Original Article

Prevalence of Secondary Lymphedema in Patients With Head and Neck Cancer

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Abstract

Context. Because surgery, radiation, and/or chemotherapy disrupt lymphatic structures, damage soft tissue leading to scar tissue formation and fibrosis, and further affect lymphatic function, patients with head and neck cancer may be at high risk for developing secondary lymphedema. Yet, no published data are available regarding the prevalence of secondary lymphedema after head and neck cancer treatment.

Objectives. The aim of this study was to examine prevalence of secondary lymphedema in patients with head and neck cancer.

Methods. The study included 81 patients with head and neck cancer who were three months or more post-treatment. External lymphedema was staged using Foldi's lymphedema scale. Internal lymphedema was identified through a flexible fiber-optic endoscopic or mirror examination. Patterson's scale was used to grade degrees of internal lymphedema.

Results. Of the 81 patients, 75.3% (61 of 81) had some form of late-effect lymphedema. Of those, 9.8% (6 of 61) only had external, 39.4% (24 of 61) only had internal, and 50.8% (31 of 61) had both types.

Conclusion. Lymphedema is a common late effect in patients with head and neck cancer, and it develops in multiple external and internal anatomical locations. During physical examination and endoscopic procedures, clinicians should assess patients with head and neck cancer for late-effect lymphedema. Referral for treatment should be considered when lymphedema is noted. Research is needed to examine risk factors of lymphedema in patients with head and neck cancer and its effects on patients' symptoms, function, and quality of life. J Pain Symptom Manage 2012;43:244–252.

Key Words
Secondary lymphedema, head and neck cancer, prevalence, late effect

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Introduction

Patients who have head and neck cancer often receive multimodality cancer treatment related to locally advanced disease. Aggressive

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multimodality treatment improves outcomes (e.g., survival, local control, and function preservation) but increases the risk of late effects, which are defined as toxicities present at least three months after the completion of cancer treatment.[1–3] A commonly neglected late effect in patients with head and neck cancer is secondary lymphedema. These patients may develop secondary lymphedema externally (e.g., face and neck)[4,5] and internally (e.g., larynx and pharynx).[6,7] Lymphedema may profoundly impact critical physical functions (e.g., breathing and swallowing), and it also affects areas (e.g., face and neck) that can lead to body image issues[7,8] and social isolation.[9] Thus, clearly understanding the frequency, site, and sequelae of lymphedema is critical. Although no studies adequately document the sites and manifestations of lymphedema in patients with head and neck cancer, European literature reports that the prevalence of secondary lymphedema is between 12% and 54%.[10–13] This wide range of estimated prevalence of secondary lymphedema in patients with head and neck cancer may be related to variations in the anatomical sites assessed for lymphedema (e.g., external vs. internal), differences in the time period of follow-up,[14] differences in grading criteria, or differences in cancer treatment regimens across studies.[15] Data related to prevalence rates in the U.S. are lacking. Thus, the purpose of this study was to examine prevalence of secondary lymphedema after head and neck cancer treatment in a sample of patients from a large comprehensive cancer center in the U.S.

Methods

Permission to conduct the study was obtained from the Institutional Review Board at Vanderbilt University and the Scientific Review Committee at Vanderbilt-Ingram Cancer Center (VICC). Written informed consent was obtained from all participants.

Participants

Eligibility for participation included 1) ≥18 years of age, 2) three or more months after completion of head and neck cancer treatment, and 3) no current evidence of cancer. Individuals were excluded if they met one of the following criteria: 1) actively undergoing chemotherapy or radiation therapy, 2) having metastatic cancer or any other active cancer, or 3) unable to understand the informed consent.

Definition of Lymphedema

For the purpose of this study, lymphedema is defined as swelling that develops at least three months after head and neck cancer treatment, beyond the time frame in which acute edema occurs in this patient population. External lymphedema is defined as visible swelling in the skin and soft tissue of the head and neck region. Internal lymphedema is defined as visible swelling occurring in the mucosa and underlying soft tissue of the upper aerodigestive tract (e.g., pharynx and larynx).

Procedures

Patients who were seen at the VICC for follow-up after completion of treatment for head and neck cancer were approached to assess interest in participation in the study. Patients who expressed interest were asked to sign a consent form. Subsequently, participants completed a demographic survey and underwent a physical examination to assess external lymphedema. All assessments for external lymphedema were completed by a licensed/registered nurse using a standard procedure to ensure consistency. This nurse was trained regarding how to evaluate external lymphedema in cancer populations (including breast cancer and head and neck cancer populations). Then, participants underwent routine endoscopy for internal lymphedema assessment conducted by one of the two study physicians. The study physicians who conducted the endoscopic examination and evaluated internal lymphedema were trained regarding how to evaluate internal lymphedema severity based on Patterson's scale (Appendix I).[16] Disease- and treatment-related data were obtained from chart review.

