

Study of Dysphagia in Patients with Advanced Oropharyngeal Cancer Subjected to an Organ Preservation Protocol Based on Concomitant Radiotherapy and Chemotherapy

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Abstract

Introduction: Organ preservation protocol (based on chemo-radiotherapy) for oropharyngeal tumors include dysphagia as a possible sequel leading to function impairment and changes in patient's quality of life. **Objectives:** The aim of this study is to assess dysphagia severity after treatment in advanced oropharyngeal cancer patients treated with concurrent chemo-radiation. **Methods:** This prospective cross-sectional study included 64 participants who had been disease free for at least six months after primary treatment. Dysphagia severity was assessed by fibre-optic endoscopic evaluation of swallowing (FEES) and the Dysphagia Outcome and Severity Scale (DOSS); the occurrence of penetration/aspiration during swallowing was also investigated. All participants also completed the M. D. Anderson Dysphagia Inventory (MDADI). The correlation of FEES results with clinical-demographic variables and MDADI scores was assessed. Descriptive analysis was performed, and qualitative variables were compared using either the chi-square or Fisher's exact test. **Results:** FEES revealed silent aspiration in 18.8% of the patients. Approximately 6.3% of the patients exhibited severe dysphagia (scores 1-2 in DOSS). Dysphagia severity was significantly associated with the MDADI physical domain scores. The participants with scores 5-7 in DOSS (no or mild dysphagia) exhibited less limitations in the MDADI physical domain ($p=0.015$). **Conclusions:** Silent aspiration was detected in one of every five patients treated with concurrent chemo-radiotherapy; almost half of the patients exhibit at least moderate dysphagia. Assessment of the participant's quality of life via the MDADI revealed an association between the physical domain scores and dysphagia severity.

Keywords: Oropharyngeal cancer- radiotherapy/chemotherapy- MDADI- deglutition

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Introduction

Dysphagia is a frequent sequela following treatment of head and neck cancer. The late effects of radiotherapy that contribute to chronic dysphagia include sensory changes, trismus, stenosis, hyposalivation and inflammation (Dysphagia Section et al., 2012). In addition, some studies have shown that the cough reflex is often absent following irradiation of the neck region (Lazarus, 2009). Although locoregional control is better and the overall and disease-free survival rates are higher in individuals treated with concomitant chemo-radiation compared to those treated with radiotherapy alone, the frequency of dysphagia to solids and the consequent need for feeding tubes or gastrostomy is higher among that group (Greven et al., 2008). Dysphagia is usually assessed

by exams, such as fibre-optic endoscopic evaluation of swallowing (FEES), swallowing videofluoroscopy and/or quality-of-life questionnaires.

Previous studies have shown that the patient's self-assessment might either complement or eventually diverge from the results of objective tests and would thus contribute to a more accurate understanding of the impact of a disease and its treatment on the quality of life of the affected individual (Hanna et al., 2004; Vartanian et al., 2004). The MDADI (M. D. Anderson Dysphagia Inventory) is a quality-of-life questionnaire recommended in clinical practice for the specific assessment of dysphagia in individuals with head and neck cancers (Schindler et al., 2008).

Accurate knowledge of the sequelae of radiotherapy and chemotherapy for oropharyngeal cancer aids

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the identification of possible risk factors that might contribute to better guidance and rehabilitation of patients, thus improving their quality of life. The aims of this study were to assess dysphagia after the treatment of individuals with advanced oropharyngeal cancer subjected to an organ preservation protocol based on concomitant chemo-radiotherapy, to identify changes in swallowing and to investigate the possible risk factors (clinical-demographic) associated with dysphagia and aspiration in this population and to assess the patient's self-perception of dysphagia by means of the MDADI.

Materials and Methods

Study Design and Participants

This is a prospective cross-sectional study including patients admitted at the Barretos Cancer Hospital, Brazil. Through telephone calls or on the occasion of a follow-up visit to the outpatient clinic, 64 individuals treated at the Head and Neck Department were invited to participate in the study protocol.

