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Reconstructive

Lymphovenous Anastomosis for the External and Internal Types of Head and Neck Lymphedema: A Case Series and Preliminary Clinical Results

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Background: Head and neck lymphedema (HNL), including external and internal types, could be a possible consequence for patients who have received neck dissection and radiotherapy for head and neck cancer. Initially, the common presentations are heaviness or tightness, followed by swelling in appearance, or difficulty speaking and swallowing in internal edema cases. Lymphovenous anastomosis (LVA) is an established approach to treat extremity lymphedema. We hereby present our preliminary experience in using LVA to treat HNL.

Methods: Between March 2021 and January 2024, six patients with HNL were treated with LVA via a preauricular or submandibular incision of the obstructed side. Lymphedema Symptom Intensity and Distress Surveys—Head and Neck (LSIDS-H&N) were used for evaluation. In addition, for the external type, MD Anderson Cancer Center Head and Neck Lymphedema (MDACC HNL) rating scale was used for evaluation. For the internal type, Swallowing Quality of Life was used for evaluation.

Results: With an average follow-up period of 15.4 ± 15.9 months, LSIDS-H&N improved from 1.11 ± 0.54 to 0.44 ± 0.66 ($P = 0.02$). For patients with the external type, within an average follow-up period of 15 ± 16.1 months, the MDACC HNL rating scale improved from level 2 to 0 or 1a ($P = 0.008$). For patients with the internal type, within an average follow-up period of 21 ± 17.3 months, Swallowing Quality of Life improved from 130.5 ± 9.2 to 151 ± 19.8 ($P = 0.5$).

Conclusions: Based on our preliminary results, LVA could be a potential solution to both external and internal HNL. *(Plast Reconstr Surg Glob Open 2024; 12:e5872; doi: 10.1097/GOX.0000000000005872; Published online 5 June 2024.)*

INTRODUCTION

Head and neck lymphedema (HNL) is not an uncommon complication in head and neck cancer patients after receiving neck lymph node dissection or radiation therapy. According to a prospective study by Ridner et al, the incidence of HNL could be as high as 90% among head and neck cancer survivors.[1] However, a retrospective study based on an integrated US healthcare database showed that only 6.5% of head and neck cancer survivors were diagnosed as HNL, and merely 3% of head and neck cancer survivors received lymphedema treatment, implying that HNL was underdiagnosed and undertreated.[2] The first-line therapy for HNL, according to the American Cancer Society head and neck cancer survivorship care guideline, is manual lymphatic drainage (MLD).[3] Currently, the most commonly used treatment for HNL is complete decongestion therapy (CDT), including MLD, customized compression garments, physical exercise, and skin care.[4] However, the financial and time burden associated with frequent MLD, and compliance of compression garments remain a major barrier for numerous patients who seek alternative therapies.

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Lymphovenous anastomosis (LVA) is an established method to treat extremity lymphedema.[5,6] However, only a few studies reported using LVA to treat HNL.[7–9] This study aimed to report our preliminary experiences using LVA to treat HNL. Additionally, HNL can be categorized into two types: external and internal. Patients with the internal type of HNL could have difficulties swallowing or speaking. To our knowledge, this is the first report using LVA to treat the internal type of HNL.

Takeaways

Question: Can lymphovenus anastomosis (LVA) be used to treat head and neck lymphedema (HNL), either the external or internal types?

Findings: A retrospective study on six patients who received LVA for HNL treatment showed positive results for both external and internal types of HNL.

Meaning: For patients with HNL, LVA could be a potential method of treating both external and internal HNL.