Instruments

External Lymphedema. External lymphedema was identified on physical examination by a trained study staff and was graded using Foldi's "Stages of Lymphedema" (Appendix II).[17] The psychometric properties of this tool have not been reported; however, it was developed based on experience treating

over 100,000 patients with lymphedema. Thus, content validity can be assumed. The scale has three major components: pathology, signs and symptoms, and diagnosis. Four stages are graded when using Foldi's scale, ranging from Stage 0 to Stage III.[17] In our study, external lymphedema was considered to be present if participants had at least Stage I lymphedema.

Internal Lymphedema. Internal lymphedema was assessed via flexible fiber-optic endoscopic or mirror examination by one of the study physicians and graded using Patterson's scale.[16] Patterson's scale grades edema involvement in 11 structures (e.g., posterior pharyngeal wall and epiglottis) and two spaces (i.e., valleculae and pyriform sinus). It has good intrarater reliability (weighted kappa, 0.84) and inter-rater reliability (weighted kappa, 0.54).[16] Four grades are used to rate edema level, which includes normal (no edema) to severe edema.[16] In this study, internal lymphedema was considered to be present if one anatomical site was edematous regardless of the severity of lymphedema.

Combined Lymphedema. In this study, the combined lymphedema category was defined as individuals with both external and internal lymphedema.

Statistical Methods

Data were double entered into the statistical software package SPSS version 17.0 (SPSS Inc., Chicago, IL). After data entry, data validation and data cleaning procedures were used to check for outliers and internal data consistency.[18] Descriptive statistics were used to describe the sample and summarize the distributions of the study variables, including demographic information, head and neck cancer disease, treatment information, and prevalence and degrees of lymphedema. Categorical (e.g., gender) and ordinal (e.g., education) data were summarized using frequency distributions. Ordinal data summaries also included median and 25th−75th interquartile ranges (IQRs). Continuous data were described using mean, median, and 25th−75th IQRs, minimum and maximum values.

Results

From December 2009 through May 2010, the study enrolled 81 adult patients with head and neck cancer who were being followed at the VICC.

Demographic Characteristics

Demographic characteristics are summarized in Table 1. The sample was 71.6% male and ranged in age from 33 to 86 years. Most participants were white (88.9%) and were at least high school graduates (88.9%). Most participants (61.7%) were married or living with a partner. More than half of the participants were receiving government insurance aid

Table 1
Demographic Characteristics

Characteristics	Frequency (%) ($n=81$)
Gender	
Male	58 (71.6)
Female	23 (28.4)
Race	
White	72 (88.9)
Black	9 (11.1)
Education level	
<12th grade	9 (11.1)
12th grade	30 (37.0)
College	36 (44.5)
Graduate	6 (7.3)
Marital status	
Married/living with partner	50 (61.7)
Single/widowed/other	31 (38.3)
Employment status	
Employed	43 (53.1)
Retired	25 (30.9)
Disabled	5 (6.2)
Unemployed	8 (9.9)
Residence area	
Metropolitan	49 (60.5)
Rural	32 (39.5)
Insurance coverage	
Medicare/Medicaid/ TennCare/TriCare	46 (56.8)
Private insurance/HMO	28 (34.6)
None/other	7 (8.6)
Smoking	
Current	12 (14.8)
Past	43 (53.1)
None	26 (32.1)
Drinking alcohol	
Current	9 (11.1)
Past	24 (29.6)
None	48 (59.3)
Age (mean, median, IQR 25−75, min, max)	59.55, 59.67, 51.28−67.37, 33.08, 86.65

(56.8%) and lived in a metropolitan area (60.5%). Sixty-eight percent reported a smoking history (14.8% currently smoked), and 40.7% reported ever drinking alcohol (11.1% currently imbibe alcohol).

Head and Neck Cancer Disease and Treatment Characteristics

Disease and treatment characteristics of the sample are summarized in Table 2. The oropharynx was the most frequent primary tumor location (42.0%). Advanced stage disease (III/IV) was present in 80.2% of all participants. Ninety percent of tumors were squamous cell carcinoma.

