Author/s:
Rajaram, R;Lee, J;Lok, E;Ng, S;Yamamoto, T

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CLINICAL REVIEW OPEN ACCESS

The Management of Head and Neck Lymphoedema: A 2025 Systematic Review

Rohan Rajaram[1,2] | Jenny Lee[1,2] | Evania Lok[1] | Sally Ng[1,3] | Takumi Yamamoto[4]

[1]Department of Plastic and Reconstructive Surgery, Austin Health, Heidelberg, Victoria, Australia | [2]Austin Clinical School, Faculty of Medicine, Dentistry and Health Sciences, the University of Melbourne, Parkville, Victoria, Australia | [3]Department of Surgery (Austin Precinct), The University of Melbourne, Parkville, Victoria, Australia | [4]Department of Plastic and Reconstructive Surgery, Centre Hospital of National Centre for Global Health and Medicine, Tokyo, Japan

Correspondence: Sally Ng (sally.ng@austin.org.au)

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ABSTRACT

Background: Head and Neck Lymphoedema (HNL) is debilitating to many domains of patients' structure and function, yet it is the most poorly researched form of lymphoedema. This is due to the variety of signs and symptoms experienced by HNL patients, and this makes it difficult to formulate standardized staging classifications and treatment algorithms. The lymphatic drainage pathway within the head and neck is also highly variable. Currently, there is no gold standard therapy or treatment algorithm for HNL. This leaves many patients with the burden of undergoing suboptimal and unverified treatment to varying degrees of success.

Methods: A PRISMA 2020 checklist adherent systematic review was conducted. Medline-OVID was queried with keywords based on HNL and its various management modalities. Title and abstract screening and subsequent full text screening were undertaken by two independent reviewers.

Results: Thirty-seven studies encompassing a sample size of 1452 were discovered from 602 initial results. Overall, the evidence base was weak with many case reports and studies. Complete Decongestive Therapy provided the largest and most consistent data. Surgical methodologies appear to provide significant benefit when cases are selected carefully for appropriateness. Other dermatological and pharmaceutical methods are promising but suffer from a lack of evidence.

Conclusion: The research base on HNL is limited by a lack of standardized severity scale, and the championing of such may encourage higher quality studies to be undertaken.

1 | Introduction

Head and Neck Lymphoedema (HNL) is an increasingly prevalent yet largely undertreated sequela to head and neck cancer management. It is estimated that between 80% and 91% of patients who undergo cancer treatment develop lymphoedema of the head and neck [1–3]. This is in addition to rarer aetiologies of HNL, such as Morbihan's disease and Kaposi's sarcoma, which contribute further to the disease burden. Pain, disfigurement, and reduction in range of motion are commonly experienced by those with HNL. Additionally, internal lymphoedema causes compression of the pharynx and larynx, resulting in compromise of vital functions such as breathing and swallowing. In severe cases, this obstruction can be fatal.

The greatest evidence base for management of HNL lies in nonsurgical modalities such as complete decongestive therapy (CDT) [4]. CDT is a management modality which focuses on four main domains to reduce the functional impact and control the complications associated with lymphoedema. The four domains

are: compression, manual lymphatic drainage, exercise, and skin care. The literature demonstrates that CDT does provide patients with a modest improvement in swelling and restoration of function [5]. Nonetheless, CDT does not resolve the structural drainage deficit seen in lymphoedema. Given that lymphatic fluid is produced constantly throughout the day, daily adherence to CDT protocols is required by patients to prevent recurrence of swelling and loss of function. Considering this, surgical options such as lymphaticovenous anastomosis (LVA), vascularized lymph node transfer (VLNT) and reductive excision are gaining popularity in HNL due to their success in managing lymphoedema in the limbs, as well as emerging evidence demonstrating radical improvements in patients with HNL [6–10]. However, published surgical case numbers are small with relatively short follow-up. For example, whereas Ayestaray et al. demonstrate a marked reduction in facial volume of up to 14.8% post LVA, this is across a cohort of four patients [11].

Appraising the efficacy of management modalities in HNL is complicated by the sheer heterogeneity of the condition. HNL affects multiple domains of patient function: vision, swallowing, pain, breathing, and as such, amalgamating multiple data points across multiple domains is challenging. This is compounded further by the need for high-quality research examining the breadth of management techniques, surgical and nonsurgical, in a pathology that, until recently, was itself severely underdiagnosed [12].

A systematic review of HNL treatment was carried out by Tyker et al. in 2019 [4]. Since this time, a greater volume of contemporary research has emerged, and an up to date synthesis of the literature is proposed in this article. This systematic review aims to present, qualitatively, the summation of research done on head and neck lymphoedema management modalities. The objective of this article is not only to consolidate heterogeneous data but, more importantly, to highlight the specific challenges encountered while attempting to arrive at a gold standard management protocol for HNL.

2 | Methods

2.1 | Study Identification

This systematic review adhered to the Preferred Reporting in Systematic Review and Meta-Analysis (PRISMA) guidelines [13] (Figure 1) and was listed prospectively on the International Prospective Register of Systematic Reviews (PROSPERO). PubMed, Cochrane Database, and Embase Library were thoroughly searched from inception until September 2024.

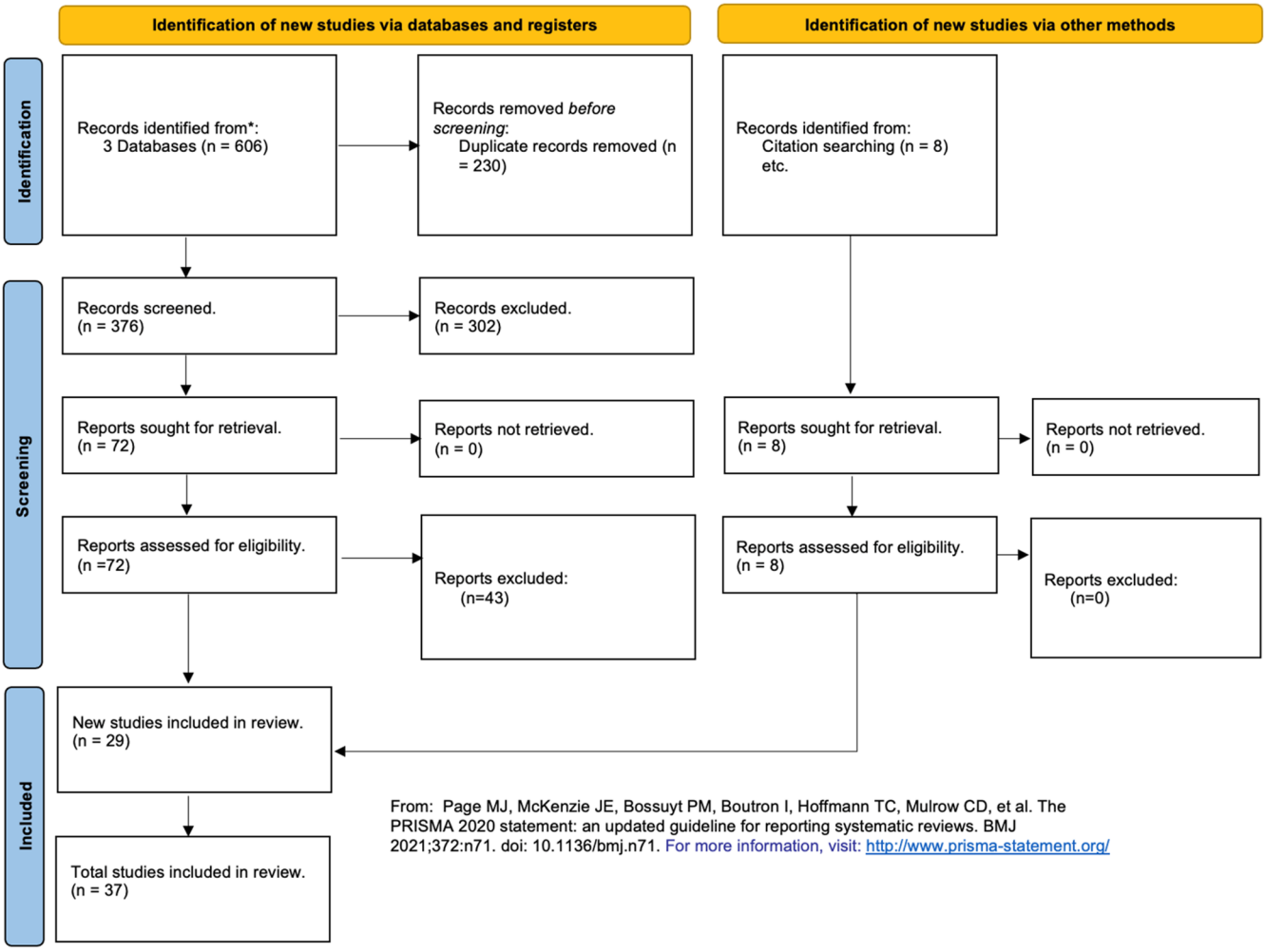


FIGURE 1 | PRISMA flow diagram demonstrating study inclusion. [Color figure can be viewed at wileyonlinelibrary.com]

The following search terms were used: ("Head" OR "Neck" OR "Laryn*" OR "Phary*" OR "Face" OR "Eyelid") AND ("Lymphed*") AND (Complete Decongestive Thera* OR CDT OR Manual Lymphatic Dra* OR MLD OR Surger* OR LVA OR VNLT OR Liposuc* OR Exci* OR Kinesio Tap*). During the review process, any relevant studies that were discovered were also added manually. All papers were independently reviewed by 2 investigators (RR and JL). Discrepancies that arose during either the title and abstract screening or the full text review were discussed and resolved.

