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Prognostic Factors and Outcomes Associated With Neck Lymphedema in Head and Neck Cancer Survivors

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Objectives: The purpose of this study is to determine the predictors of neck lymphedema and to explore its association with symptoms and patient-reported outcomes (PROs) in Head and Neck Cancer (HNC) patients who underwent non-operative treatment.

Methods: This study involved a cross-sectional secondary analysis of data from patients diagnosed with head and neck squamous cell carcinoma who underwent radiation therapy (±chemotherapy). Patients with visits <6 weeks or >2 years following completion of radiation and those with recurrent or metastatic cancer were excluded. Presence of post-treatment lymphedema, demographics, clinical characteristics, health-related behaviors, and symptoms were collected. PROs were obtained using validated questionnaires that assessed depression, anxiety, swallowing dysfunction, and quality of life (QOL). Multivariable regression models were used to examine the relationship between lymphedema with predictors and symptoms.

Results: Of the 203 patients included, 88 (43.4%) developed post-treatment lymphedema. In multivariable analysis, pre-treatment Body Mass Index (BMI) (odds ratio [OR] = 1.07, 95% confidence interval [CI] [1.01, 1.14] $p = 0.016$) and N stage (OR = 1.96, 95% CI [1.06, 3.66], $p = 0.032$) were found to be independently associated with lymphedema. Regarding PROs, lymphedema was associated with greater swallowing dysfunction (3.48, 95% CI [0.20, 6.75], $p = 0.038$), decreased mouth opening (−3.70, 95% CI [−7.31, −0.10], $p = 0.044$), and increased fatigue (1.88, 95% CI [1.05, 3.38], $p = 0.034$).

Conclusion: Higher pre-treatment BMI and greater N stage are identified as independent predictors for lymphedema development in non-operative HNC patients. Additionally, patients experiencing lymphedema reported worsening swallowing dysfunction and increased symptoms related to trismus and fatigue. Recognizing patients at elevated risk for lymphedema allows for early intervention, alleviation of symptom burden, and optimization of health care resources.

Key Words: head and neck cancer, lymphedema, patient-reported outcome measures, prognostic factors, quality of life, survivorship.

Level of Evidence: 4

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INTRODUCTION

The treatment of Head and Neck Cancer (HNC) is often multifaceted, incorporating a combination of radiation therapy, chemotherapy, immunotherapy, and/or surgery. While advances in treatment modalities have significantly improved patient survival, the morbidity and toxicities associated with treatment-related side effects continue to have profound, long-term impacts on patients' well-being and quality of life (QOL).[1–4] Among these complications, lymphedema is a notable, yet underexplored, consequence for cancer survivors. Lymphedema is characterized by chronic swelling and functional impairment caused by the accumulation of lymphatic fluid in interstitial spaces due to impaired lymphatic drainage. Although well-established as a side effect in breast, genitourinary, and gynecological cancers, lymphedema in the context of HNC remains inadequately investigated, particularly in patients treated with non-operative therapy.[5]

Reports indicate an increasing prevalence of lymphedema following HNC therapy, with some studies stating the presence of lymphedema in up to 90% of survivors.[6,7] While most reports of lymphedema have been associated with patients treated with multimodal therapy in breast cancer, the addition of radiation therapy to surgical treatment has been found to increase lymphedema risk, suggesting that radiation may play an important role in lymphedema development.[8,9] In addition, several factors have been found to be correlated with lymphedema

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development in HNC patients treated with multiple modalities. These factors include the extent of lymph node involvement during surgery, the dose and duration of radiation therapy, and the use of chemotherapy[10,11] In addition, recent years have witnessed a significant increase in the utilization of non-operative treatments such as radiotherapy (RT) and chemoradiotherapy (CRT) to treat HNC.[12] This trend is driven by advancements in organ-preserving radiation treatments and the development of new therapeutic agents for treatment. As the population of patients undergoing RT or CRT without surgery increases, it is essential that this group is well characterized to understand the unique challenges they face. Further exploration of prognostic factors, particularly in a non-operative group, is essential for identifying individuals at higher risk of lymphedema and implementing preventive strategies.

