Oral Oncology 169 (2025) 107671

Contents lists available at ScienceDirect

Oral Oncology

journal homepage: www.elsevier.com/locate/oraloncology

Head and neck lymphedema after radiotherapy – Prevalence, changes and associated factors – a prospective observational cohort study

A. Hagren [a,b,*], J. Sjövall [b,d], C. Brogårdh [a,c], K. Johansson [a], E. Ekvall Hansson [a,c]

[a] Department of Health Sciences, Lund University, Sölvegatan 19, 223 62 Lund, Sweden
[b] Department of Otorhinolaryngology, Head & Neck Surgery, Skåne University Hospital, Lasarettsgatan 21, 221 41 Lund, Sweden
[c] Department of Neurology, Rehabilitation Medicine, Memory Disorders and Geriatrics, Skåne University Hospital, Entrégatan 7, 221 85 Lund, Sweden
[d] Department of Clinical Sciences, Lund University, Sölvegatan 19, 223 62 Lund, Sweden

ARTICLE INFO

Keywords:
Lymphedema
Head and neck neoplasm
Squamous cell carcinoma
Radiotherapy
Body mass index
Physical activity
Cohort studies

ABSTRACT

Background: There is an increasing incidence of oropharyngeal squamous cell carcinoma (OPSCC) survivors living with treatment-related head and neck lymphedema (HNL). This study aimed to determine (i) the prevalence of external HNL, (ii) changes in HNL over a nine-month period post-treatment, and (iii) factors associated with HNL among patients with OPSCC treated with (chemo)radiotherapy.

Methods and Results: Fifty patients were recruited (mean age 64 years), where two thirds were male. HNL was assessed with a lymph scanner in seven facial points, and with a measuring tape at three levels, before treatment, and three and nine months post-treatment. Paired sample *t*-test was used to calculate changes in HNL and logistic regression analysis identified factors associated with HNL, including age, gender, BMI, physical activity, addition of chemotherapy and radiation dose. At three months post-treatment, 80 % of patients had HNL, which decreased to 69 % nine months post-treatment. The submental point was the most common location for HNL and showed the greatest change over the nine-month period. Differences in circumferential measurements were small. Low physical activity increased the odds of developing HNL ($p = 0.011$).

Conclusions: HNL is a common side effect after (chemo)radiotherapy treatment. The changes in HNL at the submental point seem to be greatest while the changes in neck circumferential are small. Since a low level of physical activity increased the risk of developing HNL, it may be important to encourage physical activity in this population.

Introduction

The Western world is experiencing an increasing incidence of oropharyngeal squamous cell carcinoma (OPSCC) due to human papillomavirus (HPV)-driven tumours [1–3]. The standard treatment for OPSCC is (chemo)radiotherapy, (c)RT. Regardless of treatment, i.e., surgery, (c)RT or in combination, the prognosis for the HPV-associated OPSCC is excellent [2] leaving an increasing number of survivors with common long standing side effects such as fibrosis, swallowing difficulties, xerostomia and fatigue. Another, often overlooked but frequent side effect, is head and neck lymphedema (HNL) [4–6].

The lymphatic system of the head and neck consists of superficial and deep vessels that drain into inferior deep cervical nodes in the jugular trunk and enter the right lymphatic duct or, on the left side of the neck, the thoracic duct. HNL occurs when the lymphatic system fails to transport lymph fluid either because of the direct impact of a neck dissection or tissue fibrosis caused by the surgery and/or (c)RT [7]. There are two different types of HNL: external (in the face, neck and submental region) which this study is focused on, and internal (in the oral cavity, pharynx and larynx) [8].

HNL can cause inflammation, fibrosis and reduced mobility, which may lead to sensations of swelling and heaviness. Severe HNL can result in impaired communication, respiration and swallowing [9,10]. Patients with HNL also experience a negative body image which may lead to anxiety, depression and a decreased quality of life [11–13]. Early diagnosis is therefore crucial to improve the possibility of reducing HNL before it becomes chronic.

There are several assessment methods used for diagnosing HNL,

* Corresponding author.
E-mail addresses: agneta.hagren@med.lu.se (A. Hagren), johanna.sjovall@med.lu.se (J. Sjövall), christina.brogardh@med.lu.se (C. Brogårdh), karin.johansson@med.lu.se (K. Johansson), eva.ekvall_hansson@med.lu.se (E. Ekvall Hansson).

https://doi.org/10.1016/j.oraloncology.2025.107671
Received 9 April 2025; Received in revised form 2 September 2025; Accepted 2 September 2025
Available online 12 September 2025

classifying its severity, quantifying the extent of lymphedema, and monitoring its progression. So far, there is no consensus on which method should be used to assess HNL. The various assessment methods include patient-reported and clinician-reported assessments that rely on rating scales [14]. However, these assessments are subjective and have limited evidence supporting their validity and reliability in clinical settings [15]. In addition, technical assessment methods, such as ultrasound and 3D scanning [16,17] exist but require further validation studies before they can be implemented. CT scans, an imaging-based assessment, provide valuable information but are entailed with radiation exposure and high cost, making it less suitable for routine monitoring [14,18].