PATIENTS AND METHODS

This retrospective study was approved by the Research Ethics Committee of National Taiwan University Hospital (202310092RINC). From March 2021 to January 2024, a total of six patients who had persistent HNL received lymphovenous anastomosis (Table 1). For the patients with persistent HNL, the first step of evaluation was to rule out recurrent cancer. Ultrasonography for soft tissue, computed tomography (CT) scan, or magnetic resonance imaging are all viable options for evaluating tumor status. Once the clearance of the tumor was confirmed, lymphoscintigraphy could be used to assess the lymphatic drainage. A small volume of 74MBq Tc-99m phytate (0.2 mL) was subcutaneously injected between the eyebrows. Planar images of head and neck regions were acquired using a dual-head gamma camera single photon emission computed tomography with low-energy high-resolution collimators (Symbia Intevo 6, Seimens, Germany). Patients were advised to rub the injection site immediately after injection. Early dynamic planar images were taken 5 minutes after the injection of radiopharmaceuticals. Delayed planar and subsequent single photon emission computed tomography images were obtained 90 minutes after the injection of radiopharmaceuticals (Fig. 1). Following the confirmation of impaired lymphatic drainage, appropriate assessment methods were used to evaluate the severity of HNL based on the type of either external or internal edema. The classification of edema as external or internal was primarily based on the symptoms and signs presented by patients. In contrast to an external swelling, patients with the internal type of HNL may experience challenges with swallowing or speaking. The patients diagnosed with the internal type in our case series were also confirmed by ear, nose, and throat specialists, using an endoscope. Lymphedema Symptom Intensity and Distress Surveys—Head and Neck (LSIDS—H&N) was used for both types of HNL.[10] In addition, for external edema, MD Anderson Cancer Center Head and Neck Lymphedema (MDACC HNL) rating scale was used.[11] For internal edema, Swallowing Quality of Life (SWAL-QOL) was also used.[12,13] Before the LVA surgery, no other methods of treatment were implemented, such as compression garments or MLD.

Surgical Techniques

The patient can be placed in either a supine or lateral position. If the patient had a short neck or wide shoulder, the shoulder could become a hindrance for placing a surgical microscope if a lateral position was chosen. If the patient did not have any cervical spine problems, the head could be gently rotated to a lateral position while the patient was in the supine position. A 2-hour interval of rotating the neck would not result in significant postoperative sprain or discomfort. Due to cosmetic concerns in the head and neck area, the choice of incision locations was limited. Moreover, based on an anatomical study by Pan et al, the superficial lymphatic drainage of the head and neck goes through the preauricular area.[14] Therefore, the preauricular or its downstream submandibular area could be an ideal place for identifying lymphatic ducts and leading to inconspicuous scars (Figs. 2 and 3). Based on the results of preoperative lymphoscintigraphy, 0.1–0.2 mL ICG was injected at the obstructed side of the temporal area,[15] and linear or splash ICG pattern could be identified around preauricular and submandibular areas (Fig. 2). A 3- to 4-cm incision was made over either the preauricular or submandibular area. With the help of a surgical microscope, lymphatic ducts (approximately 0.3–0.5 mm) or lymph nodes could be identified under the superficial

Table 1. Characteristics of Patients with Head and Neck Lymphedema (n = 6)

Patient No.	Age	Sex	Comorbidities	Cause and Timing of HNL Diagnosis	Type of HNL	No. LVA
1	63	M	Hypertension Diabetes	Right tongue cancer, T2N0 s/p wide excision and neck dissection, postoperative 2 months	External	3
2	43	F	Hypothyroidism	Lymphoma, nasal type, stage IIE, s/p CCRT, post CCRT 1 month	Internal	1
3	51	M	Hepatitis A	Oropharyngeal cancer, T1N2bM0, s/p excision and CCRT, post CCRT 1 month	External and internal	1
4*	36	M	Nil	NPC, T3N1M0, stage III, s/p CCRT, post CCRT 1 month,	External	1
5	50	M	Diabetes	NPC, T1N2M0, stage III, s/p CCRT, post CCRT 4 months	Internal	1 (end to side)
6	53	M	Gastric ulcer	Hypopharyngeal cancer, T2N2M0, stage IVA, s/p CCRT, post CCRT 1 months	Internal	1

*The patient had LVA twice and LNVA once for recurrent HNL.
HNL, head and neck lymphedema; LVA, lymphovenous anastomosis; CCRT, concurrent chemoradiotherapy; NPC, nasopharyngeal cancer.

