic architecture and nodal packets when oncologically feasible. Moreover, following response-adapted RT protocols may reduce HNL without compromising disease control.

6. Implications and Future Directions

Despite affecting over 70% of HNC survivors, HNL remains an unresolved issue that significantly impacts quality of life. Current management is hindered by a lack of standardized assessment tools and surveys for quantifying and tracking disease progression. Moreover, a critical gap exists in treatment options. While conservative therapies such as CDT remain the sole standard-of-care option, nearly half of patients fail to see improvement, and internal lymphedema is not addressed, leaving patients with chronic functional deficits in swallowing and speech. Furthermore, contemporary interventions are largely reactive, initiated only after HNL has declared itself. Future studies may pivot toward prophylactic therapies. A promising avenue for this may involve changes in intraoperative decision making, by which critical lymphatic and venous structures are preserved without sacrificing disease control.

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Abbreviations

The following abbreviations are used in this manuscript:

CDT	Complete decongestive therapy
HNC	Head and neck cancer
HNL	Head and neck lymphedema
ICG	Indocyanine green
PROM	Patient-reported outcome measure
QOL	Quality of life

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