Objective measurements of local tissue water can be obtained by a lymph scanner, which identifies and distinguishes different levels of lymphedema. The lymph scanner has been validated [19], demonstrated excellent interrater reliability in the head and neck region [20], and normal reference values have recently been established [21,22]. The lymph scanner has been used to assess changes in HNL at the submental measuring point [11,20]. However, after head and neck cancer (HNC) treatment, HNL develops in several different sites in the head and neck area, making it essential to measure multiple points to obtain a more accurate picture. Another objective and reliable method (showing sufficient intra- and interrater reliability) is tape measurement of the neck circumference [20,21,23].

There are large discrepancies in the reporting of the prevalence of HNL, ranging from 10 % to 90 % [10,24,25]. It is likely that the tumour location and the type of treatment affect the prevalence of HNL and subsequently vary between the HNC subsites. In addition to treatment, different factors such as gender, BMI and level of physical activity may affect the prevalence of lymphedema [26–28], but more knowledge is needed.

Taken together, there is an increasing incidence of OPSCC survivors living with treatment-related HNL. Consequently, there is a need for a deeper understanding of HNL, including its prevalence, development over time, and factors associated with its occurrence. Such knowledge is important to improve the management of HNL.

Aim

The aim of this study was to determine (i) the prevalence of external HNL, (ii) changes in external HNL over a nine-month period post-treatment, and (iii) factors associated with external HNL, among patients with OPSCC and treated with (c)RT.

Materials and methods

Study design

This study used a single-center exploratory, prospective, cohort design. It was approved by the Swedish Ethical Review Authority (ref. no.2020–01066) and was registered at ClinicalTrials.gov (ref.no. NCT05316974). Reporting has been done according to the STROBE guidelines.

Setting

The study was conducted at Skåne University Hospital, Sweden, a tertiary referral hospital where all HNC patients in the Southern Health Care Region, with a population of approximately 1.9 million, are assessed and treated. Recruitment of participants occurred from October 2022 to November 2023 and the patients were followed for nine months post-treatment.

Participants

Patients aged 18 years or older, with biopsy-confirmed OPSCC (stage I-IV), as assessed by the multidisciplinary tumour board and planned for curatively intended (c)RT, were eligible for inclusion. Exclusion criteria were pregnancy, previous treatment for HNC, as well as pre-treatment surgery or Botox injections in the head and neck area. On the first visit to the Dept. of Oncology, the patients received oral and written information about the study and were invited to participate. Informed consent was obtained from all patients before inclusion.

Data collection

HNL was assessed by two methods: with a lymph scanner to assess local tissue water, and with a measuring tape to assess neck circumference. The HNL assessments were performed before treatment began as part of clinical routine (baseline), and three and nine months after treatment completion. All patients were measured in the morning and all measurements were performed by the first author (AH).

Diagnosis, tumour stage, oncological treatment (radiation fields and dose, chemotherapy) and age at diagnosis, were extracted from medical records. Information on BMI, smoking habits, and ratings of physical activity was collected at baseline, and at three and nine months post-treatment. Physical activity level was self-assessed based on Frändin and Grimby's Activity Scale. The scale consists of six levels that categorise activity from complete rest to high-intensity physical activity [29].

As part of the standard follow-up procedure, all patients were offered an appointment with a physiotherapist and given instructions in manual lymphatic drainage for daily self-care. Any interventional therapy for HNL during the follow-up was not cause for exclusion but was registered.

Measurements of local tissue water

The lymph scanner MoistureMeterD, Delfin Technologies Ltd, Finland, was used to assess local tissue water. The technique is based on an ultrahigh-frequency electromagnetic waves of 300 MHz which penetrate the skin to a depth of 2.5 mm. The lymph scanner registers the reflected electromagnetic waves and are displayed as the percentage of tissue water content (PWC). A standardised positioning protocol, including seven facial points, was used [21]. Points 1 to 3 were identified on both sides of the face and neck (Table 1). Measuring tape and soft pen were used to identify and mark the points. The patient was placed in an upright sitting position with the head facing straight forward.

Measurements of neck circumference

Neck circumference measurements (CM), in cm, were collected by a measuring tape held flat against the skin at three levels:

Upper level: the highest possible circumferential level of the neck, inferior to the mandible.

Middle level: the circumferential level right over the thyroid cartilage.

Lower level: the lowest possible circumferential level of the neck.

Table 1
Summary of the Locations for the Measuring Points.

Measuring points (P)	
P1	The point in the middle of a line between the nasal alar cartilage and the ear lobule
P2	The point in the middle of a line between P4 and 1 cm below the mandibular angle
P3	The point in the middle of a line between the lobule and the jugular fossa
P4	The point 8 cm below the midline of the lower lip

Definition of HNL

HNL was defined as an increase in PWC or CM of 2 standard deviations (SD) or more compared to normal reference values of tissue water in the head and neck area [21], at any measuring point or circumferential level three months after the HNC treatment.

