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ORIGINAL ARTICLE

Relationship Between Pharyngeal Residues Assessed by Bolus Residue Scale or Normalized Residue Ratio SCALE and Risk of Aspiration in Head and Neck Cancer Who Underwent Videofluoroscopy

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Abstract

Dysphagia affects 60–75% of patients treated for head and neck cancer (HNC). We aimed to evaluate the association between residue severity and airway invasion severity using a videofluoroscopic swallowing study and identify risk factors for poor penetration–aspiration outcomes in patients with dysphagia treated for HNC. Penetration–Aspiration Scale (PAS) was used to assess airway invasion severity, while residue severity was assessed using both the Bolus Residue Scale (BRS) for residue location and the Normalized Residue Ratio Scale (NRRS) for residue amount. Relevant covariates were adjusted in the logistic regression models to account for potential confounding. Significantly higher abnormal PAS was reported for increased piriform sinus NRRS (NRRSp) [odds ratio (OR), 4.81; $p=0.042$] with liquid swallowing and increased BRS value (OR, 1.52; $p=0.014$) for semi-liquid swallowing in multivariate analysis. Tumor location, older age, and poorer Functional Oral Intake Scale (FOIS) were significant factors for abnormal PAS in both texture swallowings. After adjusting for confounding factors (sex, age, and FOIS score), NRRS model in liquid swallowing (area under the curve [AUC], 0.83; standard error =0.04, 95% confidence interval [CI]: 0.75, 0.91) and BRS in semi-liquid swallowing (AUC, 0.83; SE=0.04; 95% CI: 0.76, 0.91) predicted abnormal PAS. The results indicate that while assessing residue and swallowing aspiration in patients with HNC, it is important to consider age, tumor location, and functional swallowing status. The good predictability of abnormal PAS with BRS and NRRS indicated that residue location and amount were both related to the aspiration event in patients with HNC.

Keywords Head and neck cancer · Dysphagia · Swallowing · Penetration–aspiration scale · Bolus residue scale · Normalized Residue Ratio Scale

Introduction

In patients with head and neck cancer (HNC), oropharyngeal dysphagia, with a prevalence of 60%–75%, is a common side effect [1]. The common symptoms of oropharyngeal dysphagia include food remains in the throat, coughing, and choking. The longer food bolus stasis and/or easy choking characteristics in these patients may have serious consequences, such as aspiration pneumonia [2]. Therefore, evaluation of swallowing function in patients with HNC is recommended. We assessed the different characteristics of swallowing impairment in two key functional aspects: safety and efficiency [3]. Safety is usually described by the severity of airway invasion, which is associated with an increased risk of respiratory sequelae during swallowing [4–6]. Swallowing efficiency can be described by pharyngeal residue

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severity. Food bolus stasis in the pharynx is a characteristic of impaired swallowing efficiency [7].

It is necessary to determine the correlation between swallowing safety and efficiency. The more severe the food bolus residue, the higher the aspiration risk. A previous study showed this correlation in patients with neurologic dysphagia [6]. However, this study did not focus on dysphagia caused by HNC. The dysphagia characteristics in patients with HNC differ from those in patients with neurogenic dysphagia [7]. The tumor's features, such as primary location and size, could cause impaired swallowing function [7, 8]. Additionally, HNC treatment also affects swallowing function [9, 10]. The anatomic structure may be altered by treatment, such as radiotherapy and surgery, to the head and neck [11]. Treatment for different HNCs also causes different dysphagia characteristics. For example, cancer in the oral cavity and its treatment may cause difficulty in the initial part of the swallowing process. Pharyngeal resection may cause severe pharyngeal residue. Laryngeal resection may cause easy penetration and aspiration. Besides surgical treatment, radiotherapy also causes swallowing dysfunction as it causes thermal and mechanical damage and alters the sensory input, which is involved in the regulation of cough and swallowing reflexes. Salivary glands and taste buds may be affected by radiotherapy and result in xerostomia [8, 12, 13]. These HNC characteristics can cause a special pattern of dysphagia in patients with HNC. Compared with neurogenic dysphagia, usually with delayed swallowing movements, in patients with HNC, swallowing movements are usually reduced but not delayed [14]. These characteristics easily cause food stasis in the pharyngeal structure and post-deglutition residues, which may explain why aspiration events in patients with HNC often occur after swallowing [7, 14].