Moreover, HNC survivors with lymphedema experience worsened symptom burden, functional status, and overall QOL. Patients affected typically present with swelling of the skin and soft tissues of the neck, as well as internal swelling of the mucous membranes, and soft tissues of the larynx, oral cavity, and pharynx.[13] Severe cases of lymphedema can result in voice changes, throat discomfort, difficulty swallowing, difficulty speaking, and even difficulty breathing.[13–16] Therefore, investigating the functional impacts and symptom burden related to lymphedema can provide insights into the areas requiring targeted interventions to improve patients' overall well-being.

Currently, there is limited literature on the prognostic factors and outcomes associated with the development of external neck lymphedema, especially in a non-operative group. This study examines the risk factors and outcomes associated with neck lymphedema in HNC patients. Specifically, we examined the prevalence, risk factors, symptom burden, and functional impact in patients who underwent non-operative treatment.

MATERIALS AND METHODS

A cross-sectional retrospective analysis of adult survivors of head and neck squamous cell carcinoma (HNSCC) receiving care from a single multidisciplinary survivorship clinic between 2017 and 2022 was conducted (Fig. 1). Inclusion criteria for this analysis were: (1) histological diagnosis of HNSCC; (2) age 18 years or older; (3) completed radiation (±chemotherapy) treatment; and (4) finished treatment >6 weeks and <2 years from the survivorship clinic visit. A total of 3892 patients were excluded for the following reasons: diagnosis of non-squamous cell carcinoma malignancy, had undergone neck dissection, had recurrent or metastatic disease, or had second primaries. Patients who had completed treatment outside of the designated time frame were excluded, as we are focusing on secondary external lymphedema rather than acute edema. This study was covered by the University of Pittsburgh Institutional Review Board protocol STUDY20050058.

Demographics and Clinical Characteristics

Demographics, lifestyle characteristics, and information on cancer and subsequent treatment were abstracted from the medical record. Demographics included age, zip code, race, and marital status. Lifestyle characteristics obtained included alcohol and tobacco use. Tobacco use (i.e., current/former/never) defined current users as those who actively smoked or used tobacco on the day of diagnosis or prior to radiation evaluation. Alcohol use (i.e., yes/no) was defined as anyone reporting yes, occasionally, or socially at the time of diagnosis. Additionally, health comorbidities, including diabetes and hypertension, were abstracted from the patient medical record.

Cancer and cancer treatment information collected included primary tumor site, American Joint Committee on Cancer (AJCC) 7th and 8th edition staging, treatment modality, radiation laterality, and radiation dosage. Primary tumor sites included oropharynx, larynx/hypopharynx, and others (i.e., nasopharynx and maxillary sinus). Treatment modality was defined as radiation therapy alone or CRT. Radiation laterality included unilateral or bilateral neck irradiation.

Area Deprivation Index

Area deprivation index (ADI), a proxy measure of patient socioeconomic disadvantage within a specific geographical area, was used as a marker of neighborhood-level measure of deprivation. Each patient's home zip code was entered into a publicly available website, and a score indicating the national percentile was abstracted. Scores range from 0 to 100, with higher scores indicating greater deprivation.[17]

Post-Treatment Lymphedema

The majority of patients were assessed in the clinic for the presence or absence of lymphedema by a certified lymphedema therapist. To ensure all patients were captured, we also reviewed patient survivorship visit records, physical therapy orders, and post-survivorship physical therapy visits. Lymphedema was defined as swelling that persists or develops at least 6 weeks after the last day of HNC irradiation treatment.