Prevalence of Lymphedema

The prevalence of external lymphedema, internal lymphedema, and combined lymphedema are presented in Table 3. Based on physical examination and endoscopic/mirror examination, 75.3% ($n = 61$) of the participants had some form of lymphedema, that is, external lymphedema only, internal lymphedema only, or combined lymphedema.

Based on physical examination, 45.7% ($n = 37$) of participants were identified as having external lymphedema, graded using Foldi's lymphedema scale (Table 4). In this study, the most frequent sites of external lymphedema were the neck and submental areas.

The prevalence of internal lymphedema, as well as the severity and location, are summarized in Table 5. The severity of internal lymphedema was the highest level noted among all involved sites. The study found that 67.9% ($n = 55$) of the participants had internal lymphedema.

Discussion

This study is the largest to date that has conducted detailed assessments of both external and internal lymphedema in patients with

Table 2
Head and Neck Cancer Disease and Treatment Characteristics

Characteristics	Frequency (%) ($n = 81$)
Location	
Paranasal sinuses	3 (3.7)
Oral cavity	11 (13.6)
Nasopharynx	3 (3.7)
Oropharynx	34 (42.0)
Hypopharynx	4 (4.9)
Larynx	13 (16.0)
Salivary gland	1 (1.2)
Other	12 (14.8)
Tumor staging at diagnosis	
Stage I	5 (6.2)
Stage II	7 (8.6)
Stage III	10 (12.3)
Stage IVa	49 (60.5)
Stage IVb	6 (7.4)
Could not be staged	4 (4.9)
Type of tumor	
SCC	77 (95.1)
Non-SCC	4 (4.9)
Complete treatment received	
Surgery alone	8 (9.9)
Radiation alone	2 (2.5)
CCR	10 (12.3)
Surgery and radiation	8 (9.9)
Surgery and CCR	26 (32.1)
Chemoinduction and CCR	21 (25.9)
Surgery, chemoinduction, and CCR	6 (7.4)

Characteristics	Mean	Median	IQR (25–75)	Min	Max
Time since diagnosis (years)	2.55	2.00	0.86–3.58	0.45	14.58
Time since treatment ended (months)	24.71	17.74	5.59–33.12	3.09	156.39

SCC = squamous cell carcinoma; CCR = concurrent chemoradiation.

Table 3
Prevalence of Secondary Lymphedema

Type of Lymphedema	Frequency (%)
No lymphedema	20 (24.7)
Some form of lymphedema	61 (75.3)
Total	81 (100.0)
Distribution of lymphedema type	
External lymphedema only	6 (9.8)
Internal lymphedema only	24 (39.4)
Combined lymphedema	31 (50.8)
Total	61 (100.0)

Note: 81 participants completed both endoscopic and skin examination.

head and neck cancer three or more months post-treatment. Furthermore, it is the first study to report external, internal, and combined lymphedema occurrence rates, as well as being the first study to report the prevalence of secondary lymphedema in patients with head and neck cancer in the U.S. Our results demonstrate that 75.3% of the participants had some form of lymphedema, including 9.8% with external lymphedema only, 39.4% with internal lymphedema only, and 50.8% with combined lymphedema. This rate is substantially higher than previously reported.

Four European studies have reported the prevalence of secondary lymphedema after head and neck cancer treatment.[10–13] These studies have a number of limitations. The first study[10] reported 54% of the participants developed laryngeal lymphedema after concurrent chemoradiation treatment, but the authors did not include external lymphedema. The second study[11] reported 48.4% of participants who developed submental or supraglottal lymphedema after head and neck cancer treatment. However, the study did not delineate the prevalence of external lymphedema only, internal lymphedema only, and combined lymphedema, thus possibly understating the prevalence of lymphedema. The third study[12] found that 17%–36% of the participants had external lymphedema after surgery, but they did not examine the patients to determine whether or not they had developed internal lymphedema simultaneously. The last study[13] reported that 12% of the patients developed subcutaneous lymphedema and fibrosis after head and neck cancer as identified through magnifying laryngoscopy examination.

Table 4
External Lymphedema Data

Lymphedema Grade	Frequency (%)
External lymphedema	
Stage 0	44 (54.3)
Stage I	15 (18.5)
Stage II	22 (27.2)
Stage III	0 (0.0)
Total	81 (100.0)
External lymphedema distribution ($n = 37$)	
One site (e.g., neck only)	24 (64.9)
Two sites (e.g., face and neck)	10 (27.0)
Three sites (e.g., face, neck, and eyes)	3 (8.1)
Total	37 (100.0)

Note: In terms of Foldi's lymphedema scale.