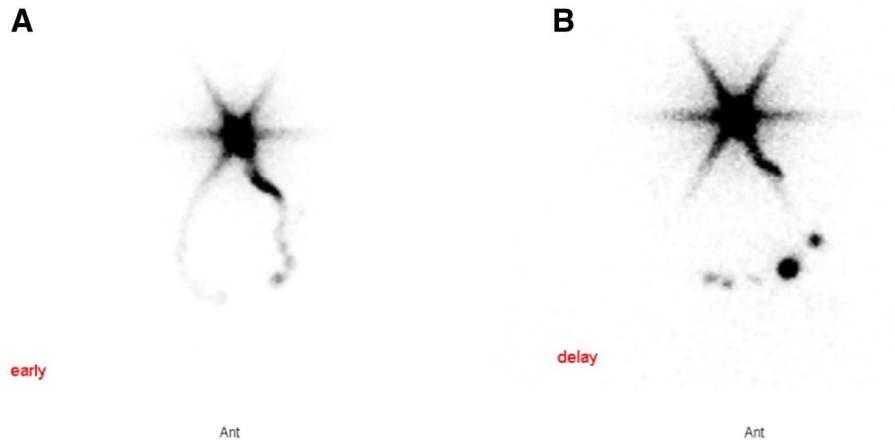

Fig. 1. An example of head and neck lymphoscintigraphy in a 55-year-old man with underlying stage IV hypopharyngeal and oropharyngeal cancer treated with surgery and concurrent chemoradiotherapy. Swelling of the right face was reported 5 months after the end of radiotherapy. A, The lymphoscintigraphy revealed diminished visualization of right infraorbital and paranasal main lymphatics, and the absence of radiotracer uptake at the right submandibular and submental lymph nodes. B, The right submental lymph nodes presented in the later image suggested partial obstruction.

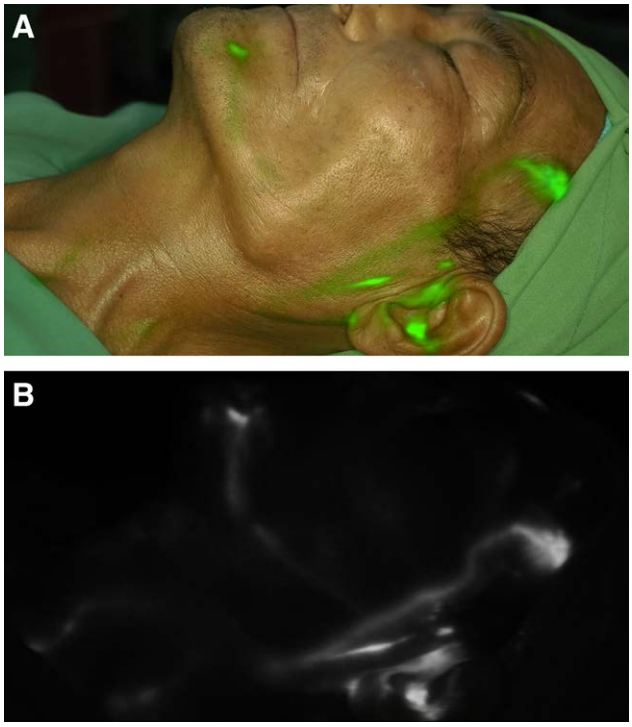

Fig. 2. Preoperative ICG lymphography showed that lymphatic drainage goes through the preauricular and lateral submandibular areas. A, Overlay mode. B, Mono mode.

musculoaponeurotic system (SMAS). No parotid gland was noticed. A branch of the superficial temporal vein was also identified. End-to-end or end-to-side LVA, or lymph node-venous anastomosis (LNVA) was performed under a surgical microscope with 11-O or 12-O nylon (Figs. 3 and 4). Patency was confirmed with the Acland test or ICG-camera–coupled microscope (Figs. 4 and 5). No postoperative compression garment was applied. (**See Video [online],** which shows LNVA through a preauricular incision.)

Statistical Analysis

Statistical analysis was performed with Stata 18.0 (StataCorp, Inc., College Station, Tex.). Fisher exact test was used to compare the difference between preoperative and postoperative status for categorical variables (MDACC rating scale for external HNL). Paired *t* test was used to compare the difference between preoperative and postoperative status for various numeric variables (LSIDS—H&N for both external and internal HNL, and SWAL-QOL for internal HNL). A *P* value of less than 0.05 was considered statistically significant.