2.2 | Study Inclusion

Inclusion criteria included the following: Clinical studies that focused on the management of lymphoedema in the head and neck region. All aetiologies of lymphoedema were included. Studies that provided quantitative reports of any of the following were included: patient demographics, location of lymphoedema, etiology of lymphoedema, severity of lymphoedema prior to and post treatment, a clear overview of treatment modality, and any complications associated with the treatment modality. Due to the limited research available in this area, case reports were included in this synthesis. Review articles, editorials, and letters to the editor were excluded since these were not primary research. Conference presentations were excluded due to their lack of peer review and methodological detail.

2.3 | Data Extraction

Data were extracted into data extraction tables, and the following data were collated: author, year of publication, type of study, country of study origin, number of patients, number within a control group if applicable, etiology of lymphoedema, cancer location if applicable, location of lymphoedema, proportion of patients with internal versus external lymphoedema or both, multiple assessments of the severity and impact of lymphoedema including quality of life (QoL) measures, patient-reported outcome measures (PROMs), specialist grading systems (e.g., MD Anderson Cancer Centre staging scale) and objective measures of lymphoedema (tape measures, imaging, bioelectrical impedance). Although the retrieved data were heterogeneous, minimal processing and cleaning was performed to preserve the integrity of the original reports. For example, specific tumor locations (e.g., lateral tongue SCC) were generalized to broader anatomical categories as outlined in Table 2. Secondly, with regard to seven- and ten-point facial volume complexes, the reports provided pre-and post-intervention measurements for all seven or 10 points. To better compare data, the percentage difference in the sum of all the measurements is given in this review. Apart from this, data were extracted as reported to allow for a comprehensive and inclusive description of the impact of treatment modalities on patients.

2.4 | Quality Assessment

Multiple tools for quality assessment were used. For randomized controlled trials, the Cochrane Risk of Bias (RoB) tool [14] was used. For cohort studies, the National Institute of Health (NIH) quality assessment tool [15] for observational cohort studies was used. For case series and reports, the Joanna Briggs Institute [16] case series assessment tool was used.

2.5 | Quantitative Analysis

Patient characteristics were provided as absolute and relative frequencies with counts and percentages, respectively.

Many papers provided means, standard deviations, and confidence intervals within their results. Where this data was not provided and the appropriate prerequisite data were present, for example raw data, sample sizes, the appropriate statistical model was used to calculate means, standard deviations, and confidence intervals. For example, in reports with a sample size of less than 30, Student's t-distribution was used. For sample sizes greater than 30, z-distribution was used.

Statistics were completed on RStudio v3.6.0 by RR.

3 | Results

3.1 | Literature Search

Of 606 initial results, 230 duplicates were removed and 376 underwent title and abstract screening. Of these, 302 were excluded and the remaining 74 qualified for full text review. A total of 37 papers were selected post full text review for data extraction based on inclusion criteria (Figure 1).

3.2 | Study Characteristics

Studies were published between 2001 and 2023. Tables 1 and 2 highlight study and patient characteristics in detail. 30/37 papers were either case series or case reports, and most (28/37) examined nonsurgical management modalities.

3.3 | Quality Assessment

Bias assessment is provided in the tables below (Tables 3–5).

Overall risk of bias amongst the included studies was moderate. Main sources of bias were found as the experimental rigor of studies increased. For example, most of the RCTs were not blinded and contained missing data. Within cohort studies, outcome data was often heterogeneous and difficult to compare; follow-up was not consistent, and intervention modalities were not consistently applied. Within case studies and series, clinicians who performed the intervention were often the same as the authors of the reports, introducing observer and reporting bias. This is in addition to the intrinsic bias that a low sample size generates.

3.4 | Pooled Patient Demographics

Across the 37 studies (total $n = 1452$), only 36 ($n = 1422$) reported on the sex of their patient population. Of these, 1078 patients (75.81%)

TABLE 1 | Included studies, level of evidence, and investigated management modality.

Authors	Date	Level of evidence	*n*	Management modality
Cinar [17]	2021	IV	1	CDT
Crane [18]	2015	IV	1	CDT
Kutlay [19]	2019	IV	2	CDT
Tacani [20]	2016	III	11	CDT
Deng [21]	2016	III	20	CDT
Pigott [22]	2018	III	10	CDT
Venchiarutti [23]	2023	III	100	CDT
Lemoine [24]	2023	III	38	CDT
Smith [25]	2015	III	733	CDT
Doke [26]	2018	III	34	CDT
Piso [27]	2001	III	11	CDT
McLaughlin [28]	2020	II	9	CDT
Ozdemir [29]	2021	II	14	CDT
Yao [30]	2020	II	25	CDT
Atar [31]	2022	II	30	Kinesio taping
Brake [32]	2014	III	9	Liposuction
Alamoudi [33]	2018	II	10	Liposuction
Hong [34]	2023	IV	1	LVA
Inatomi [35]	2018	IV	1	LVA
Hattori [36]	2021	IV	1	LVA
Mihara [37]	2011	IV	1	LVA
Ayestaray [11]	2013	IV	4	LVA
Deng [38]	2021	III	11	Photobiomodulation
Tritter [39]	2020	III	7	Pneumatic garments
Gutierrez [40]	2020	III	205	Pneumatic garments
Shires [41]	2022	III	35	Pneumatic garments
Mayrovitz [42]	2017	III	44	Pneumatic garments
Ridner [43]	2021	II	19	Pneumatic garments
Micke [44]	2003	III	36	Selenium
Zimmermann [45]	2005	II	10	Selenium
Mangla [46]	2015	IV	1	Surgical debulking
Sagili [47]	2013	IV	3	Surgical debulking
Chalasani [48]	2010	III	9	Surgical debulking
Withey [49]	2001	IV	1	Lymphatic flap
Zeng [50]	2023	IV	2	Steroids
Li [51]	2023	IV	2	Tofacitinib
Gurgenci [52]	2022	IV	1	Hypertonic packs

TABLE 2 | Demographic details of all included patients.

		(N(studies)) (N(patients))
Number of patients		37 (1452)
Age of patient		28 (1417)
Mean	54.5	
SD	2.5	
Gender		36 (1422)
% Male	75.81%	
% Female	24.19%	
Etiology of LE		37 (1452)
% Cancer management	98.83%	
% MD	0.96%	
% Kaposi's sarcoma	0.14%	
% Pemetrexed	0.07%	
Location of cancer		23 (1320)
% Oropharynx	32.08%	
% Intra oral	26.87%	
% Hypopharynx and larynx	20.98%	
% Thyroid	0.98%	
% Salivary	0.75%	
% Cutaneous	0.68%	
% Nasopharynx	0.30%	
% Other	17.36%	
Location of LE (number of mentions-not mutually exclusive)		30 (NA)
# Pan facial	17	
# Eyelid	9	
# Submental	6	
# Submandibular	3	
# Neck	3	
Intervention		37 (1452)
% CDT	69.25%	
% Pneumatic garments	21.18%	
% Selenium	3.16%	
% Kinesio taping	2.06%	
% Liposuction	1.64%	
% Surgical debulking	0.89%	
% Photobiomodulation	0.75%	
% LVA	0.55%	
% Steroids	0.14%	
% Tofacitinib	0.14%	
% Hypertonic pack	0.07%	
% VLNT	0.07%	

Abbreviations: CDT, complete decongestive therapy; LVA, lymphaticovenous anastomosis; MD, Morbihan's disease; VLNT, vascularised lymph node transfer.

were male. Similarly, the average age of patients reported across 28 studies ($n = 1417$) was 54.5 (SD = 2.4). The overwhelming majority, 98.83%, of patients measured across all 37 studies developed lymphoedema secondary to cancer management. Notably, no reports of HNL developed due to primary aetiologies (e.g., Milroy Disease, Lymphoedema tarda, Lymphoedema praecox) were found. In the 24 studies that listed the site of cancer ($n = 1325$), most were oropharyngeal cancer (32.08%), followed by intra-oral (26.78%) or hypopharyngeal and laryngeal (20.98%) cancer. Anatomical location of lymphoedema was quantified as the number of papers that mentioned a given location. Pan-facial lymphoedema was most commonly reported across 17/30 papers, followed by eyelid (9/30) and submental (6/30) lymphoedema (Table 2).