Post-Treatment Patient Symptoms

Patient symptoms were collected prospectively during a patient's survivorship visit by nursing staff. Symptoms collected include the presence of shoulder dysfunction, pain, fatigue, hearing loss, sleep disturbance, xerostomia, and body and self-image issues. The presence of trismus was defined as a mouth opening <35 mm and mouth opening was also analyzed separately as a continuous variable.[18]

Patient-Reported Outcomes

We also looked at validated patient-reported outcomes (PROs) questionnaires that were completed by patients during their survivorship visit, including the fourth version of the University of Washington Quality of Life (UWQOL) questionnaire, 8-item Patient Health Questionnaire (PHQ-8), 7-item Generalized Anxiety Disorder (GAD-7), and 10-item Eating Assessment Tool (EAT-10).

The UWQOL is a widely used tool for assessing health-related QOL in individuals with HNC. It consists of questions that cover 12 domains relevant to QOL, including pain, appearance, activity, recreation, chewing, shoulder, taste, saliva, mood, and anxiety. A physical subscale score was calculated as an average of swallowing, taste, speech, appearance, and saliva domains. A social subscale was calculated using the anxiety, mood, activity, recreation, shoulder dysfunction, and pain

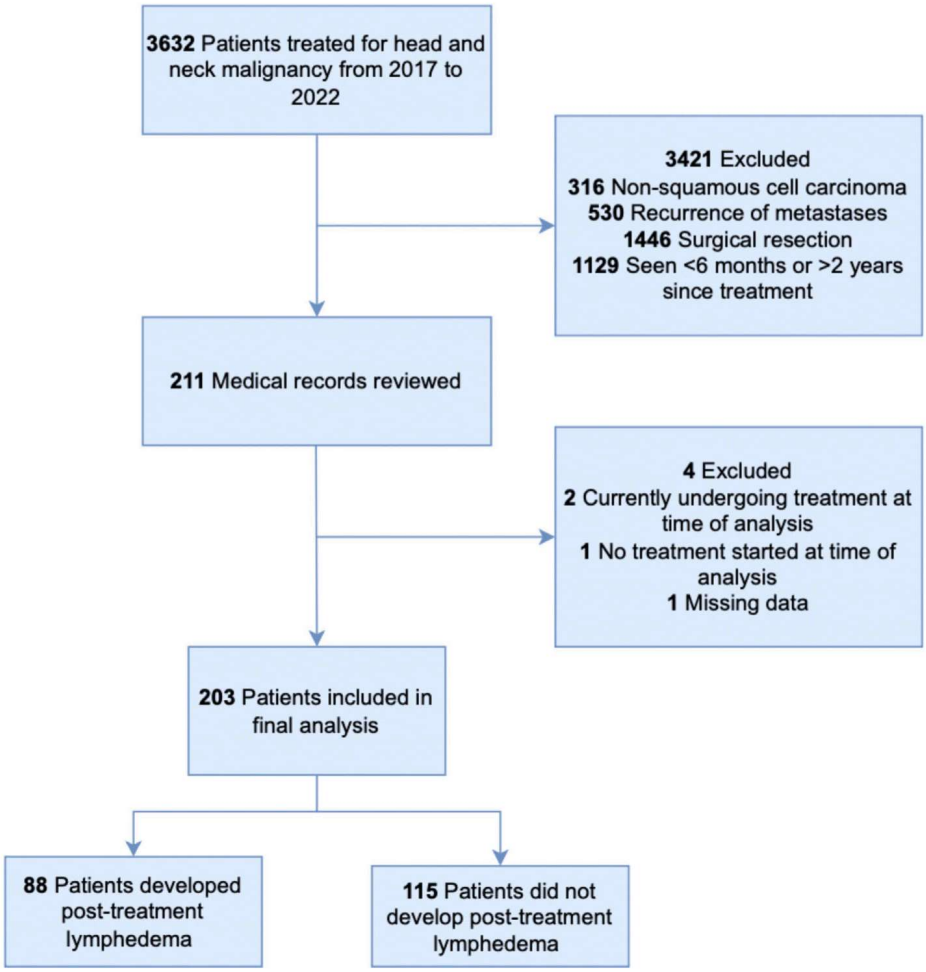

Fig. 1. Patient selection and screening flow chart. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

domains.[19] For both categories, scores ranged from 0 to 100, with higher scores demonstrating better QOL.