RESULTS

All patients were Asian, and the average age was 49.3 ± 8.4 years. One patient was a woman, and the others were men. The characteristics of operations and outcomes are listed in Table 2. Among the eight operations, four of them were for the external type of HNL, three were for the internal type, and one operation was for a combination of both external and internal HNL. The average timing of LVA surgery after the diagnosis of HNL was 6.75 ± 4.3 months. The average number of LVAs for each operation was 1.25 ± 0.71. Regarding the operation site, seven of them were preauricular areas, and one of them was a submandibular area (Fig. 2). There was one patient (patient no. 4 in Table 1 or operation no. 4, 6, and 7 in Table 2) who received LVA three times to treat HNL. The first time was to treat lymphedema over the right cheek with a satisfactory result, but lymphedema over the left cheek occurred 3 months later. He received a second LVA

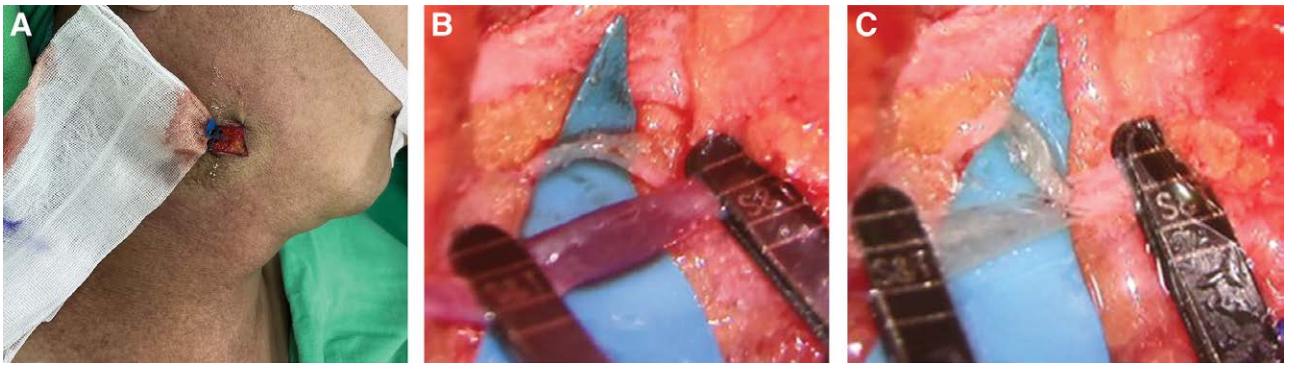

Fig. 3. A submandibular lymphovenous anastomosis for HNL. A–B, A lymphatic duct and a vein were identified via a submandibular incision. C, An end-to-side anastomosis was performed.

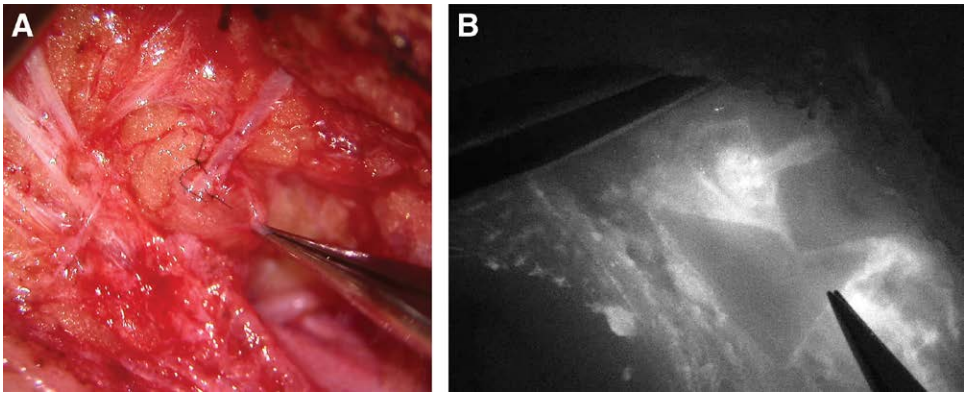

Fig. 4. A preauricular LNVA for HNL. A, An end-to-end LNVA was performed. B, Patency was confirmed by an ICG-camera–coupled surgical microscope.

operation to treat the left-side lymphedema. However, 4 months later, the lymphedema over the right cheek recurred, so he received a third LVA operation. The average duration of operations was 1.5–2 hours. With an average follow-up period of 15.4 ± 15.9 months, LSIDS-H&N improved from 1.11 ± 0.54 to 0.44 ± 0.66 (P = 0.02). For patients with the external type of HNL, within an average follow-up period of 15 ± 16.1 months, the MDACC HNL rating scale improved statistically significantly from level 2 to 0 or 1a (P = 0.008). For patients with the internal type of HNL, supraglottic edema subsided slightly. Within an average follow-up period of 21 ± 17.3 months, SWAL-QOL improved from 130.5 ± 9.2 to 151 ± 19.8 (P = 0.5).