3.5 | Management Modalities

All papers ($n = 1452$) reported management modalities. Most patients underwent Complete Decongestive Therapy (CDT) (69.25%), followed by pneumatic compression garment use (21.28%), with selenium supplementation, kinesio taping, liposuction, surgical debulking, photobiomodulation, LVA, massage therapy, steroid and tofacitinib use, hypertonic pack use, and vascularised lymph node transfer used sparingly (Table 2).

4 | Outcome Analysis

4.1 | Combined Physical Modality Treatments

4.1.1 | Complete Decongestive Therapy

CDT is a multi-modality intervention that combines Manual Lymphatic Drainage (MLD) with exercises, compressive garment wear, exercise prescription, and skin care to assist in the return of lymph to the systemic circulation [17–30].

There were 14 papers exploring CDT with a combined sample size of 1009. Together, these studies captured the impact of CDT on the following outcomes: MD Anderson Cancer Center Lymphoedema Stage, change in neck circumference and facial volume, estimated using 7- and 10-point face measurement complexes, pain scores, and head and neck range of motion (RoM).

TABLE 3 | Cochrane RoB evaluating risk of bias for included randomized controlled trials.

Study	Q1 overall	Q2 overall	Q3 overall	Q4 overall	Q5 overall	Overall RoB
Alamoudi [28]	High	Low	Low	High	Some concerns	Some concerns
Atar [26]	Low	Low	Low	High	Some concerns	Low
McLaughlin [23]	High	Some concerns	Some concerns	High	Some concerns	High
Ozdemir [24]	High	Low	High	High	Some concerns	Some concerns
Ridner [39]	High	Low	Low	High	Some concerns	Some concerns
Yao [25]	High	Low	Some concerns	High	Some concerns	High
Zimmermann [41]	High	Low	Low	High	Some concerns	Some concerns

TABLE 4 | NIH cohort study risk of bias assessment tool for included cohort studies.

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14
Brake [27]	Y	Y	Y	N	N	Y	Y	NA	Y	N	N	N	Y	Y
Chalasani [44]	N	N	Y	N	N	Y	Y	NA	Y	N	N	N	Y	Y
Deng [16]	Y	Y	Y	Y	N	Y	N	NA	Y	Y	N	N	Y	Y
Deng [53]	Y	Y	Y	Y	Y	Y	Y	NA	Y	Y	N	N	Y	Y
Doke [21]	Y	Y	Y	Y	Y	Y	Y	NA	Y	N	N	N	Y	Y
Gutierrez [36]	Y	Y	Y	Y	Y	Y	Y	NA	Y	N	N	N	Y	Y
Lemoine [19]	Y	Y	Y	N	N	N	Y	NA	Y	N	N	N	Y	Y
Mayrovitz [36]	Y	N	Y	Y	Y	N	Y	NA	N	Y	N	N	Y	Y
Micke [40]	Y	Y	Y	Y	N	Y	Y	NA	Y	N	N	N	Y	Y
Pigott [17]	Y	Y	Y	N	N	Y	Y	NA	N	N	N	N	Y	Y
Piso [22]	Y	Y	Y	Y	Y	Y	Y	NA	Y	N	N	N	Y	Y
Shires [37]	Y	N	Y	Y	Y	N	Y	NA	N	N	N	N	Y	Y
Smith [20]	Y	N	Y	N	N	Y	Y	NA	Y	N	N	N	Y	Y
Tacani [15]	Y	Y	Y	Y	N	Y	Y	NA	Y	N	N	N	Y	Y
Tritter [35]	Y	Y	Y	N	N	Y	N	NA	Y	N	N	N	Y	Y
Venchiarutti [18]	Y	Y	Y	Y	N	N	Y	NA	Y	Y	N	N	Y	Y

4.1.2 | Complete Decongestive Therapy and MD Anderson Cancer Centre Head and Neck Lymphoedema Stage

The MD Anderson Cancer Centre Head and Neck Lymphoedema staging system is a verified tool for describing the phenotypic severity of established lymphoedema of the Head and Neck (Table 6) [53].

Five studies ($n = 866$) reported the number of their participants that reduced their MDACC head and neck lymphoedema stage by at least one sub-stage (i.e., 1b to 1a) post complete decongestive therapy with variable follow-up times. Within these, Smith and colleagues' large cohort study demonstrated that 439 of 733 patients improved at least one sub-stage in their lymphoedema severity over a three-month period [25]. Likewise, the 2018 case series undertaken by Piggot et al. demonstrated that 8 of the 10 subjects reduced their MDACC lymphoedema stage by one sub-stage over five and a half months of treatment. Ozdemir et al. conducted the larger of two randomized controlled trials on CDT in head and neck lymphoedema, comparing clinic-based to home-based head and neck lymphoedema CDT. Five out of seven patients in the clinic-based group saw a remission of their lymphoedema severity, whereas two out of seven of the home-based patients saw similar improvements. None of the seven patients in the negative control group demonstrated any clinical improvement in lymphoedema severity. Follow-up was at 4 weeks. Conversely, Venchiarutti's 2023 cohort study reported only 5 of its 60 patients reducing their lymphoedema stage, with 3 patients progressing in the severity of their lymphoedema. No trends could be gleaned regarding the severity group that benefitted most from CDT; however, it is worth noting that no

TABLE 5 | JBI risk assessment tool for case series and reports, assessment of included case series and case reports.

Study ID	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10
Cinar [12]	Y	Y	Y	NA	NA	Y	Y	Y	Y	NA
Crane [13]	Y	Y	Y	NA	NA	Y	Y	Y	Y	NA
Kutlay [14]	Y	Y	Y	Y	Y	Y	Y	Y	Y	NA
Hong [29]	Y	Y	Y	NA	NA	Y	Y	Y	Y	NA
Inatomi [30]	Y	Y	Y	NA	NA	Y	Y	Y	Y	NA
Hattori [31]	Y	Y	Y	NA	NA	Y	Y	Y	Y	NA
Mihara [32]	Y	Y	Y	NA	NA	N	Y	Y	Y	NA
Ayestaray [33]	Y	Y	Y	N	NA	N	Y	Y	Y	NA
Zeng [46]	Y	Y	N	N	NA	Y	Y	Y	Y	NA
Mangla [42]	Y	Y	N	N	NA	Y	Y	Y	Y	NA
Sagili [43]	Y	Y	N	Y	Y	Y	Y	Y	Y	NA
Li [47]	Y	Y	Y	Y	N	Y	Y	Y	Y	NA
Gurgenci [48]	Y	Y	Y	Y	N	Y	Y	Y	Y	NA
Withey [45]	Y	Y	Y	Y	Y	Y	Y	Y	Y	NA

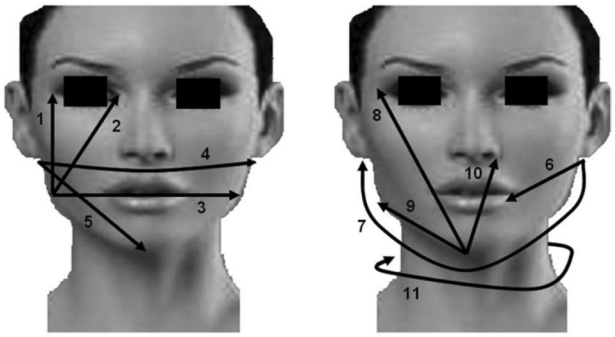
TABLE 6 | MD anderson cancer center head and neck lymphoedema staging system.

Stage	Description
0	No visible oedema but patient reports heaviness
1a	Soft visible oedema, no pitting and reversible
1b	Soft pitting oedema, reversible
2	Firm pitting oedema, not reversible, no tissue changes
3	Irreversible Tissue Changes

MDACC Stage 3 patients were included across the available literature on CDT.

4.1.3 | The Impact of Complete Decongestive Therapy on Face Complex Improvement

The face is highly compartmentalized, with multiple potential spaces for oedema to develop compared to the limbs. Therefore, developing a measurement system that tracks changes in facial volume is complex. To achieve this, both 7- and 10-point facial measurement complexes have been developed and are shown below (Figures 2 and 3). The average percentage difference in facial complex measurements after CDT is measured in 5 studies ($n = 99$). Piso et al. 2001, eleven-patient cohort study demonstrated the highest reduction in facial complex measurements of 9.66% (95% CI = 7.28%–12.04%) on average across all patients, whereas the intervention arm of Yao's 2020 paper demonstrated the most modest improvement in facial complex measurement at 2.14% (95% CI = 1.17%–3.11%). None of the papers reported an increase in measurements.



