ORIGINAL RESEARCH

Predictors of severe dysphagia following radiotherapy for head and neck cancer

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Abstract

Objective: To investigate if severe dysphagia following radiotherapy for head and neck cancer (HNC) could be predicted by patient and tumor characteristics, feeding tube use, weight factors, jaw opening function, and saliva secretion.

Methods: Data was collected from 94 HNC patients 6 to 36 months post radiotherapy. Swallowing function was assessed by videofluroscopy (VFS). Severe dysphagia was defined by Penetration Aspiration Scale (PAS) as PAS≥5 or a total score ≤60 on the M. D. Anderson Dysphagia Inventory (MDADI).

Results: Thirty-three patients (35%) had PAS ≥5 and 19 (20%) a MDADI ≤60, that is, presented with severe dysphagia. Univariable logistic regression analysis (UVA) gave that tumor of the tonsil, overweight at time of VFS and each unit increase in Body Mass Index (BMI) predicted less risk of PAS ≥5. Dependency of feeding tube at time of VFS and each month's continued use and weight loss ≥7.5% since treatment to time of VFS predicted increased risk of PAS ≥5. Predictive variables from the UVA of PAS ≥5 (tumor of the tonsil, overweight, and total duration of feeding tube), were analyzed by multivariate logistic regression analysis. All retained power as independent predictors. UVA for MDADI showed that use of feeding tube at time of VFS predicted MDADI ≤60 with the risk increasing each month. Each increasing unit of BMI decreased risk of MDADI ≤60.

Conclusion: Long time users of feeding tube and higher weight-loss are at risk of severe dysphagia. This makes collaboration between professionals working with dysphagia an important step in detecting severe dysphagia.

Level of Evidence: 3.

KEYWORDS
deglutition disorders, head and neck neoplasms, saliva secretions, trismus, weight loss

1 | INTRODUCTION

Radiotherapy is an effective treatment for head and neck cancer (HNC) and approximately 80% of HNC patients are recommended radiotherapy in some extent during cancer treatment.[1] However, as radiation impacts all tissues in the targeted area it often causes long-term, in some cases permanent, impairments.[2,3] Dysphagia is one of the most common

side-effects among HNC patients, afflicting approximately 40% to 45% of patients treated for HNC.[4,5]

Dysphagia is commonly associated with malnutrition, dehydration, aspiration, pneumonia and has been noted to effect patients perceived well-being negatively in measurements of health-related quality of life (HRQL).[6,7] HNC guidelines recommend multidisciplinary teams to monitor and optimize dysphagia outcomes and intervene when necessary.[8] HNC patients are at risk of malnutrition and weight-loss before, during and after treatment.[9] On top of this, HNC patients with dysphagia may not be able to eat and drink all consistencies, which can lead to a restricted diet.[10] A poor nutritional status has also been noted to contribute to dysphagia due to loss of muscle mass (sarcopenia).[11,12] To avoid aspiration pneumonia, malnutrition and excessive weight-loss, patients may depend on a feeding tube for nutrition, either during treatment or as a permanent solution.

Radiation induced impairment to anatomical structures involved in swallowing can result in residue after swallowing, penetration and aspiration.[10,13] Penetration and aspiration events can be difficult to detect in HNC patients as irradiation sometimes leads to sensory deficits with inability to notice food or liquid entering the airway.[14] As a result of the sensory deficits patients may fail to protect their airways by coughing or by clearing their throat. Such silent penetration and aspiration are risk factors of aspiration pneumonia and death.[15]

Trismus that is, restricted mouth opening and hyposalivation are other common radiation-induced side effects,[2,3] afflicting up to 45% and 25% to 50% of HNC patients respectively.[16,17] In terms of HRQL, the effects of dysphagia, trismus, and hyposalivation are well known and have been investigated in several studies.[7,18-22] Research has also focused on outcomes of therapeutic intervention to improve function[23-25] and on how irradiation correlates to impaired function.[26-28] However, few studies have examined how salivary secretions and trismus relate to observer rated dysphagia.[17,29]

Impaired sensation makes it difficult for patients to subjectively determine their swallowing ability in terms of penetration/aspiration events, and signal the need for referral for a swallowing examination.[28,30] Patients who do perceive swallowing difficulties often underestimate them, mainly reporting less severe dysphagia symptoms while instrumental examination shows aspiration.[31] As dysphagia can have grave impact on physical health and HRQL it would be beneficial to find easily attainable clinical markers that could predict severe dysphagia and indicate referral for dysphagia management.

The main aim of this study was to investigate if severe dysphagia following radiotherapy for HNC could be predicted by patient and tumor characteristics, feeding tube and weight factors, jaw opening function, and saliva secretion. Severe dysphagia was defined as Penetration Aspiration Scale (PAS) (Table 1)[32] 5 or higher, as well as M. D. Anderson Dysphagia Inventory (MDADI) scores below 60 points.[33] An additional aim was to investigate how the same factors influenced the score on the MDADI, a dysphagia specific HRQL questionnaire.

