The Laryngoscope

Modified Head and Neck Swallow Scale: Using EORTC-QLQ-H&N35 to Predict Overall Survival

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Objectives/Hypothesis: Dysphagia is a treatment-related complication of head and neck cancer (HNCA). We demonstrate the predictive value of a modified head and neck swallow scale (m-HNSW) adapted from the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Head and Neck 35 (EORTC-QLQ-H&N35).

Study Design: Retrospective Cohort Study.

Methods: Retrospective, single-center cohort study utilizing a prospectively collected database of HNCA patients in a high-volume tertiary referral center. 736 HNCA patients more than 2 years from completion of treatment were identified. EORTC-QLQ-H&N35 data collected from at least one of three defined episodes of care were used. The m-HNSW uses three questions to form a 9-point dysphagia scale. A Cox proportional hazards model was used to determine the effect of the m-HNSW while controlling for demographics, tumor staging, site, and treatment.

Results: Using data from 3, 6, 12 months from treatment, we analyzed a subset that included 328 patients. Three months after the completion of therapy, the m-HNSW score had a significant association with 1 (HR = 1.24, P = .0005) and 5 year survival (HR = 1.19, P = .0002) after accounting for body mass index. Six (HR = 1.14, P = .014) and 12 month (hazard ratio (HR) = 1.33, P < .0001) scores post completion of therapy predict 5-year survival. An increase of the m-HNSW score by 1 point was associated with an increase in death by 24%, and 19% at 1 and 5 years following therapy.

Conclusions: The m-HNSW is a simple assessment of dysphagia using previously validated EORTC-QLC-H&N35 data that when taken at 3, 6, and 12 months after completion of therapy is predictive of overall survival.

Key Words: Head and neck cancer, dysphagia, swallowing, survival, outcomes, quality of life.

Level of Evidence: 4

***Laryngoscope*, 131:2478–2482, 2021**

INTRODUCTION

Improved oncologic outcomes and long-term survivorship in head and neck cancer (HNCA) have increased awareness of treatment-related toxicities.[1–3] Organ preservation treatments have been shown to increase dysphagia 2.5 times compared to surgery alone in certain subsites and patients undergoing any multimodality treatment are more likely to develop esophageal stricture.[4] Radiation fibrosis syndrome of the pharyngeal, laryngeal, and esophageal musculature presents clinically with symptoms of voice, airway, and swallowing abnormalities due to neuromuscular and musculoskeletal injury.[5]

Oral alimentary nutrition can be supplemented via food modifications, that is, dysphagia diets, nasogastric tube feeding, or gastrostomy tube (GT) feeding. Decreased use of GT has been correlated with favorable pretreatment dysphagia scores, pretreatment functional status, concurrent chemotherapy, and use of gabapentin.[6] Dysphagia related treatment effects in long-term HNCA survivors (>5 years from definitive radiation therapy) demonstrate 66% GT dependence with 86% of patients developing pneumonia, half requiring hospitalization.[7]

Quality of life (QOL) assessment tools in HNCA have been increasingly used in the oncologic *evaluation*, but more recently have been suggested to provide *prognostic* information.[8–10] The European Organization for Research and Treatment of Cancer Working Group developed the Quality of Life Questionnaires: EORTC, QLQ-C30, and the HNCA specific module EORTC QLQ-HN35. The association between QOL and nutrition is well-established in HNCA patients.[9,11] "Dyspnea" and "weight loss" have been significantly associated with overall survival (OS). "Insomnia" and "appetite loss" were associated with disease-free survival (DFS).[9]

Dysphagia is a known treatment-related complication of HNCA. Using the Surveillance, Epidemiology, and

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Editor's Note: This Manuscript was accepted for publication on March 30 2021.

The authors have no funding, financial relationships, or conflicts of interest to disclose.