Statistical methods

Demographic data and clinical characteristics were presented as mean and SD (continuous variables) or numbers and percent (categorical variables). Data was analysed using IBM SPSS version 28. A p-value < 0.05 was considered statistically significant. The PWC and CM values were normally distributed at all measuring points and occasions. The prevalence of HNL was calculated three and nine months post-treatment. Paired sample *t*-test was used to calculate the changes in tissue water between the post-treatment assessments. The Bonferroni method was applied to correct for multiple comparisons related to the changes for PWC and CM. Thus, for statistical significance a p-value of $0.05/7 = 0.007$ was applied for PWC and $0.05/3 = 0.017$ for CM. Univariate logistic regression analyses (HNL as dependent variable, dichotomized as yes or no) were used to determine factors associated with HNL at three and nine months. The binary independent variables were gender (male/female), age (<65/≥65), chemotherapy (yes/no), contralateral radiotherapy at any level (yes/no), BMI (<25/≥25) and physical activity according to Frändin and Grimby's Activity Scale (1–3/4–6).

Result

Participants

Fifty patients with OPSCC, planned for (c)RT with curative intent, were recruited. In total, 84 % of the patients (n = 42) completed both post-treatment assessments. A flowchart is presented in Fig. 1.

Table 2 presents participants' demographics and clinical characteristics. Their mean age was 64 years and two-thirds were male. Only a few patients were smokers and 52 % had a BMI ≥ 25 before the start of treatment. The most common tumour subsite was the base of tongue, and most patients had stage I or II HPV-positive tumours. All macroscopic diseases were treated with IMRT to a dose of 68 Gy (2 Gy per fraction, five fractions per week). Ninety-four percent of the patients received 68 Gy ipsilaterally to one or more neck levels, usually levels two and three. Seventy-two percent of the patients received an elective dose of 54 Gy to contralateral lymph nodes.

The mean BMI decreased from baseline to nine months from 25.7 to 20.7 ($p < 0.001$). Half of the patients scored 4 to 6 on the physical activity scale at baseline. Physical activity scores were lowest three months post-treatment (Table 2).

Table 2
Patients' Demographics and Clinical Characteristics (n = 50) at Baseline and Post-Treatment.

Demographics and characteristics	*Baseline n = 50*	*3 months n = 45*	*9 months n = 45*
Male / Female, n (%)	33 (66) / 17 (34)		
Age, mean (SD, range)	64 (10.2, 46–88)		
P16, n (%)			
Positive / Negative	45 (90) / 5 (10)		
T classification, n (%)			
T1	10 (20)		
T2	26 (52)		
T3	7 (14)		
T4	7 (14)		
N classification, n (%)*			
N0	4 (8)		
N1	33 (66)		
N2	11 (22)		
N3	2 (4)		
BMI, mean (SD)	25.7 (3.5)	23.3 (2.9)	20.7 (3.0)
<25, n (%)	24 (48)	33 (73)	41 (91)
≥25, n (%)	26 (52)	12 (27)	4 (9)
Smoking, n (%)			
Smokers / Nonsmokers	5 (10) /45 (90)	2 (4) / 43 (96)	2 (4) / 43 (96)
Physical activity n, (%)**			
1—3	25 (50)	24 (55)	20 (44)
4—6	25 (50)	20 (45)	25 (56)

*The five patients with P16-negative tumours had N classification N0 n = 1, N1 n = 1, N2b n = 3, the four patients with lymph node metastasis are referred to N1 in the table. **Missing data for one patient at three months.

Prevalence of HNL

Table 3 presents the prevalence of HNL over the nine-month period. HNL, measured in PWC, was registered in 80 % (n = 36) of the patients in one or more measuring points at three months. Nine months post-treatment HNL was registered in 69 % (n = 31). At three months the female/male ratio of HNL was 36 % (n = 13)/64 % (n = 23) and at 9 months the female/male ratio was 42 % (n = 13)/58 % (n = 18).

The prevalence of HNL varied between the different measurement points. Among the patients with HNL, submental (P4) lymphedema was the most frequent three months post-treatment, occurring in 72 % (n = 26). At nine months, HNL was most frequent at the lowest point at the left side of the neck (P3), where 61 % (n = 19) of the patients had