2 | SUBJECTS AND METHODS

2.1 | Subjects

Subjects diagnosed with HNC participating at the weekly multidisciplinary tumor board meeting at Sahlgrenska University Hospital in Gothenburg were assessed for eligibility for this study by chart review. Criteria for inclusion were treatment for tumors of the tonsil, base of tongue, hypopharynx, or larynx treated by curative external beam radiation therapy (EBRT) ± brachytherapy and/or chemotherapy. Exclusion criteria were surgical treatment, previous oncological treatment for HNC, patient reported dysphagia prior to HNC, neurological or neuromuscular disease, and tracheotomy. This prospective study included patients between the years 2011 and 2018.

Patients who met criteria for inclusion were contacted by telephone and asked about their current and previous swallowing ability. They were then offered an assessment of their swallowing function by videofluoroscopy (VFS) 6 to 36 months post oncological treatment. Patients who participated in VFS and completed the MDADI were included in analysis.

TABLE 1 Rosenbek's Penetration-Aspiration Scale,[32] with definition of severe dysphagia used in the present study added

	PAS		
None	1	Material does not enter the airway	No/mild dysphagia
Penetration	2	Material enters the airway, remains above the vocal folds, and is ejected from the airway	
	3	Material enters the airway, remains above the vocal folds, and is not ejected from the airway	
	4	Material enters the airway, contacts the vocal folds, and is ejected from the airway	
	5	Material enters the airway, contacts the vocal folds, and is not ejected from the airway	Severe dysphagia
Aspiration	6	Material enters the airway, passes below the vocal folds and is ejected into the larynx or out of the airway	
	7	Material enters the airway, passes below the vocal folds, and is not ejected from the trachea despite effort	
	8	Material enters the airway, passes below the vocal folds, and no effort is made to eject	

TABLE 2 Patient characteristics and treatment information

		Mean (SD)
Age at time of VFS		63.0 (8.1)
Time between radiotherapy and VFS in months		12.7 (8.1)
		n (%)[b]
Sex	Female	27 (28.7%)
	Male	67 (71.3%)
Tumor location	Tonsil	46 (48.9%)
	Base of tongue	32 (34.0%)
	Larynx	11 (11.7%)
	Hypopharynx	5 (5.3%)
Tumor stage	I	11 (11.7%)
	II	8 (8.5%)
	III	11 (11.7%)
	IV	64 (68.1%)
External beam radiotherapy	Conventionally fractionated (once daily in 1.9-2.15 Gy fractions, total of 64.6-73.1 Gy)	89 (94.7%)
	Hyperfractionated radiotherapy (twice daily in 1.7-2 + 1.1 Gy fractions, a total of 64.4-68 Gy)	5 (5.3%)
Irradiation to lymph nodes		80 (85.1%)
Brachytherapy		20 (21.3%)
Chemotherapy	No chemotherapy	20 (21.3%)
	Concomitant	64 (68.1%)
	Induction	10 (10.6%)
Adult Comorbidity Evaluation (ACE-27)	None	46 (48.9%)
	Mild	33 (35.1%)
	Moderate	12 (12.8%)
	Severe	3 (3.2%)
Smoking status[a]	Never smoked	29 (31.2%)
	Former smoker	54 (58.1%)
	Currently smoking	10 (10.8%)
Body Mass Index (BMI) classification[a]	Underweight (BMI <18.5)	6 (6.7%)
	Normal weight (BMI 18.5-24.9)	55 (61.8%)
	Overweight (BMI 25-29.9)	25 (28.1%)
	Class I obesity (BMI 30-34.9)	3 (3.4%)
% weight-loss between oncological treatment and videofluroscopy[a]	0-4%	19 (21,3%)
	4-7.5%	14 (15.7%)
	>7.5%	56 (62.9%)
Severe dysphagia	Rosenbek's Penetration Aspiration Scale ≥5	33 (35.1%)
	M. D. Anderson Dysphagia Inventory (MDADI) total score ≤60	19 (20.4%)
Use of feeding tube during treatment		72 (76.6%)
Use of feeding tube at time of videofluroscopy		8 (8.5%)
Contact with a dietician	Yes	86 (91.5%)
	No	8 (8.5%)

[a]Missing data: Smoking status is missing for one patient. Weight and BMI values missing for five patients.
[b]Percentages rounded, therefore it does not always sum up to 100%.

2.1.1 | Oncologic treatment

Oncologic treatment was given in accordance to regional guidelines. EBRT was either conventional (n = 89) or hyperfractionated (n = 5) (Table 2).