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DOI: 10.1002/lary.29559

End Results-Medicare database, long-term dysphagia, gastrostomy or tracheostomy dependence, and pneumonia are associated with the greatest risk of late mortality.[12] However, there is a continuum of dysphagia between normal consumption of oral intake and GT dependence. Dysphagia has not yet been identified as a predictor of survival in HNCA. We sought to determine if the *severity* of dysphagia affects OS in HNCA and if dysphagia scores are modifiable by variables including age, body mass index (BMI), gender, smoking status, cancer stage, tumor site, treatment, and speech language pathology (SLP) evaluation.

MATERIALS AND METHODS

Concept

The EORTC QLQ-HN35 is a validated 35-question survey instrument that uses a four-question Likert-type categorical scale ("not at all", "a little", "quite a bit", and "very much"). This categorical scale is then transformed into a 0–100 scale, where a high score implies a high level of symptoms.[13] EORTC QLQ-HN35 is subdivided into six scales: pain, swallowing, nutrition, speech, social function, body image, and sexuality.[13] The swallowing scale (head and neck swallow scale [HNSW]) includes four items: problems swallowing liquids, problems swallowing pureed food, problems swallowing solid food, and choked when swallowing. The modified HNSW (m-HNSW) uses the same simplified Likert scale and summation but uses only three of four-questions (omitting choked when swallowing) (see Table I). The m-HNSW is a single score with a minimum of 0 (asymptomatic) to a maximum of 9; if the patient had complete gastrostomy dependence, the maximum score of 9 was assumed.

Inclusion

University of Cincinnati Institutional Review Board approval was obtained for the retrospective review of a prospectively collected HNCA database. HNCA is separated into subsites: lip/oral cavity, larynx, oropharynx, nasopharynx, hypopharynx/cervical esophagus, unknown primary, and other (sinonasal, salivary, skin). Patients at least 2 years after completion of treatment or who died within 2 years and completed at least one EORTC-QLQ-H&N35 questionnaire were identified. The EORTC-QLQ-H&N35 was administered at 10 timepoints including pretreatment, 3, 6, 12, 18, 24, 30, 36, 48, and 60 months with a varying number of patients responding ranging from 21 to 214 responders at each timepoint.

Statistical Analysis

We analyzed nine variables including age, BMI, gender, smoking status, cancer stage, tumor site, treatment, and SLP evaluation. Treatment was defined as a dichotomous variable radiation (+/−) and surgery (+/−). Although the EORTC-QLQ-H&N35 questionnaire was administered at multiple time points the response rate was variable. We did not have enough longitudinal data (i.e., patients completing multiple EORTC over time) for meaningful data analysis. We did identify relatively large responses at 3, 6, 12 months. For the survival analysis, we used a subset of 328 patients collected at 3, 6, 12 months (n = 154, 202, and 214 respectively) (Table II).

At 3, 6, 12 months, a survival analysis using Cox proportional hazards model was utilized to investigate whether the m-HNSW score at that time point had a significant effect on the hazard of death using the 9 covariates (listed above). We used a stepwise variable selection procedure to retain covariates that were significant in the final mode. The stepwise procedure although similar to the forward selection method at the beginning (entry criteria $P = .05$), allows effects that already are in the model to be removed if found to be below the staying criteria ($P = .05$) in subsequent steps similar to the backward selection method. The survival analysis was done using SAS 9.4 (SAS Inc., Cary, NC), though PHREG and LIFETEST survival plots were generated that accounted for significant covariates.

RESULTS

Demographics are included for the 3 month (n = 154), 6 month (n = 202) and 12 month (n = 213) subset of patients for a total of 328. The majority (83.2%) of tumors included in the analysis came from three subsites including lip/oral cavity, oropharynx, and larynx with an appropriate stratification of early and advanced T stage tumors (Table II). Covariates of average age, BMI, gender, smoking status, treatment (history of radiation and/or surgery), and SLP (exposure to SLP services) were similar among cohorts. Using the m-HNSW as a continuous variable from 0–9, the only covariant was BMI. Therefore, BMI, mean 27, is reported in the survival analysis.