The videofluoroscopy swallowing study (VFSS) and fiberoptic endoscopic evaluation of swallowing (FEES) are two instruments that are widely used in evaluating swallowing function. Both tools have good intra- and inter-rater agreements [15]. In the past, VFSS was considered a better tool for assessing penetration and aspiration events, while FEES was the instrument of choice for studying residue by Fattori et al. [16]. However, assessing residue severity under FEES is usually perceptual due to its limitations [17]. As a quantifying scale, such as NRRS, was developed under VFSS, the residue assessment ability of VFSS has improved. VFSS and FEES have been used to determine the association between residue and aspiration events in HNC-related dysphagia [18, 19], with inconsistent results. In this study, VFSS was used to assess swallowing.

To establish the association between residue severity and aspiration severity in patients with HNC, we used different scales to determine the severity of airway invasion and pharyngeal residue using VFSS. The Penetration–Aspiration Scale (PAS), widely used in swallowing assessment, was used to assess airway invasion severity [20]. For the residue, although several rating tools have been developed to assess its severity, which can be roughly classified as qualitative or quantitative, we used the Bolus Residue Scale (BRS) [21], a qualitative rating scale, and Normalized Residue Ratio Scale (NRRS) [22], a quantitative rating scale.

This study aimed to investigate which assessment method of food pooling (either BRS or NRRS) is better associated with aspiration risk in patients with HNC. We hypothesized that NRRS has a better association with aspiration risk, given that NRRS can represent the quantified extent of food pooling, while BRS only indicates the presence of food pooling. Moreover, this study aimed to identify risk factors of severe aspiration events other than food pooling.

Methods

Design and Study Population

This retrospective, cross-sectional study included patients treated for HNC who had swallowing dysfunction and underwent VFSS between January 2016 and March 2021. Patients with HNC after cancer treatment will be frequently followed up at the otorhinolaryngology outpatient clinic of a university hospital. Fibroscopic examinations are performed at the outpatient clinic to assess distorted anatomy and function after the treatment. Food texture modification, swallowing posture adjustment, or nasogastric tube use were applied to patients with dysphagia in the first 3 months after the HNC treatment. If the symptom persists for > 3 months and the patient complains of difficult swallowing in daily life, the patient will undergo VFSS. Patients were excluded if (1) they had underlying conditions, such as stroke that had already caused or may cause dysphagia, (2) they were > 75 years, (3) use of VFSS was contraindicated, (4) they had received treatment for dysphagia before undergoing VFSS, (5) they were diagnosed with cancer not originating in the head or neck, and (6) they had undergone total laryngectomy (which eliminates the possibility of aspiration). The HNC was staged according to the 8th edition of the American Joint Committee on Cancer's tumor, node, and metastasis classification system and staging criteria [23]. Furthermore, we determined whether the patients had been diagnosed with multiple HNCs. Treatment, including surgery and radiotherapy, and duration from treatment to VFSS were recorded. Sex, age, and functional swallowing status assessed by the Functional Oral Intake Scale (FOIS) [24] were also recorded. The swallowing efficiency of the patients was scored using NRRS and BRS. Swallowing safety was scored using PAS.

Independent Variables and Outcome Measures

The major independent variable of this study is the pooling of food residue, which was measured using BRS and NRRS. The outcome of interest was aspiration severity, which was scored using PAS. All these scores were assessed from VFSS images. The second objective of this study was to find risk factors associated with aspiration risk in patients with HNC with dysphagia. Therefore, other independent variables included patients' demographics and clinically relevant characteristics, as described in statistical analysis.

Analyses of Swallowing Function

VFSS has been performed extensively at our hospital by a well-trained speech pathologist with clinical experience. A standardized VFSS was performed using remote-controlled fluoroscopy (AXIOM Luminos dRF, Siemens, Munich, Germany). Images were recorded at a frame rate of 30 fps. Patients were asked to sit in a chair to allow for the acquisition of both lateral and anteroposterior images. Each patient swallowed two portions of a standard formula (a 5-mL liquid and 10-mL semi-liquid boluses) with a spoonful (3 mL) of barium sulfate (barium sulfate 99.5 g/100 g, Baritop LV, Kaigen Pharma Co Ltd, Osaka, Japan). According to the International Dysphagia Diet Standardization Initiative framework, the liquid and semi-liquid boluses had a thin and mildly thick consistency [25]. We video recorded the VFSS for each patient until the swallowing process was completed, which was when the whole food boluses entered the patient's esophagus. The residue was scored on the frame, while the hyoid bone was at the lowest position after swallowing. PAS was then recorded after this frame. An experienced radiologist and a licensed speech pathologist analyzed all included patients' VFSS images.