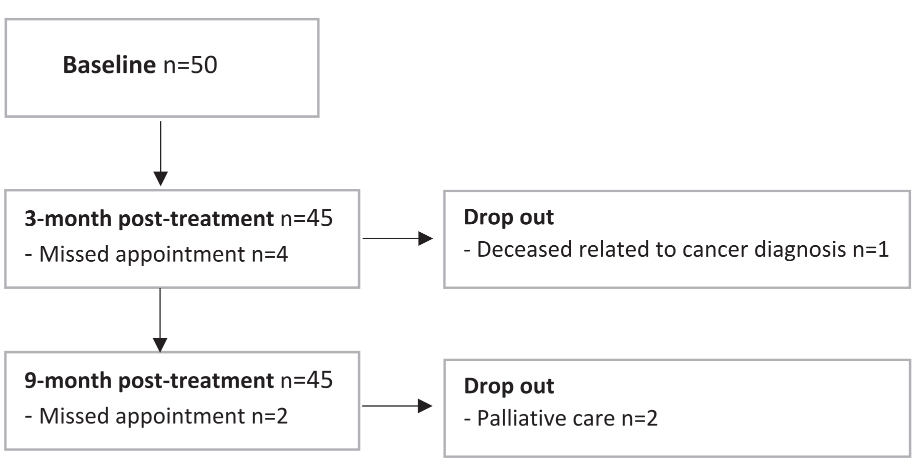

Fig. 1. Flowchart of participants for analysis at different time points.

Table 3
Percentage of Tissue Water Content (PWC) and Neck Circumferences Measurements (CM) at Baseline and Prevalence of Head and Neck Lymphedema (HNL) over the Nine-Month Period.

	MeasurementBaseline(n = 50) Mean (SD)	*Measurement 3 months (n = 45) Mean (SD)*	*Prevalence of HNL 3 months n (%)**	*Measurement9 months (n = 45) Mean (SD)*	*Prevalence of HNL 9 months n (%)**
PWC (%)					
P1 Right	35.0 (9.8)	38.0 (8.5)	2 (5.6)	41.2 (6.8)	6 (19.4)
P1 Left	35.8 (8.4)**	38.8 (9.9)	5 (13.9)	40.9 (7.2)	3 (9.7)
P2 Right	36.6 (9.4)***	45.3 (9.4)	13 (36.1)	44.6 (7.9)	11 (35.5)
P2 Left	38.5 (7.4)	48.0 (8.4)	19 (52.8)	45.2 (6.8)	12 (38.7)
P3 Right	40.4 (7.9)	47.0 (9.0)	10 (27.8)	46.7 (7.5)	9 (29.0)
P3 Left	39.3 (8.1)	49.9 (8.7)	23 (63.9)	47.3 (8.0)	19 (61.3)
P4	33.7 (10.5)	47.7 (7.9)	26 (72.2)	42.8 (9.4)	15 (48.4)
CM (cm)					
CM upper	40.6 (3.6)	41.5 (3.4)	6 (54.4)	40.6 (3.3)	4 (50.0)
CM middle	39.0 (3.2)	39.4 (2.9)	4 (36.4)	38.6 (3.0)	4 (50.0)
CM lower	38.6 (3.0)	38.8 (2.8)	7 (63.6)	38.0 (2.6)	4 (50.0)

P = measuring point, SD = standard deviation. *The prevalence of HNL is presented as the number (%) of patients with HNL at any measuring point according to PWC at 3 months post-treatment (n = 36/45), and CM (n = 11/45), and at 9 months post-treatment according to PWC (n = 31/45), and CM (n = 8/45). **Not measurable point at baseline for one patient due to beard. ***Not measurable point at baseline for one patient due to tumour.

Table 4
Changes in Percentages of Water Content (PWC) and Circumferential Measurements (CM) over the Nine-Month Period.

	Changes between baseline and 3 months Mean diff (95 % CI)	*p-value*	*Changes between 3 and 9 months Mean diff (95 % CI)*	*p-value*	*Changes between baseline and 9 months Mean diff (95 % CI)*	*p-value*
PWC (%)						
P1 Right	2.84 (0.20 to 5.47)	0.035	2.78 (0.52 to 5.04)	0.017	6.04 (3.73 to 8.35)	**<0.001**
P1 Left	3.19 (−0.35 to 6.74)	0.076	2.34 (−0.69 to 5.37)	0.127	5.27 (2.89 to 7.64)	**<0.001**
P2 Right	8.77 (6.17 to 11.37)	**<0.001**	−0.39 (−2.84 to 2.06)	0.750	8.08 (5.41 to 10.74)	**<0.001**
P2 Left	9.62 (6.75 to 12.49)	**<0.001**	−2.26 (−3.93 to −0.59)	0.009	6.81 (4.59 to 9.02)	**<0.001**
P3 Right	6.70 (4.40 to 9.01)	**<0.001**	−0.12 (−2.32 to 2.08)	0.914	6.16 (4.27 to 8.04)	**<0.001**
P3 Left	11.05 (8.25 to 13.86)	**<0.001**	−2.49 (−4.36 to −0.62)	0.010	8.07 (5.40 to 10.74)	**<0.001**
P4	14.18 (10.73 to 17.63)	**<0.001**	−4.63 (−7–20 to −2.07)	**<0.001**	8.55 (4.81 to 12.28)	**<0.001**
CM (cm)						
CM A	0.98 (0.29 to 1.67)	**0.007**	−0.98 (−1.46 to −0.49)	**<0.001**	0.00 (−0.72 to 0.72)	1.000
CM B	0.49 (−0.45 to 1.02)	0.071	−0.84 (−1.28 to −0.40)	**<0.001**	−0.42 (−1.00 to 0.16)	0.148
CM C	0.30 (−0.17 to 0.76)	0.209	−0.82 (−1.20 to −0.44)	**<0.001**	−0.59 (−1.11 to −0.07)	0.028