The PHQ-8 and GAD-7 are reliable and sensitive indices used to assess depression and anxiety severity in a patient, respectively. The PHQ-8 consists of the 8 criteria required to make a DSM-V diagnosis of depression by asking the patient to rate the frequency with which they experience certain depressive symptoms on a four-point scale. The PHQ-8 score can range from 0 to 27, with higher scores indicating more severe depressive symptoms.[20] The GAD-7 has 7 items and scores range from 0 to 21, with higher scores indicating increasing severity of anxiety symptoms.[21]

The EAT-10 is self-reported questionnaire a tool designed to assess self-perceived swallowing dysfunction and dysphagia. The EAT-10 consists of 10 items that evaluate various aspects of swallowing function and associated symptoms. Each item is rated on a scale from 0 to 4, with higher scores indicating greater impairment. The total EAT-10 scores range from 0 to 40, with higher scores indicating more severe dysfunction.[22,23]

Statistical Analysis

All statistical analysis was performed using RStudio (2023.03.0 + 386; RStudio, Inc, Boston, Massachusetts). For the descriptive analysis, we calculated frequency (percentage) for categorical variables, mean (standard deviation) for normally distributed continuous variables and median (IQR) for non-normally distributed continuous variables. The difference of distribution were tested by various statistical tests, according to different types and distributions of the variables. *T*-test and Wilcoxon Rank Sum Test were used for continuous variables, which were reported as mean ± SD and median (interquartile distance), respectively. Chi-square test and Fisher's exact test were used for categorical variables with expected cell count >5 and ≤5, respectively. Multivariable Logistic regression was used to investigate predictors for lymphedema. Multivariable Logistic regression and linear regression were utilized to assess the correlation between lymphedema and binary or continuous patient-reported outcomes, respectively. Covariates were selected using univariable regression results and stepwise selection. A p-value less than 0.05 is considered as significant.

RESULTS

Patient Characteristics

A total of 203 patients who were treated for HNSCC with radiation therapy (±chemotherapy) were included in our analysis (Fig. 1). Of these, 88 (43.3%) patients developed lymphedema >6 weeks after treatment. The mean age was 64.73 (SD = 8.51) years, with the majority being

white ($n = 172$, 84.7%) and over half ($n = 126$, 62.1%) married. The number of participants who reported smoking at the time of diagnosis was 57 (28.1%), while 82 (40.4%) reported a history of smoking. Approximately half ($n = 116$, 57.1%) reported alcohol use at the time of diagnosis.

The most common tumor subsite was the oropharynx ($n = 133$, 65.5%) followed by the larynx/hypopharynx ($n = 56$, 27.6%). Other cancer sites ($n = 14$, 6.9%) included 10 involving the nasopharynx and 3 involving the maxillary sinus. Over half (54.2%, $n = 110$) of patients had T3/T4 disease, and 43.8% ($n = 89$) had T1/T2 disease. The majority ($n = 174$, 85.7%) were treated with definitive CRT, and most ($n = 149$, 73.4%) received bilateral neck irradiation. Radiation laterality for 13 (6.4%) patients could not be determined. Table I displays the demographics and clinical characteristics of patients in our cohort.

Predictors of Lymphedema

When comparing patients who developed lymphedema with those who did not, significant differences in average pre-treatment Body Mass Index (BMI) (29.67 vs. 27.51, $p = 0.10$) and proportion of advanced N stage (58.0% vs. 42.6%, $p = 0.043$) (Table I). Multivariable logistic regression was performed to detect predictors of lymphedema and included pre-treatment BMI, N stage, treatment type, and weight loss (Table II). The odds of developing lymphedema for patients with each unit elevated pre-treatment BMI were 1.07 times higher compared to those with lower pre-treatment BMI (95% CI [1.01, 1.14], $p = 0.016$). Multivariable analysis also revealed a significant association between lymphedema development and lymph node involvement. Those with stage N2/N3 have 1.96 times higher odds of developing lymphedema compared with those who were stage N0/N1 (95% CI [1.06, 3.66], $p = 0.032$). Treatment type was not significantly associated with lymphedema.