Aspiration outcome was assessed using PAS, which is an eight-point scale, with scores ranging from 1 (the material does not enter the airway of the individual) to 8 (the material enters the airway of the individual, passes below the vocal folds, and no effort is made to eject the material) [20]. Lateral views were used to determine PAS scores. Patients with scores 1 and 2 on PAS, which stands for "material does not enter the airway" and "material enters the airway, remains above the vocal folds, and is ejected from the airway," respectively, were considered to have normal function in preventing penetration and aspiration. Therefore, PAS score >2 indicated that the patient had clinically impaired swallowing safety in this study.

Post-swallow residues were assessed by the following two methods: (1) BRS was used to score the presence of post-swallow residue in different locations, including the epiglottic vallecula, piriform sinuses, and posterior pharyngeal wall. A BRS [21] score between 1 and 6 was obtained based on the number of structures that showed residue. A BRS score of 1 indicated no residue in any of these structures, while additional scores were given by different weights according to the anatomic regions in which the residue posed an aspiration risk. The residue in the posterior pharyngeal wall and piriform sinus will acquire 1 additional point to the initial score because their anatomic location is closer to the airway. BRS scores were double checked by observing both the lateral and anteroposterior views; (2) NRRS [22] was used to measure the amount of residue in the valleculae (NRRSv) and piriform sinuses (NRRSp). This measurement involves calculating the ratio of residue occupying the pharyngeal space and normalizing it against the size of the cervical vertebrae. We collected the frame while the hyoid bone was at the lowest position after swallowing [22]. ImageJ software [22, 26] was used to analyze the images. The line and stripe tool were used to mark the height of the cervical vertebrae, which is the internal scalar in the NRRS. The freehand selection tool was used to outline the region of the vallecula, piriform sinuses, and residue. The measurement tool was then used to calculate the area and NRRS. Besides previously mentioned scores, FOIS was also collected to reveal the oral intake function of the included patients.

Statistical Analyses

The characteristics of the study population are presented using descriptive statistics. Mean and standard deviation (SD) or median and interquartile ranges are used to present continuous variables; frequencies and percentages are used to present categorical variables.

To explore which scoring scale of food pooling was better associated with aspiration risk, bivariable logistic regression was conducted separately for BRS or NRRSv and NRRSp. In the regression model, BRS and NRRS were, respectively, applied as the independent variable, while PAS >2 was used as the dependent variable. The bivariable analysis results were used to evaluate whether the independent variable is an important factor associated with aspiration risk. To identify potential risk factors, covariates other than food were tested as well to examine the association with the outcome. These covariates included demographics (sex and age), tumor location, time since last treatment (either surgery or radiotherapy), T stage of the tumor, history of surgery or radiotherapy, status of multi-site HNC, and FOIS score. Furthermore, we identified significant factors found in the bivariable analysis. These factors and patients' demographics (i.e., sex and age) underwent multivariable analysis to determine if any of these factors were significantly associated with aspiration risk under the adjustment of other covariates. To avoid collinearity, variables specified to be adjusted in the regression model are highly correlated, thus leading to over-fitting. We retained only variables with variance inflation factor value < 3 in the regression model [27].

The logistic regression results were presented as odds ratios (ORs) with 95% confidence intervals (CIs), and associated *p* values were determined for each tested variable. *P* values < 0.05 were considered statistically significant. Furthermore, we illustrated the receiver operating characteristic (ROC) curve of BRS and NRRS, with other identified risk factors in the multivariable analysis, to evaluate its outcome-predicting ability using the area under the curve (AUC). The standard error (SE) and 95% CIs were also presented. An AUC > 0.8 was considered a good explanation of the outcome by the variables included in the model. All analyses were performed using the SAS 9.4 software (SAS Institute, Cary, NC, USA).