The changes of PWC and CM are presented as mean difference (95 %CI for mean = 95 % confidence interval). Numbers of patients at baseline to three months post-treatment according to PWC n = 45 and CM n = 44 due to missing data for one patient. Numbers of patients at three months to nine months post-treatment according to PWC n = 42 and CM n = 41. Numbers of patients at baseline to nine months according to PWC and CM n = 45. The significance level after Bonferroni correction was for PWC 0.007 and for CM 0.017.

lymphedema, followed by the submental point 48 % (n = 15). HNL was least common in the measuring points at the cheeks (P1) at both three and nine months (Table 3).

The prevalence of HNL, measured as CM, was registered in 25 % (n = 11) of the patients, in one or more of the three levels three months post-treatment. Nine months post-treatment HNL was found in 18 % (n = 8). The prevalence of HNL was almost equal between the three levels (Table 3).

Changes in PWC and CM

Table 4 presents the changes in PWC and CM over the nine-month period. PWC increased in all measuring points from baseline to the three months post-treatment. After Bonferroni correction the increase was significant ($p < 0.007$) in five out of seven measuring points. All values, except at the cheeks (P1), decreased between three and nine months, with statistical significance remaining at the submental point (P4) after correction for multiple comparisons. PWC increased at all measuring points from baseline to nine months ($p < 0.001$). The changes in PWC were greatest at the submental point (P4) on both measuring occasions.

The changes in the neck CM were small. A significant increase was observed at the upper level from baseline to three months post-treatment. The changes between three and nine months decreased significantly from −0.98 (upper level) to −0.82 (lower level), and the values were lower than at baseline. No significant changes in circumferential levels between baseline and nine months post-treatment were found after Bonferroni correction was applied (Table 4).

Factors associated with HNL

Table 5 presents factors potentially associated with HNL (dependent variable) three and nine months post-treatment. The univariate logistic regression analysis revealed that a lower level of physical activity (scoring between 1–3) at baseline was significantly associated with a higher prevalence of HNL ($p = 0.011$). Odds ratio was 16.62 (CI 1.91 to 144.24). At nine months the result remained significant ($p = 0.012$).

Discussion

To the best of our knowledge, this is the first study that has evaluated the prevalence, changes, and factors associated with HNL among patients who underwent (c)RT for OPSCC. We found that HNL was common after (c)RT, most prevalent three months post-treatment and decreased slightly at nine months. More patients with HNL were identified with the lymph scanner than by the measuring tape. A low level of physical activity at baseline was significantly associated with a higher prevalence of HNL.

Table 5
Logistic Regression Analyses of Factors Associated with Head and Neck Lymphedema.

Independent variable	3 months post-treatment Odds ratio (95 % CI)	p-value	9 months post-treatment Odds ratio (95 % CI)	p-value
Gender (ref female vs male)	0.50 (0.09 to 2.80)	0.435	0.23 (0.04 to 1.21)	0.083
Age (ref < 65 vs ≥ 65)	1.79 (0.39 to 8.29)	0.457	0.72 (0.20 to 2.56)	0.615
Chemotherapy (ref no vs yes)	*	0.999	6.19 (0.71 to 54.16)	0.099
Contralateral radiotherapy (ref no vs yes)	1.50 (0.31 to 7.27)	0.615	1.36 (0.36 to 5.19)	0.655
BMI at baseline (ref < 25 vs ≥ 25)	1.40 (0.32 to 6.07)	0.655	3.46 (0.89 to 13.51)	0.074
Physical activity at baseline (ref 4–6 vs 1–3)	4.16 (0.75 to 22.90)	0.102	16.62 (1.91 to 144.24)	**0.011**
Physical activity post-treatment(ref 4–6 vs 1–3)	3.00 (0.64 to 14.02)	0.163	8.31 (1.58 to 43.62)	**0.012**

CI: confidence interval. Head and Neck Lymphedema (dependent variable) was dichotomized (yes/no). Numbers of patients with HNL at.
any measuring point according to PWC at three months (n = 36/45) and at nine months (n = 31/45). Physical activity according to Frändin and Grimby's Activity Scale. *Chemotherapy has no odds ratio at three months because all participants who received chemotherapy had HNL.

Prevalence of HNL

Several studies have examined the prevalence and progression of HNL in cancer patients with varying findings and methods used. According to Jeans et al., HNL was prevalent in 71 % of patients at three months, decreased by six months (58 %), and was almost resolved (10 %) at 12 months [25]. In contrast, Ridner et al. found that approximately 75 % of patients had HNL more than one year after treatment completion [10]. This finding is more consistent with our study, where HNL, measured by PWC, was present in 80 % of patients three months after treatment and in 69 % nine months post-treatment. However, the studies are difficult to compare due to differences in assessment methods. Ridner et al. [10] used a rating scale, and Jeans et al. [25] used various assessment techniques, including measuring local tissue water with a lymph scanner, but only in one measuring point, making it difficult to compare results directly. Additionally, our study comprised OPSCC patients treated with (c)RT and in the previous studies [10,25] different HNC diagnoses and cancer treatments were included.