1. Mandible angle up to the outer corner of the eye;
2. Mandible angle up to the inner corner of the eye;
3. Mandible angles by the line between the lips;
4. Lower implants of ear above the upper lip area;
5. Lower implant of ear up to the mental protuberance;
6. Lower implant of ear up to the mouth angle;
7. Lower implants of ear by the lower mandible area;
8. Mental protuberance up to the outer corner of the eye;
9. Mental protuberance up to the mandible angle;
10. Mental protuberance up to the nasal ala;

FIGURE 2 | 10-point facial complex, courtesy Tacani et al.

4.1.4 | The Impact of Complete Decongestive Therapy on Neck Circumference Reduction

Similar to the face complex, neck circumference complex is measured at 2 or 3 set points and averaged into a composite measure. Five studies ($n = 183$) reported on improvements in neck circumference. Doke et al. ($n = 34$) demonstrated the greatest decrease in neck circumference of 38.4% (95% CI = 37.13%–39.67%) over 12 months. Ozdemir et al. demonstrated the most variable change in neck circumference. Their clinical CDT group experienced an average increase in their neck circumference of 0.19% on average (95% CI = −26.3%–26.68%).

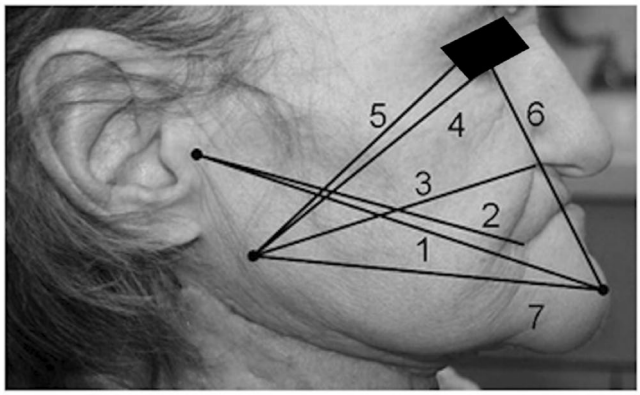


FIGURE 3 | 7-point facial complex, courtesy Ozdemir et al.

4.1.5 | Complete Decongestive Therapy and Pain Scores

Only two studies on complete decongestive therapy ($n = 45$) reported improvements in pain scores out of 10. Tacani et al. [20] reported an average improvement of 4.9 points, and Doke et al. [26] reported a 3.1-point improvement.

4.1.6 | Functional Improvements With Complete Decongestive Therapy

One case report (Crane 2015) and one cohort study (Doke 2018) assessed disparate functional deficits within their respective patient populations. The patient in Crane's case report had main functional issues of temporomandibular joint dysfunction and neck flexion restriction due to swelling from their lymphoedema. After completing the course of CDT, the active mandibular depression range of motion (ROM) improved 84% from 19 to 35 mm. This is near the often quoted normal ROM of 35–45 mm and represents a significant regain of function [54].

The 34 patients in Doke's cohort study presented with cervical spine ROM deficit, which was measured by a maximal active cervical ROM test. Prior to CDT, the patients collectively had total left to right ROM of 98.2°, which improved by 49.9% (SD = 14.05%) to 147°. This represents a significant return of neck ROM. Additionally, the Crane et al. group demonstrated that deep neck flexor endurance time improved 76% from 13.3 to 23.4 s.

4.1.7 | Complete Decongestive Therapy for Morbihan's Disease

One case report (Cinar 2021) and one case series (Kutlay 2019) examined the impact of CDT in resolving head and neck oedema associated with Morbihan's Disease. The Cinar paper used a similar 7-point facial complex and reported an 8.1% decrease in total measurements across the complex. The Kutlay 2019 paper examined two patients with Morbihan's Disease. However, their assessment of the impact of CDT was not objective, simply reporting that there was a subjective improvement in swelling in both patients.

4.1.8 | Kinesio Taping

Kinesio Taping (KT) is a method by which elastic Kinesio Tex tapes of varying tensions are used to create positive pressure in subdermal and subfascial compartments [31]. This facilitates the drainage of fluid through both the lymphatic and systemic circulations.

The RCT undertaken by Atar et al. in 2022 is the only research that has evaluated the efficacy of KT as a standalone intervention ($n = 30$ intervention, 28 control). Participants either underwent true or sham KT for 3 weeks, and a comprehensive list of objective parameters was measured at the end of the trial. Both face circumference and 7-point face complex measurements decreased modestly (approximately 1%) but with statistical significance when preprocedure and control measurements were compared. Furthermore, neck circumference reduced by a statistically significant 5% when compared to preprocedure and to the control group. MDACC staging also reduced by at least one stage in 28/30 patients. Finally, functional measures and PROMs were encouraging and significantly improved between the groups as measured by the QoL Questionnaire for Head and Neck Cancer [55]. Internal lymphoedema was unchanged as measured by the Patterson Edema Scale.

4.1.9 | Pneumatic Compression Garments

Pneumatic compression garments are intended as an adjunct within CDT, primarily to be used in reducing the self-care burden in maintenance CDT [39–43]. Therefore, outcome measures revolved mainly around comfort and adherence rather than actual improvement in lymphoedema. To this end, 5 papers ($n = 310$) examined the role of pneumatic compression garments in the management of head and neck lymphoedema. Four of these were cohort studies and one was a randomized controlled trial. All studies utilized the Flexitouch Head and Neck system, a garment that fits over the face, head, and neck and applies pressure to mimic home lymphatic drainage. The most commonly tracked outcomes were subjective patient-reported outcomes on largely proprietary, heterogeneous, and nonverified scales. The majority of participants from all 5 studies agreed that they were likely to adhere to these garments at home, given the comfort and ease of use of the product. This was reflected globally in participant responses to individual questions regarding comfort and ease of use.

With the exception of the Shires 2022 paper, all papers required patients to wear pneumatic garments for at least 4 weeks to determine the impact on lymphoedema. One such study (Mayrovitz 2017) tracked facial measurements using the 7-point facial complex and found a 1.18% (SD = 1.23%) improvement in facial volumes.

4.2 | Surgical Modalities

4.2.1 | Liposuction

The evidence base for liposuction in HNL is based entirely out of two studies on separate populations out of a single center in Canada [32, 33]. These are the cohort study undertaken by Brake

et al. in 2014 and the randomized, nonblinded control trial by Alamoudi et al. in 2018 (total $n = 29$, intervention $n = 19$). Both papers examined the effect of liposuction on patients' personal impression of their new facial shape using the modified blepharoplasty outcome evaluation (MBOE) score, which is not explicitly validated in head and neck lymphoedema [33]. All patients in both studies primarily had lymphoedema in the submental area secondary to cancer management. Tissue from the submental area was evacuated using standard liposuction technique with a 3 mm Accelerator-3 liposuction cannula under local anesthetic. Patients then completed the MBOE. Participants in the Brake study experienced 13.6 points of improvement in the MBOE, especially stating that their perception of their chin and confidence in its aesthetics were much higher than they were preoperatively. This was echoed by the Alamoudi 2018 RCT where not only did the intervention group demonstrate an average of 10.3 points of improvement from their preoperative score, but this represented a significant difference from the control group who simply underwent CDT and worsened on the MBOE by 0.5 points.

4.2.2 | Lymphaticovenous Anastomosis

Lymphaticovenous anastomosis (LVA) is a super-micro surgical technique that physiologically improves lymphatic drainage by bypassing areas with a drainage deficit through the anastomosis of draining lymphatics to a nearby vein [11, 34–37].

The management of head and neck lymphoedema using LVA was examined in 5 studies with a combined sample size of 8. Two of these were case reports (total $n = 2$) in patients with Morbius Morbihan's Disease, and another three papers covered 6 patients who developed HNL secondary to cancer management.

In patients with Morbius Morbihan's Disease, LVA was used in both case studies to relieve severe eyelid lymphoedema that restricted lid opening. Both procedures were performed under local anesthetic and used preoperative ICG lymphangiography to identify disruption in lymphatic architecture through the detection of dermal backflow [34]. In the Hattori paper, a single end-toto-end LVA was performed between a preauricular lymph vessel and a nearby subcutaneous vein. Due to increased fibrosis of lymphoedema, a concomitant blepharoplasty was also performed. The other paper, by Hong et al. performed bilateral LVAs between preauricular lymph vessels. Notably, on the left side, a venae commitantes of the transverse facial artery was selected for anastomosis. Both papers reported complete remission of swelling, without recurrence. Hong et al. followed their patient up at 41 months, and Hattori followed their patient up at 12 months. Not only did both patients regain the ability to open their eyes, but the swelling had also completely subsided with good functional as well as aesthetic outcomes.