Patient-Reported Outcomes and Symptoms

Multivariable logistic regression of binary symptoms questions (presence/absence) included the following domains: shoulder dysfunction, pain, fatigue, hearing loss, sleep disturbances, xerostomia, and body/self-image concerns. We found that lymphedema significantly increased the odds of fatigue (OR = 1.88, 95% CI [1.05, 3.38], $p = 0.034$). A significant association between lymphedema and shoulder dysfunction, pain, hearing loss, sleep disturbances, and xerostomia was not detected in this cohort. The regression results for lymphedema are summarized in Table III, while the complete results are shown in Supplementary Table 1.

For continuous PROs, multivariable linear regression showed that patients with lymphedema are estimated to have a decreased mouth opening of 3.70 mm (95% CI [−7.31, −0.10], $p = 0.044$) and 3.48 points higher swallowing dysfunction (EAT-10) scores (95% CI [0.20, 6.75], $p = 0.038$), indicating increased severity for the measured domain. This cohort does not show a significant correlation between lymphedema and severity of depression (PHQ-8), anxiety (GAD-7), and social and physical QOL subscales (UWQOL Social and UWQOL Physical). The regression results for lymphedema are summarized in Table IV, while the complete results are shown in Supplementary Table 2.

DISCUSSION

Head and neck lymphedema is a prevalent side-effect among survivors after HNC treatment. Prior studies have found that lymphedema is associated with increased symptom burden, functional decline, and reduced QOL in HNC patients who undergo surgery or multimodal therapy.[24] Beyond these impacted domains, studies in breast cancer patients have also demonstrated that the addition of radiation therapy to surgical treatment increases lymphedema risk, suggesting that radiation may play a significant role in the progression of treatment-related side effects.[25,26] This study aimed to identify prognostic factors associated with the development of external neck lymphedema in nonsurgical HNC patients and explore its outcomes in this population. This is the first study to date that has examined secondary lymphedema impacts on a non-operative group.

Our cohort consisted of HNC patients who completed radiation or chemoradiation more than 6 weeks prior, ensuring that acute edema effects had resolved. Among them, 38.8% developed external lymphedema. Previous studies that assessed external lymphedema through clinical assessment reported prevalence rates from 17% to 61%.[27] Notably, higher pre-treatment BMI was found to be a predictive factor, with those who developed lymphedema having higher average pre-treatment BMIs than those who did not (29.67 vs. 27.51). Similar findings have been reported in breast cancer literature, where increasing BMI is associated with increased lymphedema risk.[27,28] Studies in HNC patients have also shown a significant association between increasing BMI and both short-term and long-term external lymphedema.[29] While the causal link is unclear, it has been postulated that elevated BMI may impose greater stress and demand upon the circulatory system, contributing to lymphedema development.[30] Greater weight loss in patients with higher pre-treatment BMIs may also result in an increase in interstitial space. These results emphasize the importance of promoting early lifestyle and nutritional interventions in HNC management.

Greater lymph node involvement was also associated with post-treatment lymphedema. While prior studies in head and neck literature have not commonly examined N stage as an independent predictor of lymphedema, Deng et al. did not find a correlation with overall staging. Deng speculated that there was a predominance of advanced-stage disease in their study cohort or that there may not be a correlation between staging and severity of tissue damage induced by treatment.[13] However, one study conducted on breast cancer patients did find that N stage was a positive predictor, speculating that the advanced disease stage is correlated with lymphedema.[31] Other studies in breast cancer literature have also found that

TABLE I.
Demographics and Clinical Characteristics of Cohorts in Analysis.