Results

Patient Characteristics

Table 1 showed 152 eligible patients included in this study (mean age, 55.1 years [SD 9.5 years]), 142 (93.4%) were male. According to the primary tumor sites, 104 (69%), 14 (9.2%), 17 (11.2%), and 17 (11.2%) patients were classified into the oral cavity, nasopharynx, oropharynx, and hypopharynx groups, respectively. Among included patients, 87 (57.2%) had HNC of T stage 3 or 4 at diagnosis and 45 (29.6%) previously had cancer in a different region of the head and neck (multiple HNCs). Among the treatment options, 123 (80.9%), 100

Table 1 Characteristics of included patients

	n	(%)
Number of subjects	152	
Male	142	93.4
Age, mean ± SD	55.1	9.5
Tumor locations		
NPC	14	9.2
Hypo_pharynx	17	11.2
Oral cavity	104	68.4
Oropharynx	17	11.2
Duration of Dx in years, median (Q1 to Q3)	1	(0.6 to 2.8)
Time since surgery or RT in years, median (Q1 to Q3)	0.63	(0.44 to 2)
T stage of cancer		
1	22	14.5
2	36	23.7
3	31	20.4
4	56	36.8
Surgery Hx	123	80.9
Radiotherapy Hx	100	65.8
Multiple HNC	45	29.6
Dysphagia scoring, median (Q1 to Q3)		
Liquid form		
BRS	3	(1 to 4)
NRRS_v	0.09	(0.036 to 0.194)
NRRS_p	0.08	(0.018 to 0.229)
PAS	1	(1 to 4)
Semi-Liquid form		
BRS	3	(1 to 4)
NRRS_v	0.09	(0.090 to 0.287)
NRRS_p	0.02	(0.004 to 0.120)
PAS	1	(1 to 4)
FOIS, median (Q1 to Q3)	5	(4 to 6)

BRS Bolus Residue Scale, *Cl* confidence interval, *Dx* diagnosis, *FOIS* Functional Oral Intake Scale, *HNC* head and neck cancer, *Hx* history, *NPC* nasopharyngeal carcinoma, *NRRSv* The Normalized Residue Ratio Scale, measurement of residue area in valleculae, *NRRSp* measurement of NRRS residue area in pyriform sinus, *PAS* Penetration–Aspiration Scale, *Q1* first quartile, *Q3* third quartile, *SD* standard deviation

*Indicated in months

(65.8%), and 71 (46.7%) patients underwent surgery, radiotherapy, and both, respectively. The median duration between the first HNC diagnosis and VFSS time was 1 year and between the last treatments and VFSS time was 0.63 years. For swallowing function scorings, both liquid and semi-liquid forms had shown the same median BRS and PAS of 3 points (residue in the posterior pharyngeal wall or piriform sinus) and 1 point (material does not enter the airway). NRRS of the valleculae and piriform sinus also showed similar scores of 0.09 and 0.08 for liquid and 0.09 and 0.02 for the semi-liquid, respectively. In terms of FOIS, the median score was 5 points (total oral diet with multiple consistencies but requiring special preparation or compensations).

Associations Between Food Pooling and Risk of Aspiration

Table 2 shows the predictive risk factors of high PAS scores, including the NRRS score (NRRSv and NRRSp), BRS, tumor location, sex, age, duration of HNC diagnosis, T staging of HNC, history of surgery, radiotherapy, time since surgery or RT, multiple HNC history, and FOIS score. For the liquid-form swallowing results, every increased score in NRRS of piriform sinus would correspond to an OR of aspiration of 6.38 ($p = 0.008$). In the multivariable regression, NRRS of piriform sinus still remained significantly associated with aspiration after adjusting for other factors (Table 2).

In terms of semi-liquid, the initial bivariable analysis identified NRRS of the piriform sinus (OR 4.96, $p = 0.017$) and BRS (OR 1.35, $p = 0.024$) as significant factors of

Table 2 Odds ratios of different predicting factors on risk of aspiration (liquid form)

