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Lymphedema of the Head and Neck—Where Do We Stand and Where We Are Headed

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Abstract: Great advancements have been made in the management of lymphedema of the extremities with lymphatic surgery. However, lymphedema of other regions, including head and neck, has remained neglected. Recent discovery of lymphatic system in the brain and the communication between intracranial and paracranial lymphatic systems has drawn attention to the head and neck lymphatics. Lymphedema of the head and neck region can result from inherent abnormality of the lymphatic system (primary) or be caused by accidental or iatrogenic injury to lymphatics (secondary). The head and neck contain a large network of lymphatic tissue. They may be affected by direct tumor infiltration, surgical resection of tumors and surrounding cancer tissue, and/or radiotherapy. Proper screening and counseling of patients before facial aesthetic procedures may avoid managing the distress of lymphedema postprocedure. Progression of head and neck lymphedema (HNL) can lead to chronic inflammatory, fibrosclerotic, and fibrofatty deposition, resulting in permanent deformity and disability. Patients may experience functional impairment, including skin changes, pain, range of motion limitations, contracture, dysphagia, dysarthria, dyspnea, and trismus, all leading to reduced quality of life. Despite these known disabilities, HNL is underdiagnosed due to a lack of awareness about this entity and of tools available for measuring internal or external swelling. The authors' article comprehensively reviews the current diagnostic methods and management strategies and what lies ahead.

Key Words: Head and neck cancer, head and neck lymphedema, lymphatic system, lymphedema

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Lymph vessels play a vital role in the disposal of metabolic wastes and removal of excess interstitial fluid as well as transporting larger molecules such as hormones and lipids. The lymphatic system plays a role in immune surveillance and processing antigens, and lymph nodes act as a sieve for abnormal cells, including infective agents. Dysfunction of the lymphatic system, whether primary or acquired, is marked by the accumulation of protein-rich fluid in the interstitium,[1] which induces cellular proliferation and inflammation resulting in thickening and fibrosis of lymphatic vessels and surrounding tissue. Lymphedema presents as chronic swelling of the affected region—resulting in restricted range of motion in the joints, heaviness, pain, skin changes, and recurrent cellulitis.[1,2]

Great advancements have been made in the management of lymphedema of the extremities with lymphatic surgery. However, lymphedema of other regions, including head and neck, has remained neglected. Recent discovery of lymphatic system in the brain and the communication between intracranial and paracranial lymphatic systems has drawn attention to the head and neck lymphatics.

Lymphedema of the head and neck region can result from inherent abnormality of the lymphatic system (primary) or be caused by accidental or iatrogenic injury to lymphatics (secondary). HNL is an increasingly recognized complication of head and neck cancer (HNC) or its ablation, with a prevalence of 75% to 90% in HNC survivors.[3–5] Head and neck contain a large network of lymphatic tissue. They may be affected by direct tumor infiltration, surgical resection of tumors and surrounding cancer tissue, and/or radiotherapy.[6] Patients with a low baseline reserve of lymphatic function can manifest lymphedema following minor trauma or minor surgical procedures like lower blepharoplasty, facelift, or energy-based facial rejuvenation procedures. Proper screening and counseling of patients before facial esthetic procedures may avoid managing the distress of lymphedema postprocedure.

In the early phase of onco-ablation, resultant local inflammation may overload the residual lymphatics, manifesting as tissue edema. Swelling may predominantly be internal (oropharyngeal/nasopharyngeal) or external (face and neck skin and subcutaneous tissue) or both.[7] In the early stages, HNL may present vaguely as tightness or heaviness without visible edema or present as changes in voice, difficulty in swallowing, etc, due to mucosal edema.[8] Further, orbital/periorbital edema may affect vision.

Progression of HNL can lead to chronic inflammatory, fibrosclerotic and fibrofatty deposition resulting in permanent deformity and disability.[9] Patients may experience functional impairment including skin changes, pain, range of motion limitations, contracture, dysphagia, dysarthria, dyspnea, trismus, all leading to reduced quality of life.[9] Despite these known disabilities, HNL is underdiagnosed due to a lack of awareness about this entity and of tools available for measuring internal or external swelling. Our article comprehensively reviews the cur-

rent diagnostic methods and management strategies and what lies ahead.