At 3 months after the completion of therapy, the m-HNSW score had a significant association with 1 (HR = 1.24, $P = .0005$) and 5 year survival (HR = 1.19, $P = .0002$) after accounting for BMI. An increase of the m-HNSW score by 1 point was associated with an increase in death by 24%, and 19% at 1 and 5 year after completion of therapy. At 6 months post-treatment (n = 202), the dysphagia score was significantly associated with 5 year OS (HR = 1.14, $P = .014$) with an increase of 14% probability of death for a one unit increase of the m-HNSW score. At 12 months (n = 213) the dysphagia score was also significantly associated with 5 year death (HR = 1.33, $P < .0001$). An increase in the m-HNSW score at 12 months after treatment therapy by one point was associated with an increase in death by 33%.

TABLE I.
Generation of m-HNSW scores were created using responses to items from EORTC QLQ – H&N35 supplement.

EORTC QLQ – H&N35					
Item #		Not at All	A Little	Quite a Bit	Very Much
5	Have you had problems swallowing liquids?	0	1	2	3
6	Have you had problems swallowing pureed food?	0	1	2	3
7	Have you had problems swallowing solid food?	0	1	2	3

TABLE II.
Patient Characteristics. "Other" tumor site includes skin, salivary gland, sinonasal tumors. Tx stage includes unknown primary tumors. AJCC Tumor Staging by Site, 7th Edition. *P* values represent variability in all the values across three timepoints.

Characteristics	Total	3 Months	6 Months	12 Months	*P*-Value
Number of patients	328	154	202	213	
Mean age (yr), (+/−SD)	61.1 (11.7)	60.5 (11.4)	61.2 (11.3)	60.1 (11.5)	.613
Gender (n, %)					
Female	111 (33.8)	46 (30.0)	67 (33.2)	79 (37.1)	.345
Smoking status (n, %)					.341
Never	101 (30.8)	42 (27.3)	59 (29.2)	77 (36.2)	
Quit	138 (42.1)	62 (40.3)	83 (41.1)	82 (38.5)	
Active	89 (27.1)	50 (32.5	60 (29.7)	54 (25.4)	
Mean BMI (+/−SD)	27.7 (7.4)	27.7 (7.7)	28.0 (7.5)	28.1 (7.0)	.872
Radiation therapy	239 (72.9)	118 (76.6)	147 (72.8)	152 (71.3)	.521
Surgery	256 (78.1)	113 (73.4)	165 (81.7)	167 (78.4)	.170
SLP evaluation/treatment	256 (78.1)	103 (66.9)	134 (66.3)	145 (68.1)	.755
Tumor location (n)					.983
Lip/oral cavity	125 (38.1)	52 (33.8)	78 (38.6)	80 (37.6)	
Larynx	77 (23.5)	36 (23.4)	46 (22.8)	54 (25.4)	
Hypopharynx/cervical esophagus	11 (3.4)	6 (3.9)	8 (3.4)	5 (2.4)	
Oropharynx	71 (21.7)	40 (26.0)	45 (22.3)	46 (21.6)	
Nasopharynx	3 (0.9)	2 (1.3)	1 (0.5)	1 (0.5)	
Other	36 (11.0)	16 (10.4)	21 (10.4)	23 (10.8)	
Unknown primary	5 (1.5)	2 (1.3)	3 (1.5)	4 (1.9)	
T stage (I-IV)					.762
T I	86 (26.2)	35 (22.7)	58 (28.7)	64 (30.1)	
T II	92 (28.1)	42 (27.3)	56 (27.7)	60 (28.2)	
T III	56 (17.1)	30 (19.5)	35 (17.3)	35 (16.4)	
T IV	78 (23.8)	41 (26.6)	44 (21.8)	42 (19.7)	
Tx	16 (4.9)	6 (3.9)	9 (4.5)	12 (5.6)	

BMI = body mass index; SD = standard deviation; SLP = speech language pathology.