After completed EBRT, brachytherapy was given to some patients with tumors of the tonsils or base of tongue (n = 20). A majority of patients (n = 74) also received chemotherapy.

3 | ASSESSMENT AND ENDPOINTS

Information about tumor characteristics was retrieved from patient chart review. Weight-loss between oncological treatment and VFS, duration of feeding tube use, and contact with a dietician was retrieved from patient chart review. Within 2 weeks of VFS patients completed the MDADI and a sociodemographic questionnaire and measurements of stimulated saliva secretions and Maximum

Interincisal Opening (MIO) were made. The Adult Comorbidity Evaluation (ACE-27) was used to determine comorbidity.[34,35]

3.1 | Videofluoroscopic examination of swallowing

The VFS was performed by a radiologist in collaboration with speech and language pathologist (SLP). Patients were seated in an upright position. High-resolution images (video matrix 1024 × 1024) were acquired in lateral projection at 15 pulses per second. The field of view was set to the tip of tongue anteriorly, the pharyngeal wall posteriorly, the soft palate superiorly, and the seventh cervical vertebra inferiorly. Four consistencies were examined (Table 3). Each consistency was determined according to testing procedures as described by the International Dysphagia Diet Standardisation Initiative (IDDSI) framework.[36] The patients swallowed on cue by the SLP except 20 mL of thin liquid where patients were instructed to drink freely. Every bolus was performed twice. IDDSI 0 and 2 was administered by syringe while 4 and 6 were given on spoon. If a greater bolus amount of the same consistency was deemed not safe for the patient (ie, risk of severe aspiration) it was excluded.

The PAS was used to determine dysphagia severity[32] (Table 1). PAS for each bolus was decided by consensus of the radiologist and the SLP. The overall PAS-score was determined by the highest obtained PAS during the examination. PAS ≥4 has been found to correspond well to patients' own experience of difficulty and PAS 6 or more has been noted to be an indicator of aspiration pneumonia.[28,33] In this study, PAS 5 or higher was used to indicate severe swallowing difficulties in terms of swallowing safety.

3.2 | Patient reported outcome

The MDADI comprises 20 items in four domains and measures the impact of dysphagia on HRQL for patients after HNC treatment.[37] The global domain examines how overall everyday activities are limited by the swallowing ability. The emotional domain reflects what feelings the swallowing function evokes in the patients, the functional domain concerns how the swallowing ability impacts daily activities. Items in the physical domain illustrate the patient's own perception of the swallowing function. Each item is scored 1 to 5 (strongly agree-strongly disagree). The domain scores range 20 to 100. A higher MDADI score represents better day-to-day functioning. The MDADI has been translated and validated into Swedish and was found to have satisfactory psychometric properties.[38] A total score below 60 has been used to indicate moderate to severe dysphagia in previous studies and was therefore used as a cut-off for severe dysphagia for patient-reported swallowing difficulties.[26,33,39-41]

3.3 | Saliva secretion

Measurement of stimulated saliva secretion was made by patients chewing a piece of paraffin wax. All saliva produced during 3 minutes

TABLE 3 Detailed description of the boluses used in the present study

Bolus size and consistency	Consistency level according to the IDDSI framework[36]	Contrast
3 mL thin liquid	0	Mixobar Colon 1 g Ba/mL mixed with equal amount of water
5 mL thin liquid	0	
10 mL thin liquid	0	
20 mL thin liquid, drink freely	0	
5 mL mildly thick	2	Omnipaque 300 mg I/mL. 20 mL Omnipaque mixed with 2 mL instant thickener
3 mL extremely thick	4	Omnipaque 300 mg I/mL. 20 mL Omnipaque mixed with 15 mL instant chocolate pudding mix
¼ biscuit	6	Covered in Mixobar Colon 1 g Ba/mL mixed with equal amount of water

Abbreviation: IDDSI, International Dysphagia Diet Standardisation Initiative.

was collected in a test tube. Hyposalivation was defined as salivation: ≤0.7 mL/min.[42]

3.4 | Maximum interincisal opening

MIO was measured in mm, trismus defined as MIO ≤35 mm.[43]

4 | STATISTICS

Descriptive statistics was used to describe patient characteristics and treatment information. Nonparametric statistical tests were used and $P < .05$ was considered statistically significant.

UVA was constructed to examine the relationship between each variable and the endpoint PAS≥5 and MDAD ≤60 described in P-values and odds ratio (OR). Analyses were based on original values and not on stratified groups. OR represents the increased odds for the examined endpoint by the selected variables.

A multivariate logistic regression analysis (MVA) was constructed from the statistically significant variables chosen by backward selection from the endpoint of PAS ≥5. Each predictive variable in the MVA was described as the OR and P-value of developing severe dysphagia. A minimum of 10 events per variable is required for an MVA, therefore an MVA could not be performed for the endpoint MDADI.