ASSESSMENT OF HEAD AND NECK LYMPHEDEMA

Diagnosis of HNL is based on a thorough clinical history and physical examination supplemented with tape measures, tissue bioimpedance, laryngoscopy-assisted internal lymphedema evaluation, and different imaging techniques.[3] Various clinician rating and symptom scoring systems have been introduced to quantify the clinical findings. Clinician rating Foldi Scale published in 2010 was the earliest scale to be applied to patients with HNL, rating lymphedema as 0 to 3 stages based on reversibility of external swelling and skin changes. The MD Anderson Cancer Center HNL severity rating scale splits the original Foldi stage 1 (reversible swelling) into 2 substages: (1) stage 1a, accounting for edema which may be visible but not appreciable on pitting, and (2) Stage 1b, when swelling is both visible and palpable as pitting.[6,7] For symptom scoring, Head and Neck–External Lymphedema and Fibrosis (HNLEF) Scale has been validated. For quantifying external edema, MD Anderson Cancer Center employs a set of 9 point-to-point tape measurements of the face, as well as 2 facial circumferences, and 3 neck circumferences.[7] Tape measurements appear to be helpful; however, identification of facial landmarks may be difficult in the setting of severe lymphedema, obesity, and in patients with head and neck reconstruction. In addition, accuracy may be affected by patient positioning, facial movements, and tape tension. Thus tape measurements may not be as useful when only taken once or when performed by different operators.[6,7]

Although internal swelling is more common and may or may not be accompanied by appreciable external swelling, it easily goes unnoticed. Assessment of internal lymphedema requires laryngoscopy. The Patterson Scale was developed[7] to evaluate internal lymphedema. It is based on the severity of edema in 11 structures and 2 spaces within the nasopharynx. Since its original publication, a Revised Patterson Scale has been published by Starmer et al,[3] abbreviating the list of evaluated sites to make it less cumbersome.[7]

While clinician-reported rating scales are time and cost-effective, they are subjective and liable to inconsistent application. More objective measures like imaging and bioimpedance have been used to improve the reliability of diagnosis and longitudinal outcomes tracking. MoistureMeterD device has been used to estimate local tissue fluid content by measuring the tissue dielectric constant.[3,7] This technology has been proven to demonstrate a high level of discrimination between patients with HNL and healthy controls.[10] Another promising technology is a three-dimensional volumetric analysis using predetermined reference points on the face and neck to provide a quantification of the volume of soft tissue lymphedema.[10] Imaging modalities for HNL include ultrasound and computed tomography (CT). Ultrasound has been utilized for the measurement of skin-to-bone distance, skin and subcutaneous tissue thickness, and resistance to compression.[7,11] Computed tomography of the head and neck is a useful diagnostic test for both external and internal HNL. Despite radiation exposure and higher costs, CT is highly accurate for visualizing and quantifying soft tissue changes due to lymphedema. Various assessment tools have been published for CT with emphasis on different radiological parameters. Computed tomography Lymphedema and Fibrosis Assessment Tool assesses fat stranding in 5 defined superficial locations, as well as internal measurements of soft tissue change.[7,12,13] Despite their availability, HNL image-based diagnosis is not routinely performed. Furthermore, diagnosis based on volume is faulty due to fluctuations throughout the day and with changes in position. Near-infrared fluorescence lymphatic imaging (NIRFLI), which can directly image the anatomy and function of the lymphatic vessels using small volumes of Indocyanine green fluorescent dye injection, can be more reliable, as seen in extremity lymphedema. However, it remains underutilized for head and neck lymphedema.[14]