The selected participants should be: older than 18 years old, had diagnoses of oropharyngeal carcinoma stage III or IV, disease free for at least six months and underwent curative organ preservation protocol based on chemoradiation. Individuals with a second primary head and neck tumour and those who had been subjected to salvage surgery for the primary tumor were excluded.

This study was approved by the Research Ethics Committee of the Barretos Cancer Hospital (#546/2011) and all patients signed an informed consent before inclusion in the study.

Assessment of Dysphagia

Deglutition was assessed by FEES and MDADI on the same day. The FEES tests were recorded which allowed for the review of the acquired images.

The participants were given food boluses dyed with aniline blue (an edible dye) in increasing amounts and consistencies. The liquid consistency corresponded to filtered water at room temperature; a food thickener based on the addition of starch to water was used to achieve the soft consistencies; and the solid consistency corresponded to crackers. The boluses were given in the following sequence: fluid (5 and 20 mL), soft (20 mL) and solid (one-fourth of a cracker, corresponding to 3.6 cm³ of solid bolus).

During FEES, the participants were oriented to sit with the neck slightly flexed forwards, i.e., simulating the position normally adopted for eating. The fibre-optic nasopharyngoscope was introduced through the wider nostril without topical anaesthesia to avoid interfering with pharyngeal and laryngeal sensitivity.

The nasopharyngeal anatomy and function were assessed. The participants were requested to produce vocal sounds or to cough to investigate the presence of aspiration unperceived by the examiner.

The final score for the classification of the severity of dysphagia was calculated according to Dysphagia Outcome and Severity Scale (DOSS), in which deglutition is classified as seven levels of dysphagia, and then grouped

in 3 categories for statistical analysis. In level 7 normal in all situations, level 6 within functional limits, functional swallowing. In level 5 mild dysphagia, distant supervision; level 4 mild-moderate dysphagia, intermittent supervision; level 3 moderate dysphagia, total assist or strategies. In level 2 moderately severe dysphagia, maximum assistance; level 1 severe dysphagia (O'Neil et al., 1999).

The extent of aspiration and the presence and effectiveness of the defence mechanisms exhibited by the participants upon coughing or hawking were assessed. In regard to eventual penetration and/or aspiration, the time of occurrence, e.g., before, during or after deglutition, was assessed, along with whether aspiration was silent or not. Several manoeuvres, such as Effortful swallow, Mendelsohn maneuver, Supraglottic swallow, Super-supraglottic swallow, including changes of the head and neck positions, were used in cases of patients who exhibited penetration, aspiration or stasis (Swanson et al., 2009).

A tactile test was used to assess laryngeal sensation; this test consisted of directing the endoscope tip towards the pharynx wall, the laryngeal surface of the epiglottis, the aryepiglottic fold, the arytenoid cartilages or the vocal folds. As the stimulus provided by the endoscope is much stronger than the contact of food and drink, one might infer that individuals who do not react to the former, especially to the stimulus applied to the vocal cords, are insensitive to the latter (Gomes et al., 2004).

In FEES, a speech therapist and an otolaryngologist jointly assessed functional deglutition. Analyses took into consideration the alterations identified, along with their frequencies in the test, e.g., more intense or frequent stasis, penetration and/or aspiration.

The MDADI consists of 20 questions, one of which is global and 19 of which are distributed across three domains: emotional (six questions), functional (five) and physical (eight). There are five response options for each question (strongly agree; agree; no opinion; disagree; strongly disagree), which are scored from one to five (see MDADI) (Guedes et al., 2013).

According to the MDADI validation protocol, the poorer the dysphagia-specific quality of life, lower the scores in each of the questionnaire domains.

Statistical Analysis

The database was entered into the IBM SPSS software for Windows 20, which was also used for statistical analysis. Descriptive analysis was performed, mainly for the variables corresponding to the assessment of dysphagia. The association between the FEES results and the qualitative variables or the MDADI score were assessed by using either the chi-square or Fisher's exact test.