In the present study lymph node metastases in the neck were equally common on the right and left sides, although right-sided primary tumours were slightly more prevalent. The submental measuring point (P4) was the most common location for HNL. It was also more common in the lower part of the left side of the neck (P3 left) compared to the right side (P3 right). The reason that the caudal measuring points were more affected by HNL might be explained by lymph fluid flowing in all directions in the peripheral parts of the lymphatic system and can therefore be affected by gravity in an upright position [30]. If the pumping collectors of the lymphatic system are damaged by radiation, lymph accumulates on the cheeks and sinks to the lowest point (P4)[31].

Moreover, the PWC values for our patients before treatment were slightly lower than those of the healthy population [21]. This is a remarkable difference from the study by Ridner et al. who reported an HNL prevalence of 63 % before treatment [10]. Even though a more advanced cancer stage might contribute to imparity, the discrepancy in assessment methods is a more likely factor.

Changes in PWC and CM

The submental measuring point (P4) was not only the most common location for HNL, it also showed the greatest change over time. However, we recommend that all measuring points should be assessed until more is known about their clinical relevance, and further research is therefore needed.

An interesting, previously not observed, finding is that PWC at the cheeks (P1) continued to increase nine months post-treatment. Either submandibular and submental fibrosis prevents the oedema from decreasing or the remaining measuring points are in peripheral radiation fields where the system recovers more quickly. A likely explanation for the decrease is that lymphedema may undergo spontaneous regression over time, as seen in radiation treatment for breast cancer. Therefore, a later follow-up, 18 to 24 months post-treatment, would also provide further insights into the long-term progression of HNL.

The neck CM decreased at nine months and was even lower than at baseline, likely due to weight loss. However, the changes were small and HNL was detected in fewer patients when measured with a measuring tape compared to a lymph scanner. Accordingly, a measuring tape should not be the only method of choice in the assessment of HNL.

Factors associated with HNL

In the logistic regression analyses, self-reported low physical activity both before treatment (p = 0.011) and nine months post-treatment (p = 0.012) considerably increased the odds for HNL, suggesting that physical activity could have a beneficial effect on HNL. This aligns with previous studies showing that physical activity can reduce arm and leg lymphedema [32]. However, the physical activity reported by the patients was not focused on movements in the head and neck area, but on the overall amount of physical activity. The reason why our participants scored the lowest physical activity levels three months post-treatment is not entirely clear, but may be due to fatigue, appetite loss and other side effects following the treatment. Thus, more knowledge about head- and neck-specific training and the importance of exercise in managing lymphedema is warranted.

Several studies have shown a correlation between high BMI and lymphedema in breast cancer and gynaecological cancer [26–28,33,34] and our HNL results have a similar trend (p = 0.074 at nine months). Few studies have investigated the relationship between high BMI and HNL, probably because patients with HNC typically experience significant weight loss during treatment. However, an article by Tribius et al. showed that a higher BMI was a predictor of HNL after multimodal therapy in HNC treatment [35].

Furthermore, our patient population was a homogeneous group where the ipsilateral radiation dose was standardized to 68 Gy, 2 Gy/fraction. Therefore, these factors were not included in the regression analysis. Patients who received additional chemotherapy showed an increased risk of developing HNL nine months post-treatment, although only a few patients received chemotherapy, and the results were not statistically significant. Tribius et al. have shown that chemotherapy was predictive for HNL three months after treatment but not in later follow-ups [35]. A larger cohort with different treatment strategies is needed to analyse the long-term effect of chemotherapy on HNL.

Strengths and limitations

A strength of the current study is the homogenous group of patients with OPSCC receiving standardised treatment with (c)RT. In terms of cancer stage, gender, age, HPV-positivity and treatment, the cohort is consistent with the Swedish OPSCC patients [36]. We therefore believe that the results, despite being from a single-center study, are representative. Another advantage is the objective assessment methods, with confirmed interrater reliability in the head and neck area [21,23]. While a larger sample size would have been desirable, the number of patients in this exploratory study was considered sufficient to get adequate analyses. The study has a follow-up time of nine months, which may not capture long-term outcomes or late-emerging side effects. Longer follow-up post-treatment is needed to fully understand the trajectory of HNL.

As different measuring methods could be used to assess HNL and no specific method is recommended, our data is somewhat difficult to compare with other studies. Additionally, the cut-off value for HNL was based on reference values for healthy individuals. However, the patients' measurement values before treatment, at baseline, corresponded well with the values for healthy individuals [21]. HNL was defined as an increase in PWC or CM of 2 SD or more compared to normal reference values of tissue water in the head and neck area, at any measuring point or circumferential level three months after HNC treatment. The time point has also been used by Deng et al., who defined HNL as swelling that develops three months after HNC treatment [24]. At this time point, the acute side effects of radiation therapy have healed and therefore considered appropriate.