Variables	All ($N = 203$)	Lymphedema ($n = 88$)	No Lymphedema ($n = 115$)	p-Value[¶]
Age, mean (SD), year[*]	64.73 (8.51)	64.22 (8.07)	65.12 (8.85)	0.454
ADI, mean (SD)[*]	64.54 (22.42)	65.83 (22.69)	65.53 (22.25)	0.472
Pre-treatment BMI, mean (SD)[*]	28.45 (5.91)	29.67 (5.72)	27.51 (5.91)	0.010[‖]
Weight loss, mean (SD), kg[*]	9.73 (7.13)	10.56 (6.71)	9.09 (7.40)	0.152
Radiation days, median (IQR)[†]	49.00 (44.00, 51.00)	49.00 (44.00, 51.00)	49.00 (44.00, 51.00)	0.949
Radiation Gy, median (IQR)[†]	70.00 (66.00, 70.00)	70.00 (69.96, 70.00)	70.00 (66.00, 70.00)	0.414
Marital status, No. (%), (n = 189)[‡]				0.236
Married	126 (62.07)	60 (68.18)	66 (57.39)	
Not married	63 (31.03)	24 (27.27)	39 (33.91)	
Race, No. (%), ($n = 201$)[§]				0.067
White	172 (84.73)	77 (87.50)	95 (82.61)	
Black	24 (11.82)	9 (10.22)	15 (13.04)	
Other	5 (2.46)	0 (0.00)	5 (4.35)	
Tobacco, No. (%), ($n = 197$)[‡]				0.799
Current	57 (28.08)	23 (26.14)	34 (29.57)	
Never	58 (28.57)	28 (31.82)	30 (26.09)	
Former	82 (40.39)	34 (38.64)	48 (41.74)	
Alcohol, No. (%)[‡]				0.728
No	87 (42.86)	36 (40.91)	51 (44.35)	
Yes	116 (57.14)	52 (59.09)	64 (55.65)	
Diabetes, No. (%)[§]				>0.999
No	180 (88.67)	78 (88.64)	102 (88.70)	
Yes	23 (11.33)	10 (11.36)	13 (11.30)	
Hypertension, No. (%)[‡]				0.278
No	93 (45.81)	36 (40.91)	57 (49.57)	
Yes	110 (54.19)	52 (59.09)	58 (50.43)	
Cancer site, No. (%)[§]				0.296
Oropharynx	133 (65.52)	60 (68.18)	73 (63.48)	
Hypopharynx/larynx	56 (27.59)	20 (22.73)	36 (31.30)	
Other	14 (6.90)	8 (9.09)	6 (5.22)	
T stage, No. (%), ($n = 199$)[‡]				0.955
Early (T1/T2)	89 (43.84)	38 (43.18)	51 (44.35)	
Advanced (T3/T4)	110 (54.19)	48 (54.55)	62 (53.91)	
N stage, No. (%)[‡]				0.043[‖]
N0 + N1	103 (50.74)	37 (42.04)	66 (57.39)	
N2 + N3	100 (49.26)	51 (57.95)	49 (42.61)	
Treatment, No. (%)[‡]				0.301
Radiation	27 (13.30)	8 (9.09)	19 (16.52)	
CRT	174 (85.71)	79 (89.77)	95 (82.61)	
Radiation laterality, No. (%) ($n = 190$)[‡]				0.887
Unilateral	41 (20.20)	17 (19.32)	24 (20.87)	
Bilateral	149 (73.40)	66 (75.00)	83 (72.17)	

ADI = Area Deprivation Index; BMI = body mass index; CRT = chemoradiotherapy; Gy = Gray.
[*]Continuous variables reported as Mean ± SD, t-test was used.
[†]Continuous variables reported as median (interquartile distance), Wilcoxon Rank Sum Test was used.
[‡]Categorical variables with expected cell count >5, chi-square test was used.
[§]Categorical variables with expected cell count ≤5, Fisher's exact test was used.
[‖]Statistically meaningful outcome.
[¶]p-value is calculated by the above tests to compare lymphedema groups.

the stage of tumor was significantly associated with lymphedema development.[32] In the context of HNC, lymph node involvement can indicate that the cancer has affected the regional lymphatic system. Lymph nodes compromised by cancer or cancer treatment may lead to reduced lymphatic function, exacerbating the risk of

TABLE II.
Multivariable Logistic Regression of Variables Associated With Post-Treatment Lymphdema.