Results

The study included 64 patients, 58 of whom were male (90.6%). The median age was 58.5 years old (range: 40 - 75 years). The median disease free interval was 2.1 years (range: 6 months - 13 years). All 64 participants were subjected to treatment consisting in concomitant

Table 1. Clinical and Sociodemographic Characteristics of the Study Patients

Variable	Category	n (%)
Gender	Male	58 (90.6)
	Female	6 (9.4)
Age group	≤65 years	49 (76.6)
	>65 years	15 (23.4)
Tumor site	Tonsil	31 (48.5)
	Base of tongue	23 (35.9)
	Soft palate	10 (15.6)
Disease free interval	6 to 12 months	16 (25.0)
	1 to 5 years	29 (45.3)
	> 5 years	19 (29.7)
T Staging	T1/T2	15 (23.4)
	T3/T4	49 (76.6)
N Staging	N0	19 (29.7)
	N1/N2/N3	45 (70.3)
Clinical stage	III	28 (43.8)
	IV	36 (56.2)
Neck dissection	Yes	16 (25.0)
	No	48 (75.0)
Feeding tube	Yes	10 (15.6)
	No	54 (84.4)
Tracheostomy	Yes	1 (1.6)
	No	63 (98.4)

1, One case missing information

chemoradiation. The median radiation dose was 7,020 Gy (range: 6,840 - 7,100 Gy). Radiation was applied to the similar fields in all of the cases. The clinical and sociodemographic characteristics of the study patients are describing in table 1.

The static and dynamic assessments of the pharynx and larynx structures in FEES (mobility and pharyngeal contraction, laryngeal elevation and sensitivity) was evaluated. Most patients exhibited reductions in pharyngeal motility and contractility (82.8%), laryngeal elevation (75.0%) and laryngeal sensitivity (45.3%) (Table 2).

Salivary stasis assessment by anatomical location observed by FEES in oropharynx, 78,1% were absent or discrete and 21,9% were moderate or severe. In hypopharynx and larynx, 85,9% were absent or discrete and 14.1% were moderate or severe.

Table 2. Dynamic and Static Assessment by FEES for Mobility and Pharyngeal Contraction, Laryngeal Elevation and Sensitivity

Variable	Evaluation		
	Adequate n (%)	Reduced n (%)	Absent n (%)
Mobility/pharyngeal contraction	9 (14.1)	53 (82.8)	2 (3.1)
Laryngeal elevation	13 (20.3)	48 (75.0)	3 (4.7)
Laryngeal sensitivity	26 (40.6)	29 (45.3)	9 (14.1)

Table 3. Presence of Changes in Preparatory and Oral Phase Assessed by FEES with 5mL of Liquid, 20mL of Liquid, Soft and Solid Food Intake

Findings	5mL liquid	20mL liquid	Soft	Solid
	n (%)	n (%)	n (%)	n (%)
Preparatory/oral phase - bolus retention in OC1	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.6)
Not crushed food	0 (0.0)	0 (0.0)	0 (0.0)	3 (4.9)
Premature loss	5 (7.8)	3 (4.7)	3 (4.8)	3 (4.9)
Penetration before swallowing	3 (4.7)	1 (1.6)	0 (0.0)	0 (0.0)
Aspiration before swallowing	0 (0.0)	1 (1.6)	0 (0.0)	0 (0.0)
Silent aspiration before swallowing	0 (0.0)	1 (1.6)	0 (0.0)	0 (0.0)

OC, oral cavity

Assessment of the oral preparatory and oral phases of deglutition on FEES using food boluses of various consistencies revealed bolus retention in the oral cavity in only 1.6% of the participants when the solid bolus was used, while premature spillage was more frequent with the 5-mL fluid bolus (7.8%) (Table 3).

Regarding the salivary stasis, penetration and moderate/severe aspiration corresponding to the various bolus consistencies. Moderate/severe stasis occurred more frequently with the solid-consistency bolus and at the oropharynx (49.2%). Moderate/severe aspiration after deglutition occurred more frequently with the 5-mL fluid bolus (3.1%) (Table 4).

Analysis of the association between the severity of dysphagia and the dysphagia-related quality of life, as assessed by MDADI identified significant associations with the MDADI physical domain. Participants with higher scores (5 to 7) on DOSS were significantly more likely to exhibit medium/minimal limitations on MDADI (p=0.015) (Table 5).