	Unit	Bivariable analysis			Multivariable analysis[a]		
		OR	(95% CI)	*p*	aOR	(95% CI)	*p*
NRRSv	1	4.91	(0.95, 25.55)	0.058			
NRRSp	1	6.38	(1.64, 24.86)	0.008	4.81	(1.06, 21.84)	0.042
BRS	1	1.29	(1, 1.68)	0.053			
Sex							
Female		ref					
Male	1	1.24	(0.24, 6.39)	0.800	1.69	(0.31, 9.39)	0.548
Age	10	1.73	(1.14, 2.63)	0.010	2.26	(1.19, 4.28)	0.013
Tumor locations							
Oral cavity		ref					
NPC	1	2.15	(0.57, 8.04)	0.256	12.18	(2.33, 63.82)	0.003
Hypopharynx	1	3.34	(1.15, 9.72)	0.027	4.88	(0.82, 29.16)	0.082
Oropharynx	1	4.23	(1.46, 12.3)	0.008	8.52	(1.66, 43.67)	0.010
Time since last surgery or RT (year)	1	1.05	(0.9, 1.23)	0.540			
T stage							
1		ref					
2	1	1.31	(0.38, 4.5)	0.671			
3	1	1.87	(0.54, 6.46)	0.322			
4	1	1.36	(0.43, 4.31)	0.602			
Surgery Hx	1	0.55	(0.22, 1.34)	0.185			
Radiotherapy Hx	1	1.73	(0.81, 3.7)	0.158			
Multiple HNC	1	0.51	(0.22, 1.18)	0.114			
FOIS	1	0.62	(0.49, 0.79)	<0.001	0.60	(0.44, 0.81)	0.001

aOR adjusted odds ratio, *BRS* Bolus Residue Scale, *CI* confidence interval, *FOIS* Functional Oral Intake Scale, *HNC* head and neck cancer, *Hx* history, *NPC* nasopharyngeal carcinoma, *NRRSv* The Normalized Residue Ratio Scale, measurement of residue area in valleculae, *NRRSp* measurement of NRRS residue area in pyriform sinus, $p = $ p value, *PAS* Penetration–Aspiration Scale, *ref* reference

[a]Multivariate logistic regression adjusted for NRRSv, NRRSp, tumor location, sex, age, time since surgery or RT, T stage of HNC, history of surgery, history of RT, multiple HNC, and FOIS

[b]Multivariate logistic regression adjusted for BRS, tumor location, sex, age, time since surgery or RT, T stage of HNC, history of surgery, history of RT, multiple HNC, and FOIS

aspiration. However, after adjusting other variables in separated models, only BRS remained significantly associated with risk aspiration. For every increased score in BRS, the odds of aspiration would increase to 1.52 [adjusted OR (aOR) 1.52; 95% CI: 1.09, 2.12, $p = 0.014$] (Table 3).

Other Identified Risk Factors of Aspiration

From the bivariable analysis results, significant factors were further modeled in the multivariable analysis to identify risk factors of aspiration in the study population. For liquid, the multivariable regression results showed that besides NRRSp, an increase in 10 years of age also increased the risk of aspiration (aOR 2.26, 95% CI: 1.19, 4.28, $p = 0.013$). When compared to tumor location in the oral cavity, NPC (Nasopharyngeal cancer) yielded higher odds of aspiration (aOR 12.18, 95% CI: 2.33, 63.82, $p = 0.003$). Conversely, an increase in FOIS score was a protective factor against aspiration risk (aOR 0.6, 95% CI: 0.44, 0.81 for every increased score, $p = 0.001$). For semi-liquid, the final multivariable regression model showed that besides BRS, other significant risk factors included increased age (aOR 1.84, 95% CI: 1.03, 3.28 for every 10 years of increase, $p = 0.039$), tumor sites at NPC (aOR 8.53, 95% CI: 1.83, 39.81 when compared to oral cavity, $p = 0.006$), and oropharynx (aOR 5.29, 95% CI: 1.22, 22.87 when compared to oral cavity, $p = 0.026$) and decrease in FOIS score (aOR 0.56, 95% CI: 0.42, 0.75 for every increased score, $p < 0.001$).

Besides logistic regression, the ROC curve for the final multivariable regression models that comprised NRRSp and BRS, respectively, of liquid and semi-liquid form both showed AUC values of 0.83 (SE = 0.04, 95% CI: 0.76, 0.91), indicating good performance in predicting abnormal PAS (i.e., risk of aspiration) (Fig. 1).