The m-HNSW scores at 6 and 12 month were not significantly associated with 1 year death. The stratification of the m-HNSW score was evaluated with scores of 3, 6, and 9 used to create predictive 1 and 5 year OS curves using the 3 month and 3, 6, and 12 month timepoints for the 1 and 5 year survival curves respectively (Figs. 1 and 2).

The cohorts of patients that did and did not survive (survival period defined as 2 years from treatment) were also analyzed separately with regard to m-HNSW score. The average score and standard deviation for patients that died and survive at 3, 6, and 12 months, were 3.67 (3.13), 1.69 (2.16) (P = .0002); 2.88 (1.99), 1.67 (1.31) (P = .013); 3.38 (2.13), 1.13 (0.87) (P = .001) respectively.

DISCUSSION

The rising incidence of human papillomavirus (HPV) related HNCAs has meant that a proportion of HNCA patients will experience improved clinical outcomes compared to HPV-negative tumors. As patients are living longer, delineating post-treatment prognostic markers can help modify the rehabilitation strategy for improved long-term QOL. Until the de-escalation of therapy for these tumors is well-established, multimodality treatment is still standard of care for advanced locoregional head and neck carcinomas and thus patients may continue to experience treatment-related toxicities for several years.

The study of dysphagia has benefited from standardized patient reported outcome measures including the Penetration-Aspiration scale,[13] Swal-QOL,[14] EAT-10,[15] MDADI,[16] and Sydney Swallow Questionaire.[17] The former two validated questionnaires were developed specifically for the treatment of HNCA patients while the others were validated in a broader spectrum of dysphagia. Likewise, the EORTC-QLQ-H&N35 is a validated patient reported outcome measure used to evaluate HNCA before, during, and after cancer treatments.[18] The generation of the m-HNSW score allows both retrospective and prospective validation of previously assessed data. Its ease of use and simple calculation can be used to follow HNCA patients over time in institutions already using the EORTC-QLQ-H&N35.

Patients with dysphagia will often self-inflict limitations in their own diet, therefore the extent of diet modification can be used as a proxy for the severity of dysphagia. By using the patient reported questions from the HNSW regarding liquids, pureed, and solids, the m-HNSW can be easily calculated and scaled rather than the typical binary question "Do you have dysphagia, yes or no?".