A total of 6.3% participants exhibited severe dysphagia (DOSS score 1-2); however, we did not observe an association with the severity of dysphagia and the clinical-demographic variables (Table 6).

Approximately 18.8% of the patients exhibited silent aspiration. Penetration/aspiration did not show an association with any of the analysed variables. The quality of life as assessed by MDADI also did not show significant

Table 4. Stasis and Penetration/Aspiration Assessment by FEES with the Following Consistencies: 5 mL Liquid, 20 mL Liquid, Soft and Solid Food intake

	Stasis and penetration/aspiration assessment Moderate/severe			
	5mL liquid	20mL liquid	Soft	Solid
	n (%)	n (%)	n (%)	n (%)
Salivary stasis				
Oropharynx	8 (12.5)	8 (12.5)	25 (39.7)	30 (49.2)
Hypopharynx	6 (9.4)	7 (10.9)	15 (23.8)	8 (13.1)
Penetration after swallowing	2 (3.1)	1 (1.6)	7 (11.1)	2 (3.3)
Aspiration after swallowing	2 (3.1)	1 (1.6)	1 (1.6)	0 (0.0)

Table 5. Association between Severity of Dysphagia According to FEES Findings and Sociodemographic and Clinical Variables

Variables		DOOS			p-value
		1-2 n (%)	3-4 n (%)	5-6-7 n (%)	
Gender	Female	0 (0.0)	1 (16.7)	5 (83.3)	0.594
	Male	4 (6.9)	22 (37.9)	32 (55.2)	
Age group	≤65 years	3 (6.1)	18 (36.7)	28 (57.1)	1.000
	>65 years	1 (6.7)	5 (33.3)	9 (60.0)	
Tumor site	Tonsil	3 (9.7)	11(35.5)	17 (54.8)	0.890
	Base of tongue	1 (4.3)	9 (39.1)	13 (56.5)	
	Palato moleSoft palate	0 (0.0)	3 (30.0)	7 (70.0)	
Disease free interval	6m-1year	2 (12.5)	6 (37.5)	8 (50.0)	0.822
	1-5years	1 (3.4)	11 (37.9)	17 (58.6)	
	More than 5 years	1 (5.3)	6 (31.6)	12 (63.2)	
T Staging	T1/T2	1 (6.7)	3 (20.0)	11(73.3)	0.382
	T3	2 (5.3)	17 (44.7)	19 (50.0)	
	T4	1 (9.1)	3 (27.3)	7 (63.6)	
N Staging	N0	2 (10.5)	7 (36.8)	10 (52.6)	0.680
	N1/N2/N3	2 (4.4)	16 (35.6)	27 (60.0)	
TNM Staging	III	3 (10.7)	12 (42.9)	13 (46.4)	0.197
	IV	1 (2.8)	11 (30.6)	24 (66.7)	
Neck dissection	No	3 (6.2)	19 (39.6)	26 (54.2)	0.589
	Yes	1 (6.2)	4 (25.0)	11 (68.8)	
Global- MDADI	Severe/Moderate	0 (0.0)	6 (46.2)	7 (53.8)	0.608
	Mild/Minimum	4 (7.8)	17 (33.3)	30 (58.8)	
Emotional- MDADI	Severe/Moderate	1 (6.2)	7 (43.8)	8 (50.0)	0.801
	Mild/Minimum	3 (6.2)	16 (33.3)	29 (60.4)	
Functional- MDADI	Severe/Moderate	0 (0.0)	4 (66.7)	2 (33.3)	0.279
	Mild/Minimum	4 (6.9)	19 (32.8)	35 (60.3)	
Physical- MDADI	Severe/Moderate	4 (14.3)	12 (42.9)	12 (42.9)	0.015
	Mild/Minimum	0 (0.0)	11 (30.6)	25 (69.4)	
Final score- MDADI	Severe/Moderate	1 (6.2)	9 (56.2)	6 (37.5)	0.124
	Mild/Minimum	3 (6.2)	14 (29.2)	31 (64.6)	

associations with penetration and aspiration (Table 6).