Variables	OR (95% CI)	*p*-Value
Intercept	0.05 (0.01, 0.29)	0.001
Pre-treatment BMI	1.07 (1.01, 1.14)	0.016*
Weight loss	1.00 (0.96, 1.05)	0.970
N stage		
N0 + N1	[Reference]	0.032*
N2 + N3	1.96 (1.06, 3.66)	
Treatment		
Radiation	[Reference]	0.227
CRT	1.77 (0.71, 4.78)	

BMI = body mass index; CRT = chemoradiotherapy; OR = odds ratio.
*Statistically meaningful outcome.

TABLE III.
Multivariable Regression of Patient-Reported Symptoms Associated With Post-Treatment Lymphedema.

Variables	OR (95% CI)	*p*-Value
Shoulder dysfunction	1.38 (0.67, 2.83)	0.378
Pain	0.82 (0.43, 1.55)	0.545
Fatigue	1.86 (1.05, 3.38)	0.034*
Hearing loss	0.82 (0.43, 1.54)	0.530
Sleep disturbances	1.56 (0.88, 2.79)	0.129
Xerostomia	0.72 (0.26, 1.99)	0.523

CI = confidence interval; OR = odds ratio.
*Statistically meaningful outcome.

TABLE IV.
Multivariable Regression of Validated Patient-Reported Outcome Surveys Associated With Post-Treatment Lymphedema.

Variables	Coefficient (95% CI)	*p*-Value
UWQOL social	−0.30 (−5.84, 5.24)	0.915
UWQOL physical	−2.74 (−7.77, 2.28)	0.282
PHQ-8	0.40 (−1.44, 2.24)	0.669
GAD-7	0.94 (−0.71, 2.58)	0.261
EAT-10	3.48 (0.20, 6.75)	0.038*
Mouth opening	−3.70 (−7.31, −0.10)	0.044*

CI = confidence interval; EAT-10 = 10-item Eating Assessment Tool; FOIS = Functional Oral Intake Scale; GAD-7 = 7-item Generalized Anxiety Disorder; PHQ-8 = 8-item Patient Health Questionnaire; UWQOL = University of Washington Quality of Life.
*Statistically meaningful outcome.

lymphedema. In addition, increased N stage potentially necessitates an expansion of the radiation field to the neck. This is an important consideration as the extent of radiation treatment can impact the lymphatic system, potentially elevating the risk of lymphedema. Further investigation should explore the potential relationship between N stage, radiation field size, and their combined influence on lymphedema development.

No significant associations were found between lymphedema and any other demographics, health comorbidities, or health-related behaviors. Consistent with our findings, a previous study in breast cancer patients also found that while BMI was associated with breast cancer lymphedema, the effects of comorbidities such as age, hypertension, diabetes, and smoking as risk factors in lymphedema were minimal.[32] Deng et al. conducted a study in 2012 that systematically examined associations between lymphedema and various prognostic factors in HNC patients and similarly did not find that any demographic factors, comorbidities, or health-related behaviors were correlated with lymphedema.[13] Deng speculated that tumor and treatment-related effects may overshadow the role of demographics or comorbidities in lymphedema manifestation.

Our study also examined the association between lymphedema and post-treatment symptom burden. Multivariable logistic regression of PROs revealed significant associations between post-treatment lymphedema and reports of fatigue. Fatigue is a multifactorial symptom influenced by a variety of physiological, psychological, and treatment-related factors. Studies in both breast cancer and HNC literature have found that lymphedema is correlated with fatigue.[32,33] While underlying mechanisms linking fatigue to lymphedema are still unclear, the chronic inflammatory state associated with lymphedema, altered immune responses, functional limitations, and psychosocial impact of lymphedema may contribute to the experience of fatigue. Further research needs to be done to understand underlying causes and explore effective interventions to address such symptoms.