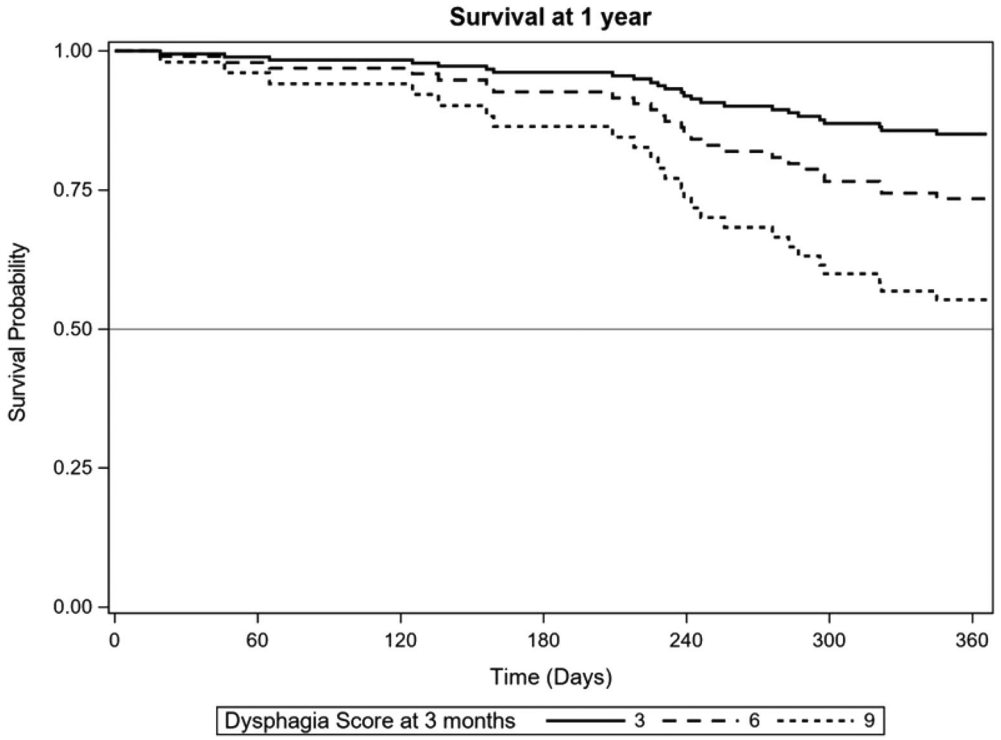

Fig 1. Estimated 1 year survival probabilities for a body mass index = 27, for three different scores of dysphagia severity scores (3, 6 and 9) measured at 3 months.

There are several important limitations in this study; we did not evaluate LRC or DFS and we did not analyze the cause of death. Our study evaluated the impact of dysphagia on OS not DFS. Disease status in this study's analysis was limited to tumor stage and site; the impact of nodal, metastatic disease, or HPV status was not evaluated. Our patient cohort included those that underwent primary surgical therapy, salvage surgical therapy, and organ-sparing definitive radiation and chemoradiation protocols. We separated into the site-specific tumor but did evaluate HPV status which may alter the algorithm comparing early and late treatment toxicity. Although our Cox proportional hazards model controlled for some patient factors, we do not assume that dysphagia causes death. It is possible that the degree of dysphagia serves as a surrogate marker for the patient's nutritional and/or functional status and more accurately predicts their individual risk of death as a result. When we looked at patients who survived compared to death at individual scores, we found no identifiable threshold. The lack of a threshold number suggests that the individual score should be monitored over time, as this decline in swallow function could be used by clinicians as a point of intervention.

Although SLP evaluation was not statistically significant in our model, this was a binary variable, that is, seen or not seen. We did not qualify evaluation or treatment, nor did we quantify number of sessions. Speech therapy is a vital component in the multidisciplinary care team for HNCA patients. Swallowing exercises are not only important in generating safe functional swallows, but also serve as a protective mechanism in the development of dysphagia.[19] Furthermore, patients who both eat and exercise have demonstrated decreased GT dependence over time.[20] Despite the significant impact of speech therapy as a preventative treatment during radiation therapy or chemoradiation therapy, this may not be standard of care nationally. Furthermore, SLP involvement in diagnostics such as functional endoscopic evaluation of swallow and modified barium swallow is commonly ordered tools used to both assess the severity of dysphagia and make treatment recommendations based on dietary restrictions. Future studies will include both dysphagia evaluation and interventions to change the outcome.

Although it is recognized that severe dysphagia put patients at increased risk for mortality, there is a paucity of literature using OS as an outcome measure. However, one recent study looking at early swallowing in patients with oral cavity cancer following surgical treatment demonstrated that early swallow dysfunction was a risk factor independent of T stage for decreased OS.[21] This study did not find a gradient difference in OS and instead swallow dysfunction was characterized as a more binary variable. A single early timepoint of 7 days postop was used in this study and this study did not account for long-term postoperative changes and or adjunctive treatment.