Clinical implications

Measuring local tissue water is a simple, objective method that allows repeated measurements and comparisons at different time points. The method is therefore well-suited for use in clinical practice. We suggest that the definition of HNL should be 2 SD above the normal reference value. The PWC changed significantly from baseline to nine months, unlike the changes in neck CM. This makes measurement of PWC more suitable than CM for assessing HNL. Furthermore, early diagnosis of lymphedema after cancer treatment and early treatment of HNL is important to prevent further development and deterioration [37–39]. If HNL is left untreated, it could be a chronic, irreversible oedema and development of fibrofatty deposits and fibrosis with lifelong discomfort and problems for the patients [6]. It is therefore important to diagnose HNL early and improve self-care and HNL treatment. Since low physical activity was associated with an increased risk of developing HNL, it is also important to encourage patients to engage in physical activity.

Conclusions

This prospective study on patients treated with (c)RT for OPSCC confirms that HNL is a common side effect and most patients had persistent HNL nine months after treatment completion. The changes in HNL at the submental point seem to be greatest while the changes in neck circumferential are small. Since a low level of physical activity increased the risk of having HNL, it may be important to encourage physical activity.

Funding

This work was supported by Sjöbergs foundation, grant number 2023-01-03:12 and Skåne University hospital Foundation, grant number 92624.

CRediT authorship contribution statement

A. Hagren: Writing – review & editing, Writing – original draft, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **J. Sjövall:** Writing – review & editing, Writing – original draft, Supervision, Data curation, Conceptualization. **C. Brogårdh:** Writing – review & editing, Writing – original draft, Supervision, Formal analysis, Conceptualization. **K. Johansson:** Writing – review & editing, Writing – original draft, Supervision, Conceptualization. **E. Ekvall Hansson:** Writing – review & editing, Writing – original draft, Supervision, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: [Eva Ekvall Hansson reports financial support was provided by Region Skåne. Eva Ekvall Hansson reports financial support was provided by Sjöberg Foundation. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.].

Acknowledgement

We also wish to acknowledge Katarina Lindbäck and Agnes Nilsson for their valuable administrative support, as well as Michael Miller for his careful language editing and Carl Walter for his assistance with the graphical abstract.

Data availability

Data will be made available on request.

References

[1] Lim YX, et al. *Clinical, morphologic and molecular heterogeneity of HPV-associated oropharyngeal cancer.* Oncogene 2023;42(40):2939–55.
[2] Lechner M, et al. *HPV-associated oropharyngeal cancer: epidemiology, molecular biology and clinical management.* Nat. Rev. Clin. Oncol. 2022;19(5):306–27.
[3] Faraji F, et al. *The prevalence of human papillomavirus in oropharyngeal cancer is increasing regardless of sex or race, and the influence of sex and race on survival is modified by human papillomavirus tumor status.* Cancer 2019;125(5):761–9.
[4] Brook I. *Late side effects of radiation treatment for head and neck cancer.* Radiat Oncol J 2020;38(2):84–92.
[5] Moroney LB, et al. *Helical intensity-modulated radiotherapy with concurrent chemotherapy for oropharyngeal squamous cell carcinoma: a prospective investigation of acute swallowing and toxicity patterns.* Head Neck 2018;40(9):1955–66.
[6] Murphy BA, et al. *Symptom control issues and supportive care of patients with head and neck cancers.* Clin. Adv. Hematol. Oncol. 2007;5(10):807–22.
[7] Rasmussen JC, et al. *Longitudinal monitoring of the head and neck lymphatics in response to surgery and radiation.* Head Neck 2017;39(6):1177–88.
[8] Deng J, et al. *Assessment and measurement of head and neck lymphedema: state-of-the-science and future directions.* Oral Oncol. 2015;51(5):431–7.
[9] Smith BG, Lewin JS. *Lymphedema management in head and neck cancer.* Curr. Opin. Otolaryngol. Head Neck Surg. 2010;18(3):153–8.
[10] Ridner SH, et al. *A prospective Study of the Lymphedema and Fibrosis Continuum in patients with Head and Neck Cancer.* Lymphat. Res. Biol. 2016;14(4):198–205.
[11] Deng J, et al. *Impact of secondary lymphedema after head and neck cancer treatment on symptoms, functional status, and quality of life.* Head Neck 2013;35(7):1026–35.
[12] McGarvey AC, et al. *Lymphoedema following treatment for head and neck cancer: impact on patients, and beliefs of health professionals.* Eur. J. Cancer Care 2014;23(3):317–27.
[13] Deng J, et al. *Differences of symptoms in head and neck cancer patients with and without lymphedema.* Support Care Cancer 2016;24(3):1305–16.
[14] Fadhil M, et al. *Systematic review of head and neck lymphedema assessment.* Head Neck 2022;44(10):2301–15.
[15] Deng J, et al. *Assessment of external lymphedema in patients with head and neck cancer: a comparison of four scales.* Oncol. Nurs. Forum 2013;40(5):501–6.
[16] Piso DU, et al. *Reproducibility of sonographic soft-tissue measurement of the head and neck.* Am. J. Phys. Med. Rehabil. 2002;81(1):8–12.
[17] Ozsoy U, Sekerci R, Ogut E. *Effect of sitting, standing, and supine body positions on facial soft tissue: detailed 3D analysis.* Int. J. Oral Maxillofac. Surg. 2015;44(10):1309–16.
[18] Akashi M, et al. *Computed Tomographic Evaluation of Posttreatment Soft-Tissue changes by using a Lymphedema Scoring System in patients with Oral Cancer.* Lymphat. Res. Biol. 2018;16(2):147–53.
[19] Nuutinen J, Ikäheimo R, Lahtinen T. *Validation of a new dielectric device to assess changes of tissue water in skin and subcutaneous fat.* Physiol. Meas. 2004;25(2):447–54.
[20] Purcell A, et al. *Measuring head and neck lymphedema: the "ALOHA" trial.* Head Neck 2016;38(1):79–84.
[21] Hagren A, et al. *Test-Retest Reliability of Local Tissue Water and Circumference Measurements in the Head and Neck Area of healthy Women and men.* Lymphat. Res. Biol. 2023;21(4):381–7.
[22] Mayrovitz HN, et al. *An Approach Toward Assessing Head-and-Neck Lymphedema using Tissue Dielectric constant Ratios: Method and Normal Reference Values.* Lymphat. Res. Biol. 2021;19(6):562–7.
[23] Chotipanich A, Kongpit N. *Precision and reliability of tape measurements in the assessment of head and neck lymphedema.* PLoS One 2020;15(5):e0233395–.
[24] Deng J, et al. *Prevalence of Secondary Lymphedema in patients with Head and Neck Cancer.* J. Pain Symptom Manage. 2012;43(2):244–52.