In addition, patients with lymphedema were also found to have decreased mouth openings, or trismus. Trismus has negative implications for patients' daily lives as it can lead to difficulties with eating, speaking, and maintaining oral hygiene. Prior studies have postulated that trismus may be a sequela of lymphedema.[33] While our study did not actively explore this causal relationship, the correlation of lymphedema and trismus suggests a complex interplay of symptoms and challenges faced by patients with lymphedema. Moreover, we also found a notable increase in the severity of perceived swallowing dysfunction (EAT-10). Our findings are consistent with other studies that also found that lymphedema was correlated with subjective measures of swallowing dysfunction.[16,34,35] These multifaced consequences emphasize the need for interventions that address these post-treatment domains. Improving functional status in patients should be a key consideration in comprehensive care and recovery.

Notably, our findings reveal a lack of significant correlation between lymphedema and social and physical QOL scales, contrasting with existing literature. For example, breast cancer studies have extensively discussed the profound impact of lymphedema on QOL.[36–38] The observed discrepancy in our results may be attributed to several factors. First, unlike breast cancer lymphedema, which primarily affects the upper extremities, head and neck lymphedema may involve other complex anatomical regions, leading to differing functional impairments and

psychosocial challenges. Moreover, distinct impacts of treatment modalities, such as radiation therapy, may contribute to variations in the manifestation and perceived burden of lymphedema. Additionally, our study population, comprised exclusively of patients from a single academic institution's HNC survivorship clinic, may exhibit specific demographic or clinical characteristics that differ from broader cancer populations. The lack of standardized grading criteria for head and neck lymphedema may also influence the correlation with QOL. Future research endeavors involving larger cohorts and standardized assessment tools will be essential for further understanding the relationship between lymphedema and patient QOL.

Some limitations of this study should be acknowledged. One limitation lies in this study's retrospective cross-sectional design, which is subject to inherent biases and a limited ability to establish causality. It is also important to recognize that a BMI of 27, indicative of a trend toward obesity, highlights challenges in diagnosing lymphedema in those with higher BMIs due to increased adipose tissue. This complicates visual inspection and measurements, potentially obscuring visual signs of lymphedema and limiting circumferential measurements. These complexities emphasize the need for further consideration in both the diagnosis and management of lymphedema in this specific population. Our identification of these challenges suggests exploring alternative mechanisms for future studies, such as advanced diagnostic techniques like pre-operative imaging with magnetic resonance imaging (MRI) or ultrasound, to gain a more detailed understanding of lymphatic and adipose tissue dynamics in individuals with higher BMI.

In addition, while the main purpose of this study was to capture lymphedema presence and discuss associated risk factors and outcomes, future studies should include degree of lymphedema and employ standardized methods (e.g., tape measures, grading scales) of assessing lymphedema to better understand the response to interventions. The patients in our study also come from a single academic institution's HNC survivorship clinic, potentially limiting the generalizability of results. Future research should involve multiple institutions with larger patient populations to diversify the cohort. Moreover, future studies may consider including objective measures of swallowing and broader related issues, such as the impact on voice. Examining the effects of speech, articulation, and vocal quality may provide valuable insights into the comprehensive impact of head and neck lymphedema. In addition, many patients in our study received post-treatment lymphedema therapy. However, due to the lack of additional data concerning the frequency and outcomes of this therapy, we were unable to assess its specific impact on the study results. Nevertheless, this aspect of therapy warrants further investigation in future research.

CONCLUSION

Our investigation highlights the prevalence of lymphedema and symptom burden in non-operative HNC patients. It also demonstrates the importance of timely detection and treatment of lymphedema, which can play a pivotal role in managing its progression and enhancing the QOL. Comprehensive approaches, including nutrition and physical health interventions prior to treatment completion, may enhance post-treatment outcomes. The associations between lymphedema and higher symptom burden highlight the comprehensive impact of lymphedema in HNC survivors. Future directions include wholistic phenotyping to examine biological markers of lymphedema as well as comparing lymphedema prognostic factors and outcomes across patient groups.

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