Patient-reported outcome measures, including pain or distress-related scales, appearance-related scales, and functional scales, have been utilized as generic assessments for patients with HNL. However, the majority of assessments are not specific to HNL patients and are unable to quantify the physical and psychological burden of HNL.[7] The Lymphedema Symptom Intensity and Distress Survey—Head and Neck is the only patient-reported outcome measure designed specifically for HNL. Lymphedema Symptom Intensity and Distress Survey—H&N (head and neck) addresses 6 domains of symptoms present in these patients: altered sensation, neck-shoulder, musculoskeletal/skin, alterations in head and neck-specific functional, psychosocial symptoms, systemic symptoms, and site-specific swelling.[7] While patient-reported outcome measures are useful for quantifying the impact of patients' symptoms on quality of life and for longitudinal outcomes tracking after treatment, they are not sufficient for diagnosis of lymphedema.

Treatment—Nonsurgical

Conservative treatment of lymphedema focuses on the promotion of fluid drainage using complete decongestive therapy (CDT). Complete decongestive therapy consists of 2 stages: (1) reductive followed by (2) maintenance.[1,8,15] This therapy focuses on reducing volume through multiple modalities, including manual lymphatic drainage, compression therapy, skincare, and exercise.[1,16,17] Manual lymphatic drainage is a form of soft-tissue massage that stretches the initial lymphatics and increases contractility, allowing lymphatic fluid to move away from damaged lymphatic vessels to alternative drainage basins. Manual lymphatic drainage is reported to be effective in reducing edema volume in combination with compression therapy. Compression therapy uses short-stretch bandages to create effective gradient compression. Exercises combined with compressive bandaging enhance the movement of lymph to adjacent areas with intact drainage.[8,17]

Benefits of compression therapy are often limited by patient compliance and other barriers to self-care, such as obesity, mobility, occupation, and caring responsibilities. To assist patient compliance, an advanced pneumatic compression device (APCD) has become available.[15,18] Pneumatic compression devices have one or more pneumatic cuffs that inflate and stimulate muscle contraction to promote lymphatic drainage. Devices offer variable pressures and cycle times.[17] In 2016, APCD was FDA-approved specifically for the management of HNL.[15,18,19] Since its approval, multiple studies have been published. Investigators have reported a significant reduction in composite measurements of the face and neck following APCD treatment.[15,19] In addition, patients reported that the use of the device decreased soft tissue symptoms such as heaviness and tightness. Further, APCD decreased neurological symptoms, including numbness, tingling, and "pins and needles" sensations. The proposed mechanism of decreased symptoms is that the device decreases pressure on the nerves and improves blood supply to affected tissues.[19] Reports have also noted improvement in swallow function. It should be noted that these studies

were funded by the company that makes the device. Therefore, further studies are warranted to ascertain efficacy. In addition, further studies are warranted to determine the effects of treatment in conjunction with CDT, optimum duration of treatment, and longitudinal outcomes of treatment.

Treatment—Surgical

Advances in microsurgical techniques have allowed for surgical treatment of lymphedema of the extremities. Early operative intervention has been found to not only delay disease progression but also reverse disease pathogenesis in some cases.[20,21] Lymphedema surgery for extremities is categorized into debulking and physiological procedures. Debulking procedures remove excess skin and subcutaneous tissue from the affected area to decrease volume, improve functional status, and facilitate CDT.[22] Physiological procedures restore or augment lymphatic drainage. These include lymphaticovenular anastomosis (LVA)/bypass, vascularized lymph node transfer (VLNT), vascularized lymph vessel transfer, and lymph node-to-vein anastomosis (LNVA).[20] Lymphaticovenular anastomosis involves utilizing a supermicrosurgical technique to form an artificial connection between a patent lymphatic vessel and adjacent venules to redirect lymphatic flow. This permits lymph to bypass obstructed vessels.[23] Lymphaticovenular anastomosis has been shown to be effective in the reduction of volume in early stages of lymphedema, but is not sufficient in the setting of irreversible tissue fibrosis.[23] Vascularized lymph vessel transfer, the transfer of a vascularized lymph node to an area of impaired lymphatic flow, is commonly used for moderate to severe lymphedema.[20,23–25]