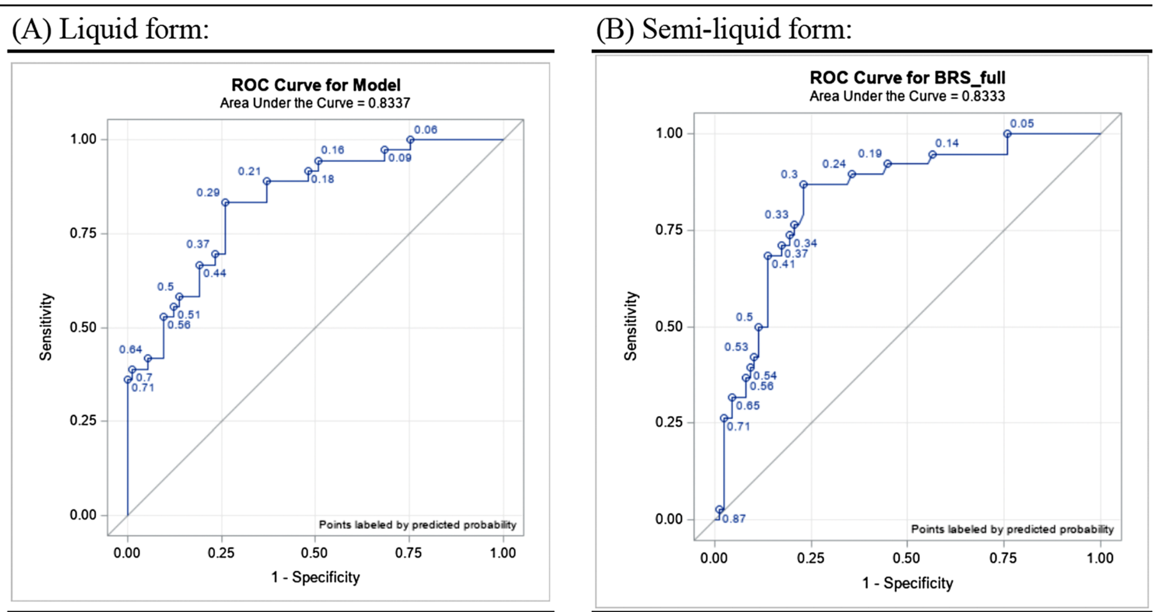
Table 3 Odds ratios of different predicting factors on risk of aspiration (semi-liquid form)

	Unit	Bivariable analysis			Multivariable analysis[a]			Multivariable analysis[b]		
		OR	(95% CI)	*p*	aOR	(95% CI)	*p*	aOR	(95% CI)	*p*
NRRSv	1	2.19	(0.72, 6.67)	0.166						
NRRSp	1	4.96	(1.33, 18.41)	0.017	6.43	(0.95, 43.53)	0.057			
BRS	1	1.35	(1.04, 1.75)	0.024				1.52	(1.09, 2.12)	0.014
Sex										
Female		Ref								
Male	1	1.19	(0.23, 6.17)	0.833	1.12	(0.22, 5.87)	0.890	1.26	(0.22, 7.38)	0.798
Age	10	1.54	(1.02, 2.32)	0.038	1.51	(0.81, 2.82)	0.199	1.84	(1.03, 3.28)	0.039
Tumor locations										
Oral cavity		Ref								
NPC	1	2.15	(0.57, 8.04)	0.256	11.04	(2.22, 54.83)	0.003	8.53	(1.83, 39.81)	0.006
Hypopharynx	1	2.63	(0.9, 7.75)	0.079	2.12	(0.35, 12.86)	0.415	2.14	(0.42, 10.92)	0.361
Oropharynx	1	4.23	(1.46, 12.3)	0.008	6.39	(1.26, 32.36)	0.025	5.29	(1.22, 22.87)	0.026
Time since last surgery or RT (year)	1	1.09	(0.93, 1.28)	0.282						
T stage										
1		Ref								
2	1	1.13	(0.32, 3.96)	0.845						
3	1	1.62	(0.46, 5.65)	0.450						
4	1	1.48	(0.47, 4.67)	0.502						
Surgery Hx	1	0.52	(0.21, 1.28)	0.157						
Radiotherapy Hx	1	1.92	(0.88, 4.16)	0.100						
Multiple HNC	1	0.64	(0.28, 1.45)	0.280						
FOIS	1	0.63	(0.5, 0.8)	< 0.001	0.53	(0.39, 0.74)	< 0.001	0.56	(0.42, 0.75)	< 0.001

aOR adjusted odds ratio, *BRS* Bolus Residue Scale, *Cl* confidence interval, *FOIS* Functional Oral Intake Scale, *HNC* head and neck cancer, *Hx* history, *NPC* nasopharyngeal carcinoma, *NRRSv* The Normalized Residue Ratio Scale, measurement of residue area in valleculae, *NRRSp* measurement of NRRS residue area in pyriform sinus, *p* = p value, *PAS* Penetration–Aspiration Scale, *ref* reference