[25] Jeans C, et al. *A prospective, Longitudinal and Exploratory Study of Head and Neck Lymphoedema and Dysphagia following Chemoradiotherapy for Head and Neck Cancer.* Dysphagia 2023;38(4):1059–71.
[26] Ribeiro Pereira ACP, Koifman RJ, Bergmann A. *Incidence and risk factors of lymphedema after breast cancer treatment: 10 years of follow-up.* Breast 2017;36:67–73.
[27] Nguyen TT, et al. *Breast Cancer-Related Lymphedema Risk is Related to Multidisciplinary Treatment and not Surgery Alone: results from a Large Cohort Study.* Ann. Surg. Oncol. 2017;24(10):2972–80.
[28] Vivekanandan P, et al. *Are post-operative preventative measures effective in breast cancer-related lymphedema? a systematic review.* Palliative Medicine. Practice 2024.
[29] Frändin K, Grimby G. *Assessment of physical activity, fitness and performance in 76-year-olds.* Scand. J. Med. Sci. Sports 2007;4:41–6.
[30] Holm-Weber T, et al. *Gravity and lymphodynamics.* Physiol. Rep. 2022:10.
[31] Suami, H.A.-O., *Anatomical Theories of the Pathophysiology of Cancer-Related Lymphoedema. LID - 10.3390/cancers12051338 [doi] LID - 1338.* (2072-6694 (Print)).
[32] Hayes SC, et al. *The effect of Exercise for the Prevention and Treatment of Cancer-Related Lymphedema: a Systematic Review with Meta-analysis.* Med. Sci. Sports Exerc. 2022;54(8):1389–99.
[33] Wu, R., et al., *Obese patients have higher risk of breast cancer-related lymphedema than overweight patients after breast cancer: a meta-analysis.* (2305-5839 (Print)).
[34] Huang J, et al. *Incidence of lower limb lymphedema after vulvar cancer: a systematic review and meta-analysis.* Medicine (Baltimore) 2017;96(46):e8722.
[35] Tribius S, et al. *Prognostic factors for lymphedema in patients with locally advanced head and neck cancer after combined radio(chemo)therapy- results of a longitudinal study.* Oral Oncol. 2020;109:104856.
[36] Regionala Cancerceter i Samverkan. *Swedish Head and Neck Cancer Register.* nd 2025–01–17 [cited 2025 28 febr]; Available from: https://cancercentrum.se/samverkan/cancerdiagnoser/huvud-och-hals/kvalitetsregister/.
[37] Smith BG, et al. *Lymphedema outcomes in patients with head and neck cancer.* Otolaryngol. Head Neck Surg. 2015;152(2):284–91.
[38] Johansson K, Branje E. *Arm lymphoedema in a cohort of breast cancer survivors 10 years after diagnosis.* Acta Oncol. 2010;49(2):166–73.
[39] Johansson K, et al. *Early intervention with a Compression Sleeve in Mild Breast Cancer-Related arm Lymphedema: a 12-month prospective Observational Study.* Cancers 2023;15. https://doi.org/10.3390/cancers15102674.