Our study demonstrates that the m-HNSW can be used to predict OS. Specifically, the 3, 6, and 12-month dysphagia score were significantly associated with increasing the hazard of death. In addition, as demonstrated by the divergence of the OS curves for those patients with low scores versus higher scores, the scale of the m-HNSW is effective in its prediction of variable risk

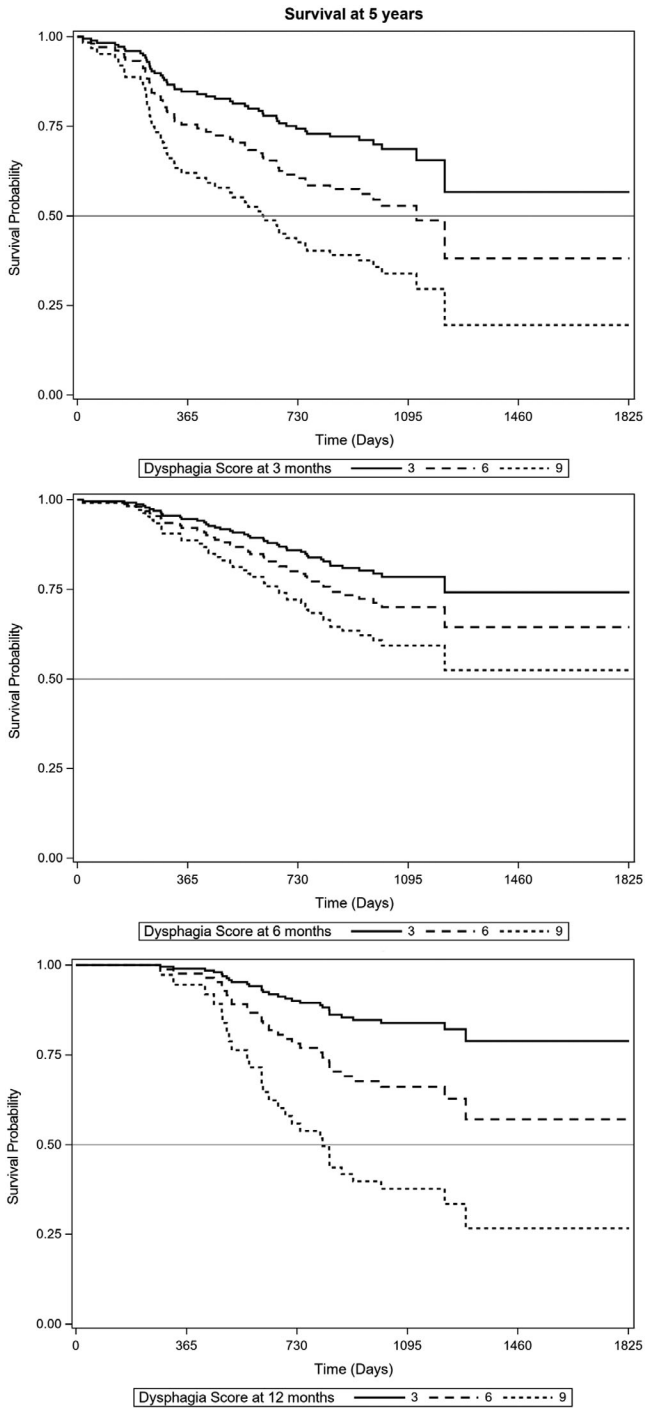

Fig 2. Estimated 5 year survival probabilities for body mass index = 27, for three different scores of dysphagia severity scores (3, 6 and 9) measured at 3, 6, and 12 months.

of death at 1 and 5 years. Our study suggests that the assessment of dysphagia in HNCA patients (especially mucosal disease, i.e., subsites including lip/oral cavity, oropharynx, and larynx) with the m-HNSW should be given at 3 and 12 months post treatment for the best predictive value at 1 and 5 years respectively. The broad inclusion criteria independent of HPV status and subsite contributes to the applicability of the m-HNSW.

CONCLUSION

This study presents a simplified dysphagia scoring system as a novel prognosticator for survival which could help clinicians identify those patients at a higher risk of death after definitive therapy for HNCA. This added metric warrants further study in a prospective manner to validate the ability to predict OS. This score may assist in initiating intervention to alter the trajectory of dysphagia and potentially survival.

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