Similar procedures have been used for HNL targeting external swelling. The prognosis of patients with HNL is expected to be superior as compared with extremity lymphedema due to the favorable effect of gravity on head and neck lymph drainage. In addition, venous reflux and venous hypertension may not be encountered as commonly, except in cases where the internal jugular vein was ligated for cancer ablation. Lower eyelids, cheeks and neck are the most commonly affected areas in patients with noticeable external swelling. For patients with swelling predominantly in the anterior neck, submental liposuction has been used and shown to improve quality of life and patients' self-perception.[26,27] As physiological procedures, both LVA and LNVA have been successfully used, as shown in various case reports, to improve periorbital and cheek swelling. Lymphatics have been mapped using indocyanine green lymphography and the anastomosis was performed in the preauricular and/or submandibular regions.[25,28–30]

We were unable to find any articles reporting the use of VLNT or vascularized lymph vessel transfer. Tissue transfers, in general, are frequently used as a reconstructive tool for skin/mucosal/bone defects after HNC ablation. Vascularized lymph node transfer performed for lymphatic restoration would be a more invasive undertaking and could result in deformity in the patient due to the flap volume.

DISCUSSION

Head and neck lymphedema is now gaining its long due attention, mainly in patients after HNC ablation. Appreciation of this condition in non-cancer scenarios remains lacking. As HNC survival continues to improve, the focus of care is shifting from mortality reduction to morbidity reduction, ensuring a good quality of life for cancer survivors. Lymphedema of the head and neck can be quite disabling, affecting basic functions like speech and swallowing. Hence, prompt intervention using a combination of nonsurgical and surgical strategies is well-indicated. Liposuction, LVA, and LNVA are all minimally invasive procedures and can be performed under general or local anesthesia. As physiological bypass procedures still have a theoretical risk of causing metastasis, patient selection criteria in terms of time duration from onco-clearance, type, and grade of primary cancer etc, will have to be determined.

Cognitive disability in these patients with HNL is recognized and is causally linked to the use of chemotherapy. With the recent discovery of a lymphatic system in the brain and the imaging studies confirming the drainage of these lymphatics to the cervical lymph nodes, it is logical to suspect that cervical lymph node ablation directly contributes to cognition damage in these patients. Hence, a systematic study of cognition change after head and neck lymphatic surgery in this patient group will be of great value.

LYMPHEDEMA: CME QUESTIONS

(1) Lymphedema is characterized by:

Acute swelling
Chronic swelling
Swelling limited to extremities
Association with renal impairment

(1) Head and neck lymphedema is noted in:

< 10% of HNC survivors
50% of HNC survivors
75% of HNC survivors
Almost 90% of HNC survivors

(1) Diagnosis of HNL is primarily based upon:

Ultrasound
Magnetic resonance imaging scans
CT scans
History and physical examination

(1) The only patient-reported outcome measurement specifically for HNL is:

Lymphedema Symptom Intensity and Distress Survey— Head and Neck
Distress-related scales
Appearance-related scales
Pain-related scales

(1) Assessment of Internal HNL is accomplished by:

MD Anderson Rating Scale
Patterson Scale*
HNLEF
Foldi Scale

(1) MoistureMeterD

Demonstrates a high level of discrimination between patients w/ HNL and controls*
Measures change in edematous surfaces
Quantifies volume of soft tissue lymphedema
Provides direct imaging of head and neck lymphatics

(1) CDT consists of 2 stages:

Inductive followed by restrictive
Constructive followed by inductive
Reductive followed by maintenance
Maintenance followed by conductive

(1) Compression therapy:

Allows lymphatic fluid to move away from damaged lymphatic vessels to intact drainage sites
Is ineffective
Benefits obese patients
Cannot be coupled with exercise

(1) Debulking procedures for HNL include:

SAL and Charles procedure
Compression therapy
Split thickness skin grafts
Fascio cutaneous flaps

(1) The mainstay of surgical management of HNL is:

LVA
VLNT
QRS
SRT

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