With regards to the cancer group, the Ayestaray et al. case series provided the greatest objective outcome data. This paper demonstrated a pi-shaped LVA technique where the lymphatic vessel is divided in two and anastomosed in an end-to-side fashion along the lateral aspect of a nearby vein to bolster drainage without impeding lymphatic flow. Improvement in lymphoedema was tracked with a proprietary facial composite measure where the circumference of the head and neck was measured at three set points and averaged. Additionally, facial volumes were also tracked using a formula that incorporated the facial composite measure. Average reduction in facial composite measures was 3.7% (SD = 2.67%) representing a nonsignificant reduction in facial oedema. A similar nonsignificant reduction in facial volumes was also noted. The remaining papers were both case studies. Inatomi et al. utilized an end-to-side LVA to relieve severe lymphoedema, and patients were able to return to normal ocular aperture post-LVA. Mihara et al. demonstrated that their end-to-end LVA can reduce buccal dermal thickness by 70% as measured radiographically on CT, a modality not used by other studies in the LVA category.

4.2.3 | Surgical Debulking

Debulking was utilized in one case report, one case series (Sagili 2013, $n = 2$) and one cohort study (Chalasani 2010, $n = 9$) over a total of 12 patients [46–48]. All patients had lymphoedema within their eyelids. Etiology was varied: 7 patients had Morbihan's Disease, 4 were postoncological treatment, and one patient developed lymphoedema as a side effect of a chemotherapy agent—Pemetrexed. The only outcome measure undertaken was clinician assessment of remaining lymphoedema without the use of a clinician assessment score. In all cases, the swelling from lymphoedema in the eyelids was resolved with surgical debulking. No mention was made about functional improvement, and no comments were made about recurrence on follow-up.

4.2.4 | Loco-Regional Lymph Node Flap

A single case report by Withey et al. in 2001 demonstrated the first and only use of a loco-regional lymph node flap in partially relieving lymphoedema for palliative reasons [49]. The case revolved around a 46-year-old male who had severe facial lymphoedema requiring tracheostomy and nasogastric tube insertion. The patient was also effectively blind due to buccal and eyelid lymphoedema. Failing conservative therapy, the patient underwent a random pattern dermal flap containing axial supraclavicular lymphatics that were transferred to the cheek to improve drainage. The patient was able to regain eye opening as a result of the lymphatic reconstruction.

4.3 | Other Modalities

4.3.1 | Photobiomodulation

The use of Photobiomodulation (PBM) is proposed as a lymphoedema therapy by mitigating the release of proinflammatory cytokines and by encouraging lymphangiogenesis [38].

Currently the Deng 2021 cohort study ($n = 11$) is the only available literature on the use of PBM as an intervention for HNL. Several assessment tools were utilized to gauge the efficacy of PBM. The Head and Neck External Lymphoedema and Fibrosis

Assessment Criteria (HN-LEF) measured the extent of external lymphoedema, the Modified Patterson Scale measured the severity of internal lymphoedema, and the HN-LEF Symptom Inventory, LSIDS-HN, Neck Disability Index, and cervical ROM all measured functional capacity. The trial demonstrated statistically significant improvement in all these fields except for internal lymphoedema. The number of sites with external lymphoedema reduced by 33% (SD = 6%), and the severity of lymphoedema at these sites improved by 72% (SD = 18%). Patients also reported fewer and less severe symptoms such as odynophagia and taste changes. Finally, the average range of motion in the neck improved to statistical significance; forward flexion and extension improved on average by 8° each.

4.3.2 | Selenium Use

Mechanistic evidence demonstrates that biological selenium increases the activity of selenium-dependent antioxidant enzymes such as glutathione peroxidase [44, 45]. The reduction of oxidation within a lymphoedema context is linked to reduced inflammatory changes in static lymphatic fluid and thus reduced fibrosis.

The use of Selenium as a biological agent was investigated in one cohort study by Micke in 2003 ($n = 36$) and one RCT ($n = 20$, $n = 10$ intervention) by Zimmerman in 2005. Both cohorts were exclusively patients who developed lymphoedema after cancer management. In the Micke 2003 study, a variety of scoring systems for internal and external lymphoedema as well as quality of life were used. These included Miller classifications, Foldi and Foldi classification, and the LENT SOMA system. Ultimately, statistically significant results were only observed in quality-of-life measures, with no significant difference in internal or external lymphoedema.

The remaining Zimmerman RCT utilized tape measurements to demonstrate a significant reduction of lymphoedema in the group treated with sodium selenite ($n = 10$) compared to the placebo group ($n = 10$) after 1 week postoperatively. However, intergroup differences were nonsignificant at 2 weeks, which was reported to be due to physiological subsidence of oedema in the placebo group.

4.3.3 | Miscellaneous

The remaining studies (2 case series and 1 case report, total $n = 5$) on the management of HNL covered using hypertonic packing, corticosteroids, and the biological agent Tofacitinib to manage lymphoedema in patients who failed CDT and were not suitable for lymphoedema surgery [50–52]. Gurgenci et al. utilized sodium carbonate packs four hourly in a patient whose periorbital lymphoedema was refractory to CDT. The author reported that after 2 weeks of packing the patient was able to open their eyes for the first time since the development of severe HNL. Zeng et al. described two cases of Kaposi's sarcoma secondary to AIDS resulting in periorbital lymphoedema. They reported the use of corticosteroids was only partially successful. One of the two patients experienced resolution of their lymphoedema whereas the other passed away before resolution could be examined. Li et al. case series followed two patients with Morbihan's disease whose eyelid lymphoedema was treated with Tofacitinib to good effect in both patients. Swelling was reduced to premorbid levels in both patients.

5 | Discussion

This systematic review presents the breadth of available information pertaining to the methodology and assessment of efficacy of the management modalities available for head and neck lymphoedema. With the inclusion of 37 papers encompassing a combined sample size of 1452, it represents the largest and most comprehensive analysis of the available evidence to date.

Most patients were male and middle aged, with the overwhelming majority of patients developing lymphoedema secondary to head and neck cancer management. This is consistent with the etiology of head and neck cancer, which seems to predominate within middle aged males. Additionally, anatomical locations of cancer were most frequently oral and oropharyngeal, which was also in keeping with epidemiological studies on head and neck cancers [56].

Overall, 12 separate management modalities were discovered. This lends weight to the notion that the management of head and neck lymphoedema is heterogeneous with no consensus on gold standard management.

Nonetheless, data on CDT was the most abundant and objective. Patients undergoing CDT for HNL saw consistent reductions in their MDACC HNL Stage as well as 7 and 10 point facial composite measurements. Of note, the Smith et al. paper demonstrated that 439 out of their 733 patients reduced their lymphoedema stage. This sample included many patients in Stage 2, suggesting that CDT reduced lymphoedema severity even when fibrotic changes had begun to occur. The effect of CDT on facial composite measurements was also consistently positive but variable in magnitude of improvement, ranging from 2.14% to 9.66%. With regard to other measured outcomes, neck circumference does not seem to significantly reduce even in the acute phase of CDT, and pain scoring demonstrates moderate improvement but is only reported across two studies.

Although these data are generally encouraging, they may be influenced by several sources of bias and inaccuracy. First is the potential for inaccuracy with facial complex measurement. Tape measurements rely on the accuracy of the investigator to measure contoured surfaces with a straight measuring tape. Additionally, patients are required to maintain a consistent head position throughout the measurement. Inter-patient consistency is also necessary. When several point-to-point measures are combined, small human errors across individual points may be compounded and become a source of inaccuracy in reporting. Furthermore, interviewing patients on pain scores after performing a purportedly therapeutic intervention introduces the potential for social desirability bias, where patients may feel obligated to report lower pain scores.

Ultimately, the largest barrier that patients experience with complete decongestive therapy is the necessity for daily adherence. This is echoed in the 2016 paper by Deng et al. demonstrating that the cognitive and time burden of CDT was a consistent

and salient detractor from patient compliance [21]. Therefore, the overall efficacy of CDT as it is currently practiced can be described as variable, modest, and associated with barriers to treatment adherence.

To this end, the efficacy and objectivity of CDT may be improved by the adjunct use of ICG lymphography [57, 58]. Since ICG and near infrared lymph node mapping can visualize the flow through lymphatic channels in real time, visualizing the immediate effect of MLD to distribute lymph past points of blockage may prove helpful in increasing the precision of MLD. Furthermore, therapy may be targeted to the individual and treatment response, and the requirement for adjunctive therapies could be assessed in real time—potentially increasing the individual efficacy of CDT. Current evidence on this is nascent but does demonstrate a proof of concept [59, 60].