In addition to problems related to the lack of a comprehensive lymphedema assessment, lymphedema studies in the population with head and neck cancer have additional measurement issues. Currently, there is no clearly defined "gold standard" available to capture the critical characteristics of secondary lymphedema in patients with head and neck cancer. In patients with breast cancer, arm lymphedema can be assessed using tape measures. Although tape measurements have been used to assess external head and neck lymphedema in three studies,[5,19,20] there is a lack of consensus on how to perform the measurement. Moreover, the National Cancer Institute's "Common Toxicity Criteria for Adverse Events," version 3.0, provides a grading scale to describe external head and neck lymphedema.[21,22] The American Cancer Society also provides a similar scale for evaluating external lymphedema of the head and neck.[23] Thus, in the population with head and neck cancer, lymphedema is usually assessed using one of several available scales.[15] We chose to use Foldi's scale to assess external lymphedema. Based on findings from a pilot observational study conducted at our institution, we believed it was important to use a tool that captured the late stage or fibrotic manifestations of lymphedema. Foldi's scale is the only one that captured the continuum of soft-tissue abnormalities, ranging from reducible pitting edema to brawny hard edema that does not recede with elevation. For internal lymphedema, we chose to use Patterson's scale because 1) it was developed to evaluate edema in irradiated

Table 5
Location and Extent of Internal Lymphedema

Prevalence of Lymphedema ($n = 81$)	Frequency (%)
No lymphedema	26 (32.1)
Mild lymphedema	19 (34.5)
Moderate lymphedema	25 (45.5)
Severe lymphedema	11 (20.0)
Total	81 (100)

		Frequency (%)				
Location of Lymphedema	Sample Sizes (n)	No Lymphedema	Mild	Moderate	Severe	Total
Base of tongue	80	53 (66.3)	26 (32.5)	1 (1.3)	0 (0.0)	80 (100.00)
Posterior pharyngeal wall	81	54 (66.7)	26 (32.1)	1 (1.2)	0 (0.0)	81 (100.00)
Epiglottis	72	35 (48.6)	22 (30.6)	12 (16.7)	3 (4.2)	72 (100.00)
Pharyngoepiglottic folds	73	36 (49.3)	24 (32.9)	10 (13.7)	3 (4.1)	73 (100.00)
Aryepiglottic folds	73	34 (46.6)	20 (27.4)	16 (21.9)	3 (4.1)	73 (100.00)
Interarytenoid space	74	36 (48.6)	16 (21.6)	17 (23.0)	5 (6.8)	74 (100.00)
Cricopharyngeal prominence	69	51 (73.9)	17 (24.6)	1 (1.4)	0 (0.0)	69 (100.00)
Arytenoids	74	32 (43.2)	26 (35.1)	14 (18.9)	2 (2.7)	74 (100.00)
False vocal folds	74	38 (51.4)	21 (28.4)	13 (17.6)	2 (2.7)	74 (100.00)
True vocal folds	74	58 (78.4)	9 (12.2)	7 (9.5)	0 (0.0)	74 (100.00)
Anterior commissure	73	62 (84.9)	10 (13.7)	1 (1.4)	0 (0.0)	73 (100.00)
Valleculae	76	41 (53.9)	17 (22.4)	17 (22.4)	1 (1.3)	76 (100.00)
Pyriform sinus	75	42 (56.0)	16 (21.3)	10 (13.3)	7 (9.3)	75 (100.00)

Note: In terms of Patterson's scale.

head and neck cancer patients,[16] and 2) it has been found that Patterson's scale is the only one directed specifically at internal edema in the pharynx and larynx based on anatomical sites and spaces.[16]

As part of this study, the sites of lymphedema involvement were clearly documented. The most frequently involved external anatomical sites were the submental region and the neck. This is consistent with other reports in the literature and clinical experience.[4,5,11] Of those participants with external lymphedema, 64.9%, 27.0%, and 8.1% were found to have one, two, or three sites of involvement, respectively. Thirty-seven (45.7%) participants had Stage I (18.5%) or Stage II (27.2%) lymphedema based on Foldi's scale. Stage III lymphedema was not seen in any participants. Stage III disease, "invalidism," is a phenomenon not expected to occur frequently in patients with head and neck cancer/treatment-associated lymphedema. Thus, modification of Foldi's scale may be warranted to make this tool more applicable to the population with head and neck cancer.