TABLE 4 Association between patient related variables and severe dysphagia defined as level 5 or more by Rosenbek's Penetration Aspiration Scale (n = 33)

Variable	Value	n (%) PAS ≥5 (n = 33)	OR (95%CI) PAS ≥5	P-value	Area under ROC-curve (95%CI)
Tumor location	Tonsil	11 (23.9%)	0.37 (0.15-0.90)	.028[a]	0.62 (0.52-0.72)
	Base of tongue	14 (43.8%)	1.76 (0.73-4.26)	.21	0.56 (0.46-0.67)
	Larynx	5 (45.5%)	1.64 (0.46-5.84)	.45	0.53 (0.45-0.60)
	Hypopharynx	3 (60.0%)	2.95 (0.47-18.61)	.25	0.53 (0.47-0.58)
Tumor stage	Early (stage I-II)	6 (31.6%)			
	Advanced (stage III-IV)	27 (36.0%)	1.22 (0.42-3.57)	.72	0.52 (0.43-0.60)
Dependency on feeding tube at time of videofluroscopy	Yes	6 (75.0%)	6.55 (1.24-34.59)	.027[a]	0.57 (0.50-0.65)
Dependency on feeding tube during treatment	Yes	29 (40.3%)	3.03 (0.93-9.89)	.065	0.59 (0.51-0.67)
Total duration of dependency on feeding tube in months	0-<2	6 (18.8%)			
	2-<4	7 (24.1%)			
	4-19	19 (61.3%)	1.35 (1.14-1.60)	.0005[a]	0.73 (0.62-0.84)
% weight-loss between oncological treatment and videofluroscopy	0-4%	3 (15.8%)	1.00		
	4-7.5%	5 (35.7%)	2.96 (0.57-15.39)	.20	
	>7.5%	25 (44.6%)	4.30 (1.13-16.44)	.033[a]	0.62 (0.52-0.71)
Body Mass Index (BMI) Classification at time of videofluroscopy	Normal weight BMI 18.5-24.9	27 (47.4%)	1.00		
	Underweight BMI <18.5	2 (50.0%)	1.11 (0.15-8.44)	.92	
	Overweight BMI 25-29.9	4 (14.3%)	0.19 (0.06-0.60)	.0051[a]	0.67 (0.58-0.76)
Body Mass Index (BMI) at time of VFS	17.5-<22.7	14 (46.7%)			
	22.7-<24.7	14 (46.7%)			
	24.7-31.6	5 (17.2%)	0.81 (0.69-0.95)	.0097[a]	0.66 (0.54-0.77)
Maximum interincisal mouth opening (MIO)	MIO ≤35 mm	8 (61.5%)			
	MIO >35 mm	24 (33.3%)	0.31 (0.09-1.06)	.062	0.58 (0.49-0.66)
Stimulated saliva secretions ml/min	Secretion ≤0.7	14 (43.8%)			
	Secretion >0.7	17 (30.4%)	0.56 (0.23-1.38)	.21	0.57 (0.46-0.68)
Swallowing function according to M. D. Anderson Dysphagia Inventory (MDADI)	None to moderate dysphagia (>60)	22 (29.7%)			
	Severe dysphagia (<60)	10 (52.6%)	2.63 (0.94-7.35)	.066	0.58 (0.49-0.68)
Adult Comorbidity Evaluation (ACE-27)	None	14 (30.4%)	1.00		
	Mild	11 (33.3%)	1.14 (0.44-2.98)	.78	
	Moderate	6 (50.0%)	2.29 (0.63-8.34)	.21	
	Severe	2 (66.7%)	4.57 (0.38-54.66)	.23	0.58 (0.46-0.69)

Note: All tests are performed with univariable logistic regression. *P*-values and OR are based on original values and not on stratified groups. OR is the ratio for the odds for an increase of the predictor of one unit.
[a]*P*-values = statistically significant values *P* <.05.

An event is the number of patients who fulfills both the endpoint criteria (in this case MDADI ≤60) and the predictive variable tested.

Analyses of the variables influence on the total score of MDADI and subdomains were done using the Mann-Whitney *U*-test for dichotomous variables, the Kruskal-Wallis test for nonordered values, and the Jonckheere-Terpstra test for ordered values. For categorical variables distribution of scores was analyzed and for ordered variables trends of the scores. The relationship between the domain scores of MDADI and the continuous variables are analyzed with Spearman's correlation coefficient.