DISCUSSION

For the management of HNL, the nonsurgical solutions include manual lymph drainage (MLD), CDT, or taking orally administered selenium, with CDT being the most widely used option.[4] Regarding surgical solutions, liposuction focusing on the submental area has been reported,[16–18] including one small randomized controlled trial with 10 patients in each arm.[18] Lymphovenous anastomosis (LVA) is a minimally invasive approach to treat extremity lymphedema.[5] However, to date, only two case reports and one case series involving four patients have documented the successful use of LVA in treating external HNL.[7–9] To the best of our knowledge, this study is the largest case series and the first of its kind to use LVA for internal HNL treatment. In addition, the concept of using LNVA to treat extremity lymphedema was first proposed by Pak et al.[19] Their innovative work proved that direct drainage from a functioning lymph node could improve the symptoms of lower extremity lymphedema. As far as we know, our study was the first to use LNVA to treat HNL (Fig. 4) (operation no. 6 and 8).

Currently, unlike extremity lymphedema being defined as a 10% increase in limb circumference by volume measurement,[20] there is no clear definition for diagnosing HNL because there is no contralateral comparison, like extremities. Current diagnosis of HNL relies on the edema of the external surface of the head and neck area, or patients' reports of their own discomfort in the scenarios of internal edema. However, in the early stage of lymphedema, LVA surgery is more likely to be effective because the lymphatic ducts are less sclerotic.[21] Therefore, to identify the patients with a high risk of HNL, such as the location of the tumor, time since the end of tumor treatment, dosage of radiation therapy, radiation status of surgical bed, or number of treatment modalities,[22] and to implement regular follow-up would be an optimal approach to manage HNL more effectively.

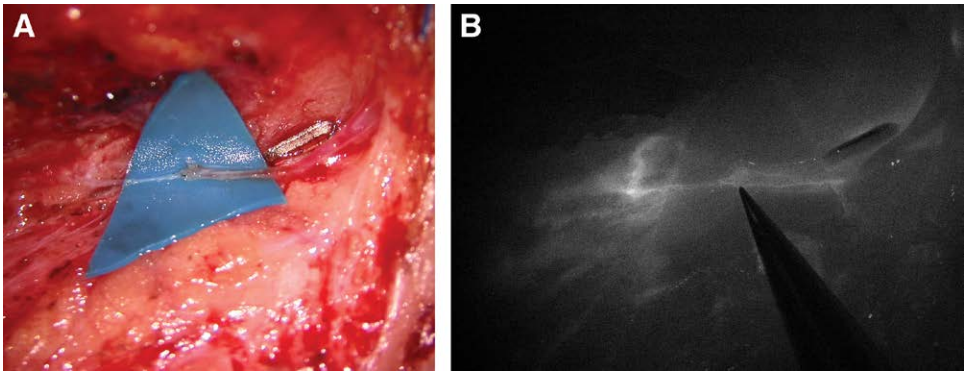

Fig. 5. A preauricular LVA for HNL. A, An end-to-end LVA was performed. B, Patency was confirmed by an ICG-camera–coupled surgical microscope.

Table 2. Results of Lymphovenous Anastomosis Operations for Head and Neck Lymphedema (n = 8)

Operation No.	Type of HNL	Timing of LVA Surgery* (mo)	Operation Site	No. LVA (LNVA)	Follow-up Duration (Mo)	Outcome† (Preoperative → Postoperative)
1	External	6	Right preauricular	3	35	LSIDS-H&N: 1 → 0.3 MDACC rating scale: 2 → 0
2	Internal	12	Right preauricular	1	32	LSIDS-H&N: 0.35 → 0.19 SWAL-QOL: 124→ 165
3	External & internal	4	Left preauricular	1	30	LSIDS-H&N: 1.73 → 0 SWAL-QOL: N/A (difficulty breathing instead of swallowing problem) MDACC rating scale: 2 → 0
4‡	External	7	Right preauricular	1	3	LSIDS-H&N: 0.92 → 0.23 MDACC rating scale: 2 → 1a
5	Internal	8	Right submandibular	1	N/A	N/A
6‡	External	1	Left preauricular	1§	4	LSIDS-H&N: 0.92 → 0.23 MDACC rating scale: 2 → 1a
7‡	External	2	Right preauricular	1	3	LSIDS-H&N: 0.92 → 0.23 MDACC rating scale: 2 → 1a
8	Internal	14	Left preauricular	1§	1	LSIDS-H&N:1.92 → 1.92 SWAL-QOL: 137 → 137

*Duration after the diagnosis of HNL.
†External type HNL was evaluated by Lymphedema Symptom Intensity and Distress Surveys—Head and Neck (LSIDS—H&N) and MD Anderson Cancer Center (MDACC) rating scale, and internal type was evaluated by Lymphedema Symptom Intensity and Distress Surveys—Head and Neck (LSIDS—H&N) and SWAL-QOL.
‡Same patient.
§Lymph node-venous anastomosis.