[a]Multivariate logistic regression adjusted for NRRSv, NRRSp, tumor location, sex, age, time since surgery or RT, T stage of HNC, history of surgery, history of RT, multiple HNC, and FOIS

[b]Multivariate logistic regression adjusted for BRS, tumor location, sex, age, time since surgery or RT, T stage of HNC, history of surgery, history of RT, multiple HNC, and FOIS



Full model	AUC	SE	Wald 95% CI	AUC	SE	Wald 95% CI
NRRSp[a]	0.83	0.04	(0.75, 0.91)	-	-	-
BRS[b]	-	-	-	0.83	0.04	(0.76, 0.91)

[a]Full model contained adjustment of NRRSp score, sex, age, tumor locations and FOIS score.
[b]Full model contained adjustment of BRS score, sex, age, tumor locations and FOIS score.
Abbreviation: BRS=Bolus Residue Scale; Cl=confidence interval; NRRS=Normalized Residue Ratio Scale.SE=standard error.

Fig. 1 ROC of identified risk factor on prediction of aspiration risk

Discussion

This study determined the association between residue and penetration–aspiration events in patients with HNC. Using univariate and multivariate logistic regression analyses, worse residue severity, older age, specific tumor location, and worse FOIS score were associated with higher penetration and aspiration severity. Furthermore, different residue assessment tools could predict aspiration risk for swallowing liquids of different textures. The prediction abilities reached the "good "AUC classification level.

Pharyngeal residue and aspiration worsen in patients with HNC [28–31]. The pharyngeal residue is a risk factor for penetration–aspiration in healthy adults and patients with neurogenic dysphagia [6, 32]. However, the relationship between pharyngeal residue and aspiration in patients with HNC remains controversial. Pisegna et al. presented weak correlations between residue and PAS in patients with HNC while swallowing thin liquid, nectar-thick liquid, and pudding [19]. A previous study had presented another result under FEES by showing that the residue in the valleculae and piriform sinus in thick-liquid swallowing were associated with aspiration [18].

In our study, NRRSp was associated with a higher PAS in liquid swallowing. The piriform sinus is close to the larynx and could easily cause aspiration events due to residue spilling [21]. Impairment of the pharyngeal constrictor muscle, which causes decreased residue clearing force, may cause bolus stasis in the piriform sinus and aspiration by liquid spillage [33]. Besides, impaired oropharyngeal muscle contractility is another common presentation in HNC causing dysphagia and is correlated with residue in the piriform sinus [34]. As NRRS is used to calculate the ratio of the residue and piriform sinus areas, it may be a useful tool to assess the risk of liquid spillage in the piriform sinus.

With respect to semi-liquid swallowing, higher penetration–aspiration severity was associated with higher BRS, but the association with NRRS was not significant. Higher BRS score implies the presence of multiple locations of pharyngeal residue. Reduced base of tongue retraction, reduced laryngeal elevation, and cricopharyngeal dysfunction have been reported as the most common dysphagia patterns [35] that may easily cause residue from the initial to the end of the oropharyngeal phase [36]. Thicker viscosity of the semi-liquid also causes residues relatively easily [37]. However, as NRRS was not statistically significantly associated with higher PAS, the amount of residue could be less important in semi-liquid swallowing than in liquid swallowing.

The difference between liquid and semi-liquid swallows may be explained by food viscosity. A systematic review showed that thicker liquids reduce the risk of penetration–aspiration and increase the risk of post-swallow residue in the pharynx [38]. This may be explained by a thicker liquid having a higher viscosity and is more prone to stasis in any anatomic structure, including the vallecula and piriform sinus. Compared with semi-liquid residue, liquid residue may have a relatively higher portion remaining in the piriform sinuses due to its lowest location in the oropharyngeal swallowing phase and high cricopharyngeal dysfunction in patients with HNC, but with the lower portion of stasis in the vallecula. This may explain why BRS, which focuses on multiple locations of the residue, was more suitable for thicker liquid swallowing than NRRS. Additionally, NRRSp, which focuses on the amount of residue in the piriform sinus, was more suitable for thinner liquid swallowing.