TABLE 5 Association between patient related variables and severe dysphagia defined as a lower or equal to 60 total score on the M. D. Anderson Dysphagia Inventory (n = 19)

Variable	Value	n (%) MDADI ≤60 (n = 19)	OR (95%CI) MDADI ≤60	P-value	Area under ROC-curve (95%CI)
Tumor location	Tonsil	10 (21.7%)	1.17 (0.43-3.22)	.76	0.52 (0.39-0.65)
	Base of tongue	5 (16.1%)	0.66 (0.21-2.04)	.47	0.54 (0.43-0.66)
	Larynx	2 (18.2%)	0.85 (0.17-4.30)	.84	0.51 (0.43-0.59)
	Hypopharynx	2 (40.0%)	2.78 (0.43-17.99)	.28	0.53 (0.46-0.61)
Tumor stage	Early (stage I-II)	3 (16.7%)			
	Advanced (stage III-IV)	16 (21.3%)	1.36 (0.35-5.27)	.66	0.52 (0.43-0.62)
Dependency on feeding tube at time of videofluroscopy	Yes	6 (75.0%)	16.61 (3.02-91.47)	.0012[a]	0.64 (0.54-0.75)
Dependency on feeding tube during treatment	Yes	17 (23.9%)	3.15 (0.67-14.86)	.15	0.58 (0.50-0.67)
Total duration of dependency on feeding tube in months	0-<2	3 (9.4%)			
	2-<4	6 (21.4%)			
	4-19	10 (32.3%)	1.19 (1.04-1.37)	.014[a]	0.67 (0.53-0.81)
% weight-loss between oncological treatment and videofluroscopy	0-4%	2 (10.5%)	1.00		
	4-7.5%	2 (14.3%)	1.42 (0.17-11.51)	.74	
	>7.5%	15 (27.3%)	3.19 (0.66-15.49)	.15	0.61 (0.50-0.72)
Body Mass Index (BMI) classification at time of videofluroscopy	Normal weight BMI 18.5-24.9	14 (25.0%)	1.00		
	Underweight BMI <18.5	3 (75.0%)	9.00 (0.86-93.67)	.066	
	Overweight BMI 25-29.9	2 (7.1%)	0.23 (0.05-1.10)	.065	0.64 (0.53-0.75)
Body Mass Index (BMI) at time of VFS	17.5-<22.7	9 (30.0%)			
	22.7-<24.7	7 (24.1%)			
	24.7-31.6	3 (10.3%)	0.77 (0.64-0.94)	.0091[a]	0.67 (0.54-0.81)
Maximum interincisal mouth opening (MIO)	MIO ≤35 mm	5 (38.5%)			
	MIO >35 mm	13 (18.3%)	0.36 (0.10-1.28)	.11	0.58 (0.46-0.69)
Stimulated saliva secretions mL/min	Secretion ≤0.7	10 (31.3%)			
	Secretion >0.7	8 (14.3%)	0.37 (0.13-1.06)	.063	0.62 (0.49-0.75)
Adult Comorbidity Evaluation (ACE-27)	None	10 (22.2%)	1.00		
	Mild	6 (18.2%)	0.78 (0.25-2.41)	.66	
	Moderate	3 (25.0%)	1.17 (0.26-5.14)	.84	
	Severe	0 (0.0%)	0.00 (0.00-infinity)	.98	0.56 (0.43-0.69)

Note: All tests are performed with univariable logistic regression. *P*-values and OR are based on original values and not on stratified groups. OR is the ratio for the odds for an increase of the predictor of one unit.
[a]*P*-values = statistically significant values *P* <.05.

5 | ETHICAL CONSIDERATIONS

The study was conducted in accordance with the Declaration of Helsinki, was approved by the Regional Ethical Review Board, Gothenburg, Sweden. All patients gave their informed consent before inclusion in the study.

6 | RESULTS

The study included a total of 94 patients. Seventy-one percent of the participants were male and the mean age was 63 years. Thirty-three

patients (35%) had PAS ≥5 and 19 patients (20%) had a total MDADI score ≤60. Patient characteristics and treatment information are listed in Table 2.

6.1 | UVA of possible predictors of PAS ≥5

Associations between all patient related variables and PAS ≥5 are listed in Table 4. Regarding tumor location, tumor of the tonsil predicted a decreased risk of severe dysphagia compared to tumors of the base of tongue, larynx, or hypopharynx (OR = 0.37, P = .028). Tumor stage, analyzed as early (I-II) vs advanced stage (III-IV), had no

TABLE 6 Multivariate logistic regression of variables predicting severe dysphagia defined as level 5 or more by Rosenbek's Penetration Aspiration Scale

Variable	OR (95%CI)	P-value
Body Mass Index (BMI) Classification at time of videofluroscopy—Overweight BMI 25-29.9	0.771 (0.635-0.935)	.0083[a]
Total duration of dependency on feeding tube in months	1.344 (1.121-1.611)	.0014[a]
Tumor location—Tonsil	0.244 (0.079-0.749)	.0137[a]