Of those participants with internal lymphedema, 34.5% were graded as mild, 45.5% as moderate, and 20% as severe. In patients with mild internal lymphedema, the most frequently noted sites included the arytenoids, base of tongue, posterior pharyngeal wall, and pharyngoepiglottic folds. In patients with moderate internal lymphedema, the most often noted anatomical sites included the interarytenoid space, valleculae, and aryepiglottic folds. In patients with severe internal lymphedema, the most frequently involved sites included the pyriform sinus and the interarytenoid space.

Although the arytenoids and the interarytenoid space are intimately related to a single region, they are still different structures with their own unique lymphatic drainage and/or lymphatic tissue density. Thus, our present study found that mild lymphedema occurred most frequently in the arytenoids and, yet, the interarytenoid space was most often rated to be moderately and severely involved in lymphedema. Moreover, our study found that some patients had moderate lymphedema, and other patients had severe lymphedema in the interarytenoid space. Thus, the interarytenoid space was rated both moderately and severely involved in lymphedema in our study. In addition, the finding of severe internal lymphedema in 20% of participants was surprising and concerning. The most frequent internal anatomical sites involved were the pyriform sinus and interarytenoid space. Although no literature addressing lymphedema in these anatomical sites is available for comparison, severe internal

lymphedema has the potential to significantly impair critical functions, including alterations in swallow function, voice, and airways. Thus, studies are needed to examine the relationship between internal lymphedema, function loss, and symptom burden.

Although more research is clearly needed, given the high prevalence of lymphedema found in this and other studies, several clinical recommendations can be made that could be implemented in the patient care environment. First, health care professionals need to be aware that lymphedema is a frequent late effect in patients with head and neck cancer. Informed consent for treatment needs to include information regarding the potential risk for developing lymphedema as a result of therapy. Patients need to be educated about the manifestations of lymphedema and the importance of notifying health care providers if lymphedema-related signs or symptoms develop. Health care providers need to include lymphedema assessment as a component of the routine clinical examination. When conducting endoscopic examinations of patients with head and neck cancer, routine observation for lymphedema and any lymphedema involving vital structures needs to be documented. Finally, patients with lymphedema can be referred to a certified lymphedema specialist for education and therapy.

A limitation of this study is that the participants were recruited from a single comprehensive cancer center. Thus, the findings from this study may not be generalizable. The accessible population was primarily Caucasian, with a small percentage of African Americans. Other minorities were not represented. In addition, this was a cross-sectional study, with its associated limitations. A prospective longitudinal study with a baseline assessment followed by repeated measures during acute and late recovery would provide a better understanding of the natural history and implications of late-effect lymphedema in the population with head and neck cancer.

Conclusions

Secondary lymphedema is a frequent late effect in patients with head and neck cancer.[19] It may involve external or internal structures. In many patients, both external and internal structures are involved simultaneously. Thus, secondary lymphedema is an important clinical phenomenon that has the potential to cause significant symptom burden and function loss. Routine screening for lymphedema is warranted and, once identified, treatment is indicated. More studies are required to examine incidence, prevalence, natural progression of secondary lymphedema, and its impact on patients' quality of life.

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The authors declare no conflicts of interest.

References

1. Barker CL, Routledge JA, Farnell DJJ, et al. The impact of radiotherapy late effects on quality of life in gynecological cancer patients. Br J Cancer 2009; 100:1558–1565.

2. Maher EJ, Denton A. Survivorship, late effects and cancer of the cervix. Clin Oncol (R Coll Radiol) 2008;20:479–487.

3. Trotti A, Mocharnuk RS. Radiation-induced toxicity in patients with head and neck cancer: the need for standardized toxicity criteria. Medsc Hematol Oncol 2001;4:2. Available from http://www.medscape.com/viewarticle/430701_2. Accessed May 26, 2011.

4. Hammond T. Symptoms of head and neck edema. Available from http://www.lymphnotes.com/article.php/id/378/. Accessed January 10, 2008.

5. Zimmermann T, Leonhardt H, Kersting S, et al. Reduction of postoperative lymphedema after oral tumor surgery with sodium selenite. Biol Trace Elem Res 2005;106:193–203.

6. Bruns F, Buntzel J, Mucke R, et al. Selenium in the treatment of head and neck lymphedema. Med Prin Pract 2004;13:185–190.

7. Micke O, Bruns F, Mucke R, et al. Selenium in the treatment of radiation-associated secondary lymphedema. Int J Radiat Oncol 2003;56: 40–49.