Furthermore, the examined literature shows that pneumatic compression garments and kinesio taping may assist in reducing the burden of daily adherence to CDT. Early data on pneumatic compression garments suggest that patients report that these garments are comfortable, easy to operate, and result in a subjective reduction in swelling for patients with both long- and short-term use, particularly in the maintenance phase of CDT. Additionally, kinesio taping demonstrates, in the only true blinded randomized control trial seen in this review, that it can be used to facilitate modest yet significant improvements in lymphoedema burden.

With regards to surgical management modalities, liposuction demonstrates promise for improving the appearance and functional burden of lymphoedema. However, neither of the papers on liposuction presents follow-up data on their patients to track recurrence beyond the reported period of 6 months.

The available literature on LVA is sparse and low powered. Nonetheless, each case on LVA seems to demonstrate beneficial improvements for carefully selected patients whose lymphoedema is severe yet confined to a single area. For example, LVA is able to resolve intractable and severe swelling in the eyelids or in the cheek. Conversely, there are no reports of LVA being used to resolve diffuse and widespread pan-facial or whole neck lymphoedema. This is potentially due to the necessity for accurate identification of the exact area of lymphatic insufficiency such that it can be bypassed with an LVA [61]. Owing to the complex and heterogeneous lymphatic organization in the head and neck and that widespread lymphoedema can block a potentially large area of lymphatic drainage from the face [62], LVA may show therapeutic benefit in select head and neck lymphoedema cases. So far, it has been used largely to treat cases of Morbus Morbihan disease successfully where patients present with lymphoedema confined to the eyelids [63]. However, there is no long-term data on the patency rate for LVA and whether there is recurrence.

Surgical debulking is also prevalent in cases of lymphoedema confined to the eyelids. Conventional understanding of surgical management of lymphoedema follows that simply excising lymphoedematous tissue without ways of restoring the drainage deficit will lead to recurrence [64]. However, in most debulking cases, such as those reported by Chalasani et al. patients are followed up with no mention of recurrence. This could potentially be due to the fact that most patients who undergo excision have lymphoedema as a result of Morbihan's Disease. In Morbihan's Disease, instead of an upstream lymphatic disruption causing an accumulation of lymph, lymph vessels themselves lose their integrity and become more permeable [63]. Therefore, it is understandable that removing tissue including the lymphatic vasculature could provide a permanent solution to Morbihan's Disease lymphoedema. In order to see long-term results in lymphoedema resultant from cancer therapy, debulking may be required to be combined with physiological surgery (LVA/VLNT) and CDT.

This systematic review has demonstrated the disparity between the various assessment and management modalities for HNL with insufficient evidence to provide a consensus for gold standard assessment and intervention [65]. This is a significant barrier to undertaking replicable and comparable research in head and neck lymphoedema. Not only are there many domains of structure and function that are impacted by lymphoedema, such as swelling, range of motion, phonation, and swallowing, as well as psychosocial considerations, each of these domains does not seem to have unified severity assessment criteria. For example, within the studies in this paper, external lymphoedema severity includes assessment that utilizes the following tools: 7-point facial composite, 10-point facial composite, volumetric analysis, and CT and MR dermal thickness measurements. This trend holds true for most domains, with each domain at times using proprietary and nonstandardized scales to quantify improvement. Since a true measure of the effect of an intervention relies on standardization and repeatability, utilizing outcome measures that are standardized within the HNL cohort can contribute to the production of higher quality research in HNL management. This is currently being attempted with the introduction of the Assessment of Lymphoedema of the Head and Neck (ALOHA) [66] measure as well as the Head and Neck Lymphoedema and Fibrosis (HN- LEF) [65, 67] criteria which amalgamate objective and patient-reported outcomes. As such, the use of one of these criteria may assist in standardizing severity measurement and quantifying the effect of different management modalities. The development of 3D volumetric measurement software and scanning devices is likely to improve the accuracy in detecting the more subtle changes from treatment intervention in the future if the high costs of these devices to healthcare systems can be surmounted.

Beyond this, another weakness of this review was the paucity of high-quality data resulting in potential inaccuracy of narrative and statistical conclusions drawn. Furthermore, as many studies reported raw data, this review was required to process this data to generate percentages, means, and standard deviations. This may have been done in ways that the authors of the original papers did not intend. As mentioned earlier, the standardization of outcome measures may encourage more randomized controlled clinical studies to be undertaken, resulting in a stronger research base permissive of more robust statistical analysis.

6 | Conclusion

Lymphoedema in the head and neck is especially debilitating due to the range of deficits that it can cause. As such, it is imperative that data demonstrating the efficacy of treatment modalities in relieving the burden of this disease are investigated

with future research. However, the variety of problems caused by lymphoedema of the head and neck also results in heterogeneous and scattered methods of quantifying the efficacy of lymphoedema management modalities. The current research demonstrates that CDT, while cumbersome for patients, is most consistently effective and may be bolstered by adjuvant pneumatic compression garments and Kinesio Taping. Furthermore, interventions such as LVA and reductive surgery have been used to improve focal lymphoedema of specific aetiologies. With the development of more standardized classifications and outcome measures, this could allow more robust study methodology to provide more robust data on treatment efficacy.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

References

1. C. R. Arends, L. Van Der Molen, J. E. Lindhout, et al., "Lymphedema and Trismus After Head and Neck Cancer, and the Impact on Body Image and Quality of Life," *Cancers* 16, no. 3 (2024): 653, https://doi.org/10.3390/cancers16030653.

2. C. Jeans, B. Brown, E. C. Ward, et al., "Comparing the Prevalence, Location, and Severity of Head and Neck Lymphedema After Postoperative Radiotherapy for Oral Cavity Cancers and Definitive Chemoradiotherapy for Oropharyngeal, Laryngeal, and Hypopharyngeal Cancers," *Head & Neck* 42, no. 11 (2020): 3364–3374, https://doi.org/10.1002/hed.26394.

3. K. R. Rogacki, P. T. Teo, M. Gopalakrishnan, et al., "Clinical, Pathologic, and Dosimetric Predictors of Head and Neck Lymphedema Following Definitive or Adjuvant Radiation Therapy for Head and Neck Cancer," *Advances in Radiation Oncology* 9, no. 9 (2024): 101545, https://doi.org/10.1016/j.adro.2024.101545.

4. A. Tyker, J. Franco, S. T. Massa, S. C. Desai, and S. G. Walen, "Treatment for Lymphedema Following Head and Neck Cancer Therapy: A Systematic Review," *American Journal of Otolaryngology* 40, no. 5 (2019): 761–769, https://doi.org/10.1016/j.amjoto.2019.05.024.

5. H. Z. Zhang, Q. L. Zhong, H. T. Zhang, Q. H. Luo, H. L. Tang, and L. J. Zhang, "Effectiveness of Six-Step Complex Decongestive Therapy for Treating Upper Limb Lymphedema After Breast Cancer Surgery," *World Journal of Clinical Cases* 10, no. 25 (2022): 8827–8836, https://doi.org/10.12998/wjcc.v10.i25.8827.

6. S. H. Azhar, H. Y. Lim, B. K. Tan, and V. Angeli, "The Unresolved Pathophysiology of Lymphedema," *Frontiers in Physiology* 11 (2020): 137.

7. J. Deng, S. H. Ridner, M. S. Dietrich, et al., "Prevalence of Secondary Lymphedema in Patients With Head and Neck Cancer," *Journal of Pain and Symptom Management* 43, no. 2 (2012): 244–252, https://doi.org/10.1016/j.jpainsymman.2011.03.019.

8. B. G. Smith and J. S. Lewin, "Lymphedema Management in Head and Neck Cancer," *Current Opinion in Otolaryngology & Head and Neck Surgery* 18, no. 3 (2020): 153–158, https://doi.org/10.1097/MOO.0b013e32833aac21.

9. H. Hara and M. Mihara, "Lymphaticovenous Anastomosis for Advanced-Stage Lower Limb Lymphedema," *Microsurgery* 41, no. 2 (2021): 140–145, https://doi.org/10.1002/micr.30689.

10. M. V. Schaverien, I. Badash, K. M. Patel, J. C. Selber, and M. H. Cheng, "Vascularized Lymph Node Transfer for Lymphedema," *Seminars in Plastic Surgery* 32, no. 1 (2018): 28–35, https://doi.org/10.1055/s-0038-1632401.