Note: The odds ratio was estimated by multivariate logistic regression with above variables.
[a]P-values = statistically significant values P <.05.

predictive power. Patients with a feeding tube at time of VFS had a greater risk of presenting with PAS >5 (OR = 6.55, P = .027). So was the total duration of feeding tube where each month of feeding tube use increased the OR by 1.35 (P = .0005) with each month of feeding tube use. Weight-loss between oncological treatment and VFS ≥7.5% predicted PAS ≥5 (OR = 4.3, P = .033), while overweight (BMI >24.9) showed a decreased risk (OR = 0.19, P = .0051). Each increasing BMI unit predicted a decreased risk of PAS ≥5 (OR = 0.8, P = .0097). MIO >35 mm showed a tendency toward decreased risk of PAS≥5 (OR = 0.31, P = .062). No predictive power of PAS ≥5 was demonstrated by MDADI ≤60 or by stimulated saliva secretions.

6.2 | UVA of possible predictors of MDADI ≤60

All analyzed variables of MDADI score ≤60 are found in Table 5. Dependency on feeding tube at time of VFS was a predictor of severe dysphagia with OR 16.61 (P = .0012) as was total duration of feeding tube use with OR increasing by 1.19 each month of feeding tube use (P = .014). A decreased risk of severe dysphagia was seen with each increasing unit of BMI with OR 0.77 (P = .0091). A tendency toward prediction was seen by saliva secretions with OR 0.37 (P = .063). No predictive power of dysphagia according to the MDADI was demonstrated by MIO, tumor location, or tumor stage.

6.3 | Multivariate logistic regression analysis

A minimum of 10 events per variable is required for an MVA. Three out of six predictive variables of UVA from PAS ≥5 met this criterion: tonsil as tumor locality, duration of feeding tube dependency, and overweight at time of VFS were included in the MVA. Tumor of the tonsil and overweight retained their power as predictor for a decreased risk and duration of feeding tube in months for an increased risk of severe dysphagia (Table 6).

6.4 | Influencing factors of the M. D. Anderson Dysphagia Inventory

All possible predictive variables were analyzed regarding their impact on the MDADI scores (Table 7). Lower scores represent worse day-to-day functioning within the domain.

More advanced tumor stage resulted in worse scores in the physical domain as well as total score. Patients who had been dependent on a feeding tube during tumor treatment presented with statistically significant lower scores in the functional, physical, and total domains compared to those who had been able to maintain a total oral intake during treatment. Patients who were still feeding tube dependent at time of VFS reported statistically significant lower outcomes for all domains compared to patients with a full oral intake. Weight-loss between oncological treatment and VFS impacted scores in the functional and total domain where patients who had a weight loss of 7.5% or more presented with lower scores compared to patients with less weight-loss. Patients with trismus demonstrated lower scores in the functional, physical, and total domain, while hyposalivation had an impact on the emotional domain.

7 | DISCUSSION

The aim of this study was to investigate if easily attainable clinical markers could be considered predictors for severe dysphagia, among patient data, tumor and treatment characteristics. 35% of the cohort in the present study had a PAS ≥5, which corresponds well to other studies reporting prevalence around 35% for aspiration and/or penetration among HNC patients.[44,45] According to the results increasing BMI and patients with tumor of the tonsil and overweight were less likely suffer from severe dysphagia. Weight-loss following treatment of 7.5% or more and use of feeding tube at time of VFS were predictors of severe dysphagia, with increasing risk with each month's use of a feeding tube.

The present study demonstrates variables concerning weight as important to detect severe dysphagia as increasing BMI and weight-loss between oncological treatment and VFS impacted the results, where a higher BMI seem to have a protective effect on the risk of developing severe dysphagia. Similarly, a study on HNC patients post RT found that patients who aspirated on VFS had a significantly higher mean weight-loss and lower BMI compared to nonaspirating patients.[46] Still only 10% of the patients who aspirated were categorized as underweight. This corresponds well to the present study as only 7% of patients with PAS ≥5 were categorized as underweight. Decreasing weight and BMI is usually monitored to detect malnutrition among HNC patients, but these results suggest that a high weight-loss and/or decrease in BMI even among patients who are able to maintain a normal weight could indicate severe dysphagia.