8. Ridner SH. Lymphedema of the head and neck: an overview. NLN Lymph Link 2008;20:1–3.

9. Murphy BA, Gilbert J, Ridner SH. Systemic and global toxicities of head and neck treatment. Expert Rev Anticancer Ther 2007;7:1043–1053.

10. Dietz A, Rudat V, Nollert J, et al. Chronic laryngeal edema as a late reaction to radiochemotherapy. [in German]. HNO 1998;46:731–738.

11. Buntzel J, Glatzel M, Mucke R, Micke O, Bruns F. Influence of amifostine on late radiation-toxicity in head and neck cancer—a follow-up study. Anticancer Res 2007;27:1953–1956.

12. Schiefke F, Akdemir M, Weber A, et al. Function, postoperative morbidity, and quality of life after cervical sentinel node biopsy and after selective neck dissection. Head Neck 2009;31:503–512.

13. Wolff HA, Overbeck T, Roedel RM, et al. Toxicity of daily low dose cisplatin in radiochemotherapy for locally advanced head and neck cancer. J Cancer Res Clin Oncol 2009;135:961–967.

14. Bruns F, Micke O, Bremer M. Current status of selenium and other treatments for secondary lymphedema. J Support Oncol 2003;1:121–130.

15. Deng J, Ridner SH, Murphy BA. Lymphedema in patients with head and neck cancer. Oncol Nurs Forum 2011;38:E1–E10.

16. Patterson JM, Hildreth A, Wilson JA. Measuring edema in irradiated head and neck cancer patients. Ann Otol Rhinol Laryngol 2007;116:559–564.

17. Foldi ME, Foldi E, Strobenreuther RHK, Kubik S. Foldi's textbook of lymphology for physicians and lymphedema therapists, 2nd ed. Munich, Germany: Elsevier GmbH, 2006.

18. Polit DF, Beck CT. Nursing research: Principles and methods, 7th ed. Philadelphia, PA: Lippincott Williams and Wilkins, 2004.

19. Smith BG, Lewin JS. Lymphedema management in head and neck cancer. Curr Opin Otolaryngol Head Neck Surg 2010;18:153–158.

20. Piso DU, Eckardt A, Liebermann A, et al. Early rehabilitation of head-neck edema after curative surgery for orofacial tumors. Am J Phys Med Rehabil 2001;80:261–269.

21. National Cancer Institute. Common terminology criteria for adverse events [v3.0]. Available from http://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcaev3.pdf. Accessed January 10, 2009.

22. Trotti A, Colevas AD, Setser A, et al. CTCAE v3.0: development of a comprehensive grading system for the adverse effects of cancer treatment. Semin Radiat Oncol 2003;13:176–181.

23. American Cancer Society. Lymphedema: Understanding and managing lymphedema after cancer treatment. Atlanta, GA: American Cancer Society, 2006.

Appendix I
Patterson's Scale for Edema in Larynx and Pharynx

Based on Your Examination of the Participant, Please Use the Following Scale to Grade Lymphedema/Edema in the Laryngopharyngeal Structures

	Rating of Edema			
	Normal	Mild	Moderate	Severe
Structures				
1) Base of tongue	1) ___	____	____	____
2) Posterior pharyngeal wall	2) ___	____	____	____
3) Epiglottis	3) ___	____	____	____
4) Pharyngoepiglottic folds	4) ___	____	____	____
5) Aryepiglottic folds	5) ___	____	____	____
6) Interarytenoid space	6) ___	____	____	____
7) Cricopharyngeal prominence	7) ___	____	____	____
8) Arytenoids	8) ___	____	____	____
9) False vocal folds	9) ___	____	____	____
10) True vocal folds	10) ___	____	____	____
11) Anterior commissure	11) ___	____	____	____
Spaces	Normal	Mildly Reduced	Moderately Reduced	Severely Reduced
12) Valleculae	12) ___	____	____	____
13) Pyriform sinus	13) ___	____	____	____

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Appendix II
Stages of Lymphedema

Stage	Pathology	Signs and Symptoms	Diagnosis
0 Latency	Focal fibrosclerotic tissue alterations	None	Functional isotope lymphography
I Reversible	High protein edema; focal fibrosclerotic tissue alterations	Pitting edema; elevation reduces the swelling; possibly "pain of congestion"	Basic diagnostic procedures
II Spontaneously irreversible	Extensive fibrosclerosis, proliferation of adipose tissue	Brawny, hard swelling that does not recede with elevation	Basic diagnostic procedures
III Elephantiasis	Extensive fibrosclerosis, proliferation of adipose tissue	Like Stage II; invalidism	Basic diagnostic procedures

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