To reduce the risk of arm lymphedema in breast cancer patients, the practice of immediate lymphatic reconstruction (ILR) by performing lymphovenous anastomosis in the axillary wound immediately after axillary lymph node dissection has become more accepted since its introduction by Boccardo et al,[23–26] given the fact that the incidence of breast cancer-related lymphedema in breast cancer patients receiving axillary lymph node dissection is about 20%,[27] and it is still difficult to cure once the arm lymphedema has occurred. However, the incidence of HNL in head and neck cancer patients receiving surgery or irradiation could be as high as 90%. Therefore, ILR with LVA in head and neck cancer patients might also have benefits for improving patients' quality of life after surviving head and neck cancer. In addition, two major concerns about ILR in breast cancer patients are the LVA patency after adjuvant irradiation and the oncological safety while artificially diverting lymphatic drainage into a nearby venule in a node-positive surgical field, both of which would not be the issues in head and neck cancer since the location of LVA at the preauricular area is away from neck dissection and the irradiated field.

In 2022, Yang et al reported that LVA treatment for affected lower limbs resulted in a significant alleviation of muscle edema in the contralateral lower limbs.[28] In 2023, Chen et al also noted that the impact of LVA extended beyond the anatomic region where it was performed.[29] Both above findings might imply the potential systemic effect brought by LVA. In 2018, Mesquita et al demonstrated that using vascular endothelial growth factor C to treat aged mice could improve meningeal lymphatic drainage, enhancing learning and memory performance.[30] In 2023, Chen et al proposed that extra-cranial LVA may help alleviate symptoms of Alzheimer disease and other neurodegenerative proteinopathies by "de-clogging" the

brain.[31] In the future, the therapeutic effect of LVA in the head and neck field might be expanded to treat some of the currently incurable neurological diseases, such as Alzheimer disease.

There are several limitations in this study. First, this preliminary report only included a small number of patients without a comparative group. Larger studies with comparison groups and longer follow-up durations are needed to confirm the effectiveness of LVA for HNL treatment. Nevertheless, our report on the preliminary treatment outcomes will hopefully bring more attention to this treatment option for HNL among healthcare professionals, allowing more patients to gain benefit from this minimally invasive surgery. Second, our patients with the internal type of HNL mainly had supraglottic edema, causing dysphagia. Therefore, we chose the SWAL-QOL for evaluation. For the internal type of HNL involving the vocal cord, patients would have dysphonia, which could be instead evaluated with Voice Handicap Index-10.[32] In addition, the Revised Patterson Edema scale, which used endoscopy to rate a total of eight anatomical structures (epiglottis, vallecula, pharyngoepiglottic folds, aryepiglottic folds, arytenoids, false vocal folds, true vocal folds, and pyriform sinuses), could provide an independent and objective tool for clinician-reported evaluation for the internal type of HNL and will be included in our further studies.[33] Meanwhile, there are other imaging-based assessment methods such as postoperative lymphoscintigraphy to assess the treatment outcome, 3D scanning of the head and neck to calculate the volume of soft tissue swelling,[34,35] ultrasound to measure the subcutaneous tissue thickness or resistance to compression,[36,37] and computed tomography, which seems the promising tool for both external and internal HNL.[38] Further studies should incorporate these assessment modalities. Finally, some might be concerned that certain HNL will subside spontaneously, and our approach of LVA surgery might result in unnecessary treatment. However, our patients had persistent HNL for an average of 6.75 months before receiving LVA surgery, and most patients had subjective improvement within a few days postoperatively. Therefore, even if the lymphedema might eventually subside without intervention, the LVA surgery could still be beneficial by providing faster relief from HNL.

CONCLUSIONS

Our preliminary study in using LVA to treat both external and internal types of HNL has shown a promising result. Further studies including more patients, longer follow-up, and more objective evaluation modalities are necessary to corroborate the therapeutic effect of LVA in the head and neck area.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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