As expected, feeding tube dependency was also a predictor, both with every increasing month of use and dependency on feeding tube at time of VFS. Use of feeding tube during treatment was not associated to severe dysphagia, indicating that short time use following

TABLE 7 Influence of patient related variables on subjective swallowing function measured by the M. D. Anderson Dysphagia Inventory (MDADI)

Variable	Value	Emotional domain Mean (SD)	P-value	Functional domain Mean (SD)	P-value	Physical domain Mean (SD)	P-value	MDADI total score Mean (SD)	P-value
Tumor location	Tonsil	82.7 (19.0) n = 46		80.7 (24.8) n = 46		71.5 (20.4) n = 46		77.4 (19.6) n = 46	
	Base of tongue	86.3 (14.9) n = 31		84.4 (17.6) n = 31		72.3 (18.3) n = 31		79.8 (15.6) n = 31	
	Larynx	87.2 (15.6) n = 11		85.8 (19.5) n = 11		75.8 (26.4) n = 11		81.9 (20.6) n = 11	
	Hypopharynx	68.2 (27.16) 67 (30; 100) n = 5	.45	58.4 (29.2) n = 5	.27	55.2 (26.6) n = 5	.34	59.8 (26.6) n = 5	.34
Tumor stage	I	89.3 (16.7) n = 10		90.0 (18.8) n = 10		79.5 (26.3) n = 10		85.1 (20.6) n = 10	
	II	91.3 (11.7) n = 8		92.0 (17.1) n = 8		82.4 (18.9) n = 8		87.6 (15.7) n = 8	
	III	83.6 (17.7) n = 11		82.2 (16.8) n = 11		70.9 (14.8) n = 11		77.8 (14.6) n = 11	
	IV	81.8 (18.8) n = 64	.10	78.5 (24.2) n = 64	.066	68.9 (20.8) n = 64	.040[a]	75.4 (19.6) n = 64	.046[a]
Dependency on feeding tube at time of videofluroscopy	No	85.5 (16.7) n = 85		85.1 (19.2) n = 85		73.9 (19.8) n = 85		80.4 (17.4) n = 85	
	Yes	63.6 (20.1) n = 8	.0044[a]	41.5 (18.9) n = 8	<.0001[a]	44.6 (11.7) n = 8	.0003[a]	49.8 (13.8) n = 8	.0002[a]
Dependency on feeding tube during treatment	No	86.1 (17.6) n = 22		90.9 (16.2) n = 22		80.8 (19.9) n = 22		85.1 (17.1) n = 22	
	Yes	82.9 (18.2) n = 71	.33	78.4 (23.6) n = 71	.0091[a]	68.5 (20.4) n = 71	.013[a]	75.5 (19.2) n = 71	.020[a]
% weight-loss between oncological treatment and videofluroscopy	0-4%	86.9 (18.2) n = 19		88.4 (16.7) n = 19		80.6 (19.9) n = 19		84.6 (17.5) n = 19	
	4-7.5%	86.4 (18.8) n = 14		83.7 (24.1) n = 14		70.9 (20.2) n =		78.9 (19.9) n = 14	
	>7.5%	81.5 (18.4) n = 55	.11	77.2 (24.1) n = 55	.049[a]	67.9 (21.4) n = 55	.051	74.6 (19.6) n = 55	.043[a]
Body Mass Index (BMI) Classification at time of videofluroscopy	Underweight BMI <18.5	70.7 (24.7) n = 6		65.3 (31.0) n = 6		68.2 (27.7) n = 6		68.3 (27.1) n = 6	
	Normal weight BMI 18.5-24.9	82.4 (18.2) n = 54		78.4 (24.7) n = 54		68.6 (21.4) n = 54		75.5 (20.0) n = 54	
	Overweight BMI 25-29.9	86.8 (16.9) n = 25		87.8 (14.5) n = 25		75.5 (18.8) n = 25		82.2 (15.2) n = 25	
	Class I obesity 30-34.9	99.0 (1.7) n = 3	.034[a]	92.0 (13.9) n = 3	.089	86.0 (24.3) n = 3	.11	91.7 (14.4) n = 3	.056
Maximum interincisal mouth opening (MIO)	MIO ≤35 mm	79.4 (14.9) n = 13		66.8 (23.6) n = 13		57.8 (18.0) n = 13		66.9 (16.8) n = 13	
	MIO >35 mm	84.4 (18.7) n = 71	.16	83.2 (22.4) n = 71	.013[a]	73.5 (21.2) n = 71	.016[a]	79.5 (19.5) n = 71	.025[a]
Stimulated saliva secretions ml/min	Secretion ≤0.7	79.4 (18.8) n = 32		75.6 (26.1) n = 32		66.7 (21.8) n = 32		73.0 (20.4) n = 32	
	Secretion >0.7	87.7 (15.6) n = 56	.041[a]	85.4 (19.3) n = 56	.11	75.0 (20.1) n = 56	.100	81.6 (17.3) n = 56	.076

TABLE 7 (Continued)