Different characteristics of the tumor itself and treatment in HNC patients make residue assessment difficult. The possible limitations of these residue assessment tools in patients with HNC should be discussed. BRS focuses on the location of the residue and is weighted by aspiration risk according to the distance to the laryngeal entrance. The weighted score of BRS should be reconsidered in patients with HNC and impaired epiglottis structure and function. Impairment of the epiglottis function in patients with HNC may cause the vallecular residue to spill out, leading to aspiration [39–41]. For NRRS, which depends on the shape of the vallecula or piriform sinus, the changing shape of the anatomic structure could lead to a misleading result of residue severity. Fibrosis resulting from radiotherapy and changes in anatomic structure caused by surgical treatment may increase or decrease the capacity of the vallecula and piriform sinus. These factors can cause the residue to either accumulate more easily or not at all. Therefore, the association between aspiration risk and residue may not be a simple cause-and-effect relationship in patients with HNC.

In previous studies, tumor location has been reported as a risk factor for aspiration. Patients with laryngeal and hypopharyngeal cancers were more likely to be aspirators [42], and hypopharyngeal and nasopharyngeal cancers were independent risk factors for aspiration pneumonia in patients with HNC [43]. High rates of silent aspiration have also been reported in patients with NPC [44]. Oropharyngeal tumors were significantly more likely to have poor PAS and BRS scores than oral cavity tumors [45]. Tumor location should be assessed in HNC-related dysphagia. Age was another risk factor that may have caused abnormal PAS in our study. Aging reduces muscle mass and connective tissue elasticity, which results in loss of strength. Moreover, age-related decrements in oral moisture, taste, and smell acuity may contribute to reduced swallowing performance in the elderly [46]. For functional status, Meyer et al. showed an association between the residue and penetration–aspiration event [47], and our study also showed an association between FOIS and PAS in patients with HNC. These results implied that these objective studies of residue and aspiration are related to clinical function status.

Since we identified the residue scales as risk factors of higher aspiration risk, a full model, including these factors, was used to predict aspiration risk. To the best of our knowledge, this is the first study to present the ROC curve of the residue predicting abnormal PAS in patients with HNC. The AUC could reach a good prediction level of PAS for liquid and semi-liquid swallowing by NRRS and BRS, respectively. Therefore, when assessing the aspiration risk of patients with HNC, residue assessment under VFSS may be an important assessment. By adjusting for other important risk factors, including age, sex, tumor location, and FOIS, residue severity assessment tools could still predict penetration–aspiration severity.

There are some limitations to our study. First, solid food boluses were not examined in the present study because a validated NRRS is not yet available for solid swallowing. Another limitation of our study was that we focused on treated patients with HNC with subjective dysphagia complaints. This may cause loss of the patient with hidden dysphagia problems, such as silent aspiration. Finally, our sample size was small and was from Taiwan, where the HNC population had different characteristics from the worldwide HNC population [48]. Taiwan has a high incidence of HNC, especially oral cancer; it has one of the highest incidences in the world, which may be caused by betel quid consumption. The oral cavity group outnumbered the groups with other tumor locations. The majority of the patients in our study were male. Therefore, subgroup analyses could be valuable. However, the study population was representative of patients at our outpatient clinic. Further study should focus on larger and worldwide populations.

Conclusion

In our study, NRRS, a pixel-based quantifying tool focusing on residue amount, could predict abnormal aspiration severity in semi-liquid swallowing, while BRS, the residue assessment tool that focuses on residue location, could predict abnormal aspiration severity in liquid swallowing in patients with HNC. This implied that the association between food residue and aspiration risk may be affected by food texture. Therefore, while assessing the residue of swallowing in these patients, it is important that the location and amount both need to be considered and assessed using different residue assessment tools. Moreover, other risk factors, including age, tumor location, and FOIS, should be considered when assessing the risk of abnormal penetration–aspiration events.

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Data Availability Raw data were generated at the National Cheng Kung University Hospital. Derived data supporting the findings of this study are available from the corresponding author on request.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Ethics Approval Ethical approval for this study was obtained from the Institutional Review Board of the National Cheng Kung University Hospital

Informed Consent Verbal informed consent was obtained from legally authorized representatives before the study.

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