11. B. Ayestaray, F. Bekara, and J. B. Andreoletti, "π-Shaped Lymphaticovenular Anastomosis for Head and Neck Lymphoedema: A Preliminary Study," *Journal of Plastic, Reconstructive & Aesthetic Surgery* 66, no. 2 (2013): 201–206, https://doi.org/10.1016/j.bjps.2012.08.049.

12. M. D. Stubblefield and D. Weycker, "Under Recognition and Treatment of Lymphedema in Head and Neck Cancer Survivors—A Database Study," *Supportive Care in Cancer* 31, no. 4 (2023): 229, https://doi.org/10.1007/s00520-023-07698-3.

13. M. J. Page, M. K. JE, P. M. Bossuyt, et al., "The PRISMA 2020 Statement: An Updated Guideline for Reporting Systematic Reviews," *British Medical Journal*, no. 372 (2021): n71, https://doi.org/10.1136/bmj.n71.

14. J. A. C. Sterne, J. Savović, M. J. Page, et al., "RoB 2: A Revised Tool for Assessing Risk of Bias in Randomised Trials," *British Medical Journal* 366 (2019): l4898.

15. National Heart Lung and Blood Institute, "Study Quality Assessment Tools," accessed December 29, 2023, https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools.

16. For Use in JBI Systematic Reviews Checklist for Case Series 2019, https://jbi.global/sites/default/files/2019-05/JBI_Critical_Appraisal-Checklist_for_Case_Series2017_0.pdf.

17. G. N. Çinar, S. Özgül, G. Nakip, et al., "Complex Decongestive Therapy in the Physical Therapist Management of Rosacea-Related Edema (Morbus Morbihan Syndrome): A Case Report With a New Approach," *Physical Therapy* 101, no. 9 (2021): pzab133, https://doi.org/10.1093/ptj/pzab133.

18. P. Crane, L. Feinberg, and J. Morris, "A Multimodal Physical Therapy Approach to the Management of a Patient With Temporomandibular Dysfunction and Head and Neck Lymphedema: A Case Report," *Journal of Manual & Manipulative Therapy* 23, no. 1 (2015): 37–42, https://doi.org/10.1179/2042618612Y.0000000021.

19. S. Kutlay, E. C. Ozdemir, Z. Pala, S. Ozen, and H. Sanli, "Complete Decongestive Therapy Is an Option for the Treatment of Rosacea Lymphedema (Morbihan Disease): Two Cases," *Physical Therapy* 99, no. 4 (2019): 406–410, https://doi.org/10.1093/ptj/pzy155.

20. P. M. Tacani, J. P. Franceschini, R. E. Tacani, et al., "Retrospective Study of the Physical Therapy Modalities Applied in Head and Neck Lymphedema Treatment," *Head and Neck* 38, no. 2 (2016): 301–308, https://doi.org/10.1002/hed.23899.

21. J. Deng and B. A. Murphy, "Lymphedema Self-Care in Patients With Head and Neck Cancer: A Qualitative Study," *Supportive Care in Cancer* 24, no. 12 (2016): 4961–4970, https://doi.org/10.1007/s00520-016-3356-2.

22. A. Pigott, J. Nixon, J. Fleming, and S. Porceddu, "Head and Neck Lymphedema Management: Evaluation of a Therapy Program," *Head & Neck* 40, no. 6 (2018): 1131–1137, https://doi.org/10.1002/hed.25086.

23. R. L. Venchiarutti, S. Templeton, L. Mathers, E. Charters, and J. R. Clark, "Treatment Approaches and Outcomes of a Head and Neck Lymphedema Service at an Australian Comprehensive Cancer Center," *Head & Neck* 45, no. 6 (2023): 1539–1548, https://doi.org/10.1002/hed.27369.

24. J. C. Lemoine, V. Vaitaitis, T. Jarreau, et al., "Inpatient Decongestive Therapy for Lymphedema in Acute Postsurgical Head and Neck Cancer Patients," *International Archives of Otorhinolaryngology* 27, no. 2 (2023): e329–e335, https://doi.org/10.1055/s-0042-1745726.

25. B. G. Smith, K. A. Hutcheson, L. G. Little, et al., "Lymphedema Outcomes in Patients With Head and Neck Cancer," *Otolaryngology and*

Head and Neck Surgery 152, no. 2 (2015): 284–291, https://doi.org/10.1177/0194599814558402.

26. K. N. Doke, L. Bowman, Y. Shnayder, et al., "Quantitative Clinical Outcomes of Therapy for Head and Neck Lymphedema," *Advances in Radiation Oncology* 3, no. 3 (2018): 366–371, https://doi.org/10.1016/j.adro.2018.04.007.

27. D. U. Piso, A. Eckardt, A. Liebermann, C. Gutenbrunner, P. Schäfer, and A. Gehrke, "Early Rehabilitation of Head-Neck Edema After Curative Surgery for Orofacial Tumors," *American Journal of Physical Medicine & Rehabilitation* 80, no. 4 (2001): 261–269, https://doi.org/10.1097/00002060-200104000-00006.

28. T. M. McLaughlin, J. J. Broadhurst, C. J. Harris, S. McGarry, and S. L. Keesing, "A Randomized Pilot Study on Self-Management in Head and Neck Lymphedema," *Laryngoscope Investigative Otolaryngology* 5, no. 5 (2020): 879–889, https://doi.org/10.1002/lio2.455.

29. K. Ozdemir, I. Keser, M. Duzlu, O. P. Erpolat, U. Saranli, and H. Tutar, "The Effects of Clinical and Home-Based Physiotherapy Programs in Secondary Head and Neck Lymphedema," *Laryngoscope* 131, no. 5 (2021): E1550–E1557, https://doi.org/10.1002/lary.29205.

30. T. Yao, B. Beadle, C. F. Holsinger, and H. M. Starmer, "Effectiveness of a Home-Based Head and Neck Lymphedema Management Program: A Pilot Study," *Laryngoscope* 130, no. 12 (2020): E858–E862, https://doi.org/10.1002/lary.28549.

31. S. Atar, Y. Atar, U. Uygan, et al., "The Efficacy of Kinesio Taping on Lymphedema Following Head and Neck Cancer Therapy: A Randomized, Double Blind, Sham-Controlled Trial," *Physiotherapy Theory and Practice* 39, no. 9 (2023): 1832–1846, https://doi.org/10.1080/09593985.2022.2056862.

32. M. K. Brake, L. Jain, R. D. Hart, J. R. Trites, M. Rigby, and S. M. Taylor, "Liposuction for Submental Lymphedema Improves Appearance and Self-Perception in the Head and Neck Cancer Patient," *Otolaryngology and Head and Neck Surgery* 151, no. 2 (2014): 221–225, https://doi.org/10.1177/0194599814529401.

33. U. Alamoudi, B. Taylor, C. MacKay, et al., "Submental Liposuction for the Management of Lymphedema Following Head and Neck Cancer Treatment: A Randomized Controlled Trial," *Journal of Otolaryngology - Head & Neck Surgery* 47, no. 1 (2018): 22, https://doi.org/10.1186/s40463-018-0263-1.

34. J. H. Hong, C. C. Yi, J. W. Lee, Y. C. Bae, R. S. Kim, and J. H. Kim, "Lymphaticovenular Anastomosis for Morbihan Disease: A Case Report," *Archives of Craniofacial Surgery* 24, no. 3 (2023): 124–128, https://doi.org/10.7181/acfs.2022.01067.

35. Y. Inatomi, S. Yoshida, K. Kamizono, M. Hanada, R. Yasumatsu, and H. Kadota, "Successful Treatment of Severe Facial Lymphedema by Lymphovenous Anastomosis," *Head & Neck* 40, no. 7 (2018): E73–E76, https://doi.org/10.1002/hed.25206.

36. Y. Hattori, H. Hino, and A. Niu, "Surgical Lymphoedema Treatment of Morbihan Disease: A Case Report," *Annals of Plastic Surgery* 86, no. 5 (2021): 547–550, https://doi.org/10.1097/SAP.0000000000002797.

37. M. Mihara, G. Uchida, H. Hara, et al., "Lymphaticovenous Anastomosis for Facial Lymphoedema After Multiple Courses of Therapy for Head-And-Neck Cancer," *Journal of Plastic, Reconstructive & Aesthetic Surgery* 64, no. 9 (2011): 1221–1225, https://doi.org/10.1016/j.bjps.2011.01.006.

38. J. Deng, J. N. Lukens, S. Swisher-McClure, et al., "Photobiomodulation Therapy in Head and Neck Cancer-Related Lymphedema: A Pilot Feasibility Study," *Integrative Cancer Therapies* 20 (2021): 15347354211037938, https://doi.org/10.1177/15347354211037938.