Variable	Value	Emotional domain		Functional domain		Physical domain		MDADI total score	
		Mean (SD)	P-value	Mean (SD)	P-value	Mean (SD)	P-value	Mean (SD)	P-value
Adult Comorbidity Evaluation (ACE-27)	None	85.7 (16.3) n = 45		81.9 (23.4) n = 45		71.2 (20.4) n = 45		78.5 (18.3) n = 45	
	Mild	81.7 (18.8) n = 33		79.8 (22.6) n = 33		71.2 (21.4) n = 33		76.6 (19.7) n = 33	
	Moderate	77.2 (22.0) n = 12		79.7 (23.2) n = 12		68.1 (22.49) n = 12		73.9 (21.5) n = 12	
	Severe	100.0 (0.0) n = 3	.54	97.3 (4.6) n = 3	.72	91.0 (13.9) n = 3	.80	95.3 (7.2) n = 3	.96

Note: In all domains, a lower score indicates a worse self-perceived swallowing function.

[a] P-values = statistically significant values P < .05.

acute adverse effects such as hyposalivation, pain while swallowing due to mucositis, nausea, or loss of taste does not seem to cause persistent severe dysphagia. In the present study, 72% of all patients were at some point dependent on a feeding tube but only 8% at time of VFS. The increased risk of severe dysphagia among longtime feeding tube users may seem obvious since it is often placed to secure nutrition because of dysphagia. However, previous findings suggest that pretreatment sarcopenia, that is, low skeletal muscle mass, is a greater risk factor for prolonged feeding tube dependency than BMI and dysphagia.[11] Therefore, it can be speculated whether patients with pretreatment sarcopenia who become feeding tube dependent might be at higher risk of nonuse atrophy and long-term swallowing difficulties. Hence, it is of great importance to minimize the effect of nonuse atrophy by trying to maintain an oral intake even if minimal, use of preventive exercise programs targeting swallowing function and optimizing nutritional status.[47-49]

A better outcome was seen among patients treated for tonsil tumors. This is in line with a previous study concerning aspiration pneumonia following radiotherapy for HNC, which demonstrated that tumors of the nasopharynx or hypopharynx were risk factors for aspiration pneumonia, while oral cavity, oropharynx, and larynx had the least reported cases of aspiration pneumonia.[15]

Trismus and hyposalivation are associated to problems concerning eating.[2,3] In the present study, trismus only demonstrated a trend toward prediction of PAS≥5, which differs from a study where a statistically significant association between trismus and aspiration was found more than 10 years post radiotherapy.[29] Even though trismus was not a predictor for severe dysphagia, it impacted patient-reported swallowing ability, as patients with trismus reported worse scores on the functional and physical domain of the MDADI as well as the total score. Regular exercise targeting mouth opening function has been found to improve MIO and HRQL, suggesting that exercise to increase mouth opening is important and has potential to improve patients' well-being and swallowing function.[22]

Hyposalivation did not demonstrate predictive power, which is in line with a study by Vainshtein et al, who found only a weak correlation between observer rated dysphagia and stimulated saliva secretions.[17] However hyposalivation often requires patients to wash down food with liquids and is linked to a deteriorated oral status.

Only 31% of patients with a MDADI score below 60 coincided with patients with a PAS ≥5. This underlines what is known from previous research, namely that observer-rated and patient-perceived impairment often do not correspond.[28] Health and well-being are complex matters. Severe dysphagia measured by the PAS scale and a MDADI score below 60 seem to represent different aspects of dysphagia. This is further illustrated by the fact that 69% of patients who were suffering from penetration and/or aspiration reported only mild to no impact of dysphagia on MDADI. It is common for HNC patients to suffer from sensory changes and silent penetration/aspiration,[31] and some might not recognize that they have swallowing difficulties if asked by their physician. This could be a great health risk as the mortality rate due to aspiration pneumonia following radiotherapy goes up to 14%.[50] The PAS is useful to describe dysphagia that presents a

medical risk but is not sensitive to other symptoms and discomfort due to dysphagia, such as residue, effort while swallowing and impact on daily life. For this purpose, questionnaires like the MDADI is more apt. Therefore, it is important that management of dysphagia include both instrumental assessment of swallowing function as well as dysphagia specific questionnaires to evaluate HRQL.

8 | LIMITATIONS

A limitation to the study is that there was no blinded assessment of PAS, which would have improved the reliability of the PAS assessment. As would the use of two separate analysists to establish inter-judge reliability. However, all assessments were performed by consensus of the SLP and the radiologist, which may be beneficial.

9 | CONCLUSION

HNC patients with longtime feeding tube dependency, decreasing BMI, and high weight-loss are at risk of severe dysphagia. Since self-perceived swallowing ability and penetration/aspiration events are not always correlated patients presenting with risk factors for severe dysphagia could benefit from dysphagia management. Collaboration between professionals working with dysphagia from different perspectives is important to detect patients at risk and to monitor and improve nutritional status.

CONFLICT OF INTEREST
The authors declare no potential conflict of interest.

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