39. A. G. Tritter, P. T. Spiller, M. L. Brown, P. M. Weinberger, and C. O. Nathan, "Pilot Study: Pneumatic Compression Garment Therapy for Postradiotherapy Laryngopharyngeal Edema," *Ear, Nose, & Throat Journal* 101, no. 1 (2022): 54–58, https://doi.org/10.1177/0145561320942362.

40. C. Gutiérrez, H. N. Mayrovitz, S. H. S. Naqvi, and R. J. Karni, "Longitudinal Effects of a Novel Advanced Pneumatic Compression Device on Patient-Reported Outcomes in the Management of Cancer-Related Head and Neck Lymphedema: A Preliminary Report," *Head & Neck* 42, no. 8 (2020): 1791–1799, https://doi.org/10.1002/hed.26110.

41. C. B. Shires, P. Harris, and K. Dewan, "Feasibility of Machine-Delivered Sequential Massage for the Management of Lymphedema in the Head and Neck Cancer Survivor," *Laryngoscope Investig Otolaryngol* 7, no. 3 (2022): 774–778, https://doi.org/10.1002/lio2.810.

42. H. N. Mayrovitz, S. Ryan, and J. M. Hartman, "Usability of Advanced Pneumatic Compression to Treat Cancer-Related Head and Neck Lymphedema: A Feasibility Study," *Head & Neck* 40, no. 1 (2018): 137–143, https://doi.org/10.1002/hed.24995.

43. S. H. Ridner, M. S. Dietrich, J. Deng, S. L. Ettema, and B. Murphy, "Advanced Pneumatic Compression for Treatment of Lymphedema of the Head and Neck: A Randomized Wait-List Controlled Trial," *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer* 29, no. 2 (2021): 795–803, https://doi.org/10.1007/s00520-020-05540-8.

44. O. Micke, F. Bruns, R. Mücke, et al., "Selenium in the Treatment of Radiation-Associated Secondary Lymphedema," *International Journal of Radiation Oncology, Biology, Physics* 56, no. 1 (2003): 40–49, https://doi.org/10.1016/s0360-3016(02)04390-0.

45. T. Zimmermann, H. Leonhardt, S. Kersting, S. Albrecht, U. Range, and U. Eckelt, "Reduction of Postoperative Lymphedema After Oral Tumor Surgery With Sodium Selenite," *Biological Trace Element Research* 106, no. 3 (2005): 193–203, https://doi.org/10.1385/BTER:106:3:193.

46. N. Mangla, A. Carlson, A. Wakil, N. Wu, and E. J. Wladis, "Pemetrexed-Associated Eyelid Edema: Effective Treatment by Excision of Lymphedematous Eyelid Tissue," *Ophthalmic Plastic & Reconstructive Surgery* 31, no. 6 (2015): e155–e157, https://doi.org/10.1097/IOP.0000000000000186.

47. S. Sagili, D. Selva, and R. Malhotra, "Eyelid Lymphedema Following Neck Dissection and Radiotherapy," *Ophthalmic Plastic & Reconstructive Surgery* 29, no. 6 (2013): e146–e149, https://doi.org/10.1097/IOP.0b013e3182831c11.

48. R. Chalasani and A. McNab, "Chronic Lymphedema of the Eyelid: Case Series," *Orbit* 29, no. 4 (2010): 222–226, https://doi.org/10.3109/01676831003695735.

49. S. Withey, P. Pracy, F. Vaz, and P. Rhys-Evans, "Sensory Deprivation as a Consequence of Severe Head and Neck Lymphoedema," *Journal of Laryngology and Otology* 115, no. 1 (2001): 62–64, https://doi.org/10.1258/0022215011906830.

50. Y. Zeng, R. Prasad, R. D. King, et al., "AIDS-Related Kaposi Sarcoma Associated With Steroid-Unresponsive Periorbital Lymphedema That Responded to Chemotherapy," *American Journal of Case Reports* 24 (2023): e938801, https://doi.org/10.12659/AJCR.938801.

51. Z. Y. Li, C. C. Chi, and S. Q. Cai, "Case Report: Morbihan Disease Treated With Tofacitinib Successfully," *Frontiers in Immunology* 14 (2023): 1177316, https://doi.org/10.3389/fimmu.2023.1177316.

52. T. Gurgenci, R. Cree, M. Jessop, J. Lomas, and P. Good, "Hypertonic Packs to Reverse Blindness Caused by Facial Lymphoedema in the Setting of Head and Neck Cancer—A Case Report," *Palliative Medicine* 36, no. 3 (2022): 555–559, https://doi.org/10.1177/02692163211069768.

53. B. G. Smith and J. S. Lewin, "Lymphedema Management in Head and Neck Cancer," *Current Opinion in Otolaryngology & Head and Neck Surgery* 18, no. 3 (2010): 153–158.

54. J. Lomas, T. Gurgenci, C. Jackson, and D. Campbell, "Temporomandibular Dysfunction," *Australian Journal of General Practice* 47, no. 4 (2018): 212–215, https://doi.org/10.31128/AFP-10-17-4375.

55. S. Singer, J. Arraras, I. Baumann, et al., "Quality of Life in Head and Neck Cancer Patients Receiving Multimodal or Targeted

Therapy—Update of the EORTC QLQ-H&N35, Phase I," *Head & Neck* 35 (2013): 1331–1338.

56. A. Pigott, B. Brown, N. White, et al., "A Prospective Observational Cohort Study Examining the Development of Head and Neck Lymphedema From the Time of Diagnosis," *Asia-Pacific Journal of Clinical Oncology* 19, no. 4 (2023): 473–481, https://doi.org/10.1111/ajco.13843.

57. I.-C. Tan, E. A. Maus, J. C. Rasmussen, et al., "Near-Infrared Fluorescence Imaging of Lymphatics in Head and Neck Lymphedema," *In Advanced Biomedical and Clinical Diagnostic Systems IX* 7890 (2011): 69–78, https://doi.org/10.1117/12.873673.

58. T. Yamamoto, T. Iida, and N. Matsuda, "Indocyanine Green (ICG)-Enhanced Lymphography for Evaluation of Facial Lymphoedema," *Journal of Plastic, Reconstructive & Aesthetic Surgery* 64, no. 11 (2011): 1541–1544, https://doi.org/10.1016/j.bjps.2011.05.025.

59. A. Piggot, A. McCann, H. Suami, and S. Trevethan, "Lymphatic Drainage Patterns in Head and Neck Lymphoedema: A Preliminary Imaging Study With Indocyanine Green Lymphography," *Wounds International* 18, no. 1 (2023): 28–33.

60. E. A. Maus, I. C. Tan, J. C. Rasmussen, et al., "Near-Infrared Fluorescence Imaging of Lymphatics in Head and Neck Lymphedema," *Head & Neck* 34, no. 3 (2012): 448–453, https://doi.org/10.1002/hed.21538.

61. E. M. Verhey, L. A. Kandi, Y. S. Lee, et al., "Outcomes of Lymphovenous Anastomosis for Lower Extremity Lymphedema: A Systematic Review," *Plastic and Reconstructive Surgery. Global Open* 10, no. 10 (2022): e4529, https://doi.org/10.1097/GOX.0000000000004529.

62. R. P. Tart, S. K. Mukherji, A. J. Avino, S. P. Stringer, and A. A. Mancuso, "Facial Lymph Nodes: Normal and Abnormal CT Appearance," *Radiology* 188, no. 3 (1993): 695–700, https://doi.org/10.1148/radiology.188.3.8351335.

63. F. Cabral, L. C. Lubbe, M. M. Nóbrega, D. L. Obadia, R. Souto, and A. C. Gripp, "Morbihan Disease: A Therapeutic Challenge," *Anais Brasileiros de Dermatologia* 92, no. 6 (2017): 847–850, https://doi.org/10.1590/abd1806-4841.20174485.

64. S. G. Rockson, "Lymphedema," *American Journal of Medicine* 110 (2001): 288–295.

65. H. Starmer, M. G. Cherry, J. Patterson, B. Young, and J. Fleming, "Assessment of Measures of Head and Neck Lymphedema Following Head and Neck Cancer Treatment: A Systematic Review," *Lymphatic Research and Biology* 21, no. 1 (2023): 42–51, https://doi.org/10.1089/lrb.2021.0100.

66. A. Purcell, J. Nixon, J. Fleming, A. McCann, and S. Porceddu, "Measuring Head and Neck Lymphedema: The "ALOHA" Trial," *Head & Neck* 38, no. 1 (2016): 79–84, https://doi.org/10.1002/hed.23853.

67. J. Deng, M. S. Dietrich, K. J. Niermann, et al., "Refinement and Validation of the Head and Neck Lymphedema and Fibrosis Symptom Inventory," *International Journal of Radiation Oncology, Biology, Physics* 109, no. 3 (2021): 747–755, https://doi.org/10.1016/j.ijrobp.2020.10.003.