Discussion

Concomitant use of chemo-radiotherapy in advanced oropharyngeal cancer has succeeded in increasing the survival of patients compared to radiotherapy alone. For that reason, this treatment combination became the standard choice in organ preservation protocols (Budach et al., 2006). Those advances notwithstanding, the risk of swallowing disorders is still high in this patient population. Dysphagia is a common sequela, and it is more severe in oropharyngeal cancer patients undergoing combination therapy as a function of the combined toxicities of radiotherapy and chemotherapy (Greven et al., 2008; Starmer et al., 2014).

Dysphagia might lead to the need for feeding tubes to avoid dehydration and malnutrition. However, the prolonged use of such tubes might be associated with muscle atrophy and, consequently, sustained dysphagia (Hanna et al., 2004). In the present study, 15.6% of the

sample required feeding tubes during or after treatment. However, a different study reported that 77% of the patients subjected to concomitant radiotherapy and chemotherapy required feeding tubes or gastrostomy during or after treatment (Greven et al., 2008).

A few patients reported discomfort during the passage of the fibre-optic nasopharyngoscope through the nostril, mainly consisting of those patients with the lowest education levels or those who had never undergone this test before. Nevertheless, the occurrence of discomfort was not sufficient to interrupt the test. As FEES might be performed at the medical office and its results are similar to those from a VFSS, we agree with the authors who assert that FEES should be used for the initial clinical assessments of patients, thus reducing the amount of radiation to which they are exposed (Singh et al., 2009).

The presence of aspiration is usually perceived by cough or hawking before or after food intake. However, in almost half of individuals with head and neck cancer, the cough reflex is ineffective or absent, allowing silent aspiration (Dysphagia Section et al., 2012). The cough

Table 6. Association between Penetration/Aspiration According to FEES Findings and Sociodemographic and Clinical Variables

Variables		Penetration/aspiration FEES			p-value
		Normal n (%)	Penetration n (%)	Aspiration n (%)	
Gender	Female	6 (100.0)	0 (0.0)	0 (0.0)	0.141
	Male	31 (53.4)	15 (25.9)	12 (20.7)	
Age group	≤65 years	30 (61.2)	10 (20.4)	9 (18.4)	0.517
	>65 years	7 (46.7)	5 (33.3)	3 (20.0)	
Tumor site	Tonsils	16 (51.6)	5 (16.1)	10 (32.3)	0.075
	Base of tongue	14 (60.9)	8 (34.8)	1 (4.3)	
	Soft palate	7 (70.0)	2 (20.0)	1 (10.0)	
Disease free interval	6 to 12 months	7 (43.8)	4 (25.0)	5 (31.3)	0.646
	1 to 5 years	18 (62.1)	7 (24.1)	4 (13.8)	
	> 5 years	12 (63.2)	4 (21.1)	3 (15.8)	
T Staging	T1/T2	11 (73.3)	1 (6.7)	3 (20.0)	0.100
	T3	20 (52.6)	13 (34.2)	5 (13.2)	
	T4	6 (54.5)	1 (9.1)	4 (36.4)	
N Staging	N0	8 (42.1)	6 (31.6)	5 (26.3)	0.256
	N1/N2/N3	29 (64.2)	9 (20.0)	7 (15.6)	
TNM Staging	III	13 (46.4)	8 (28.6)	7 (25.0)	0.258
	IV	24 (66.7)	7 (19.4)	5 (13.9)	
Neck dissection	No	26 (54.2)	13 (27.1)	9 (18.8)	0.522
	Yes	11 (68.8)	2 (12.5)	3 (18.8)	
Global- MDADI	Severe/Moderate	7 (53.8)	2 (15.4)	4 (30.8)	0.476
	Mild/Minimum	30 (58.8)	13 (25.5)	8 (15.7)	
Emotional- MDADI	Severe/Moderate	8 (50.0)	5 (31.2)	3 (18.8)	0.625
	Mild/Minimum	29 (60.4)	10 (20.8)	9 (18.8)	
Functional- MDADI	Severe/Moderate	3 (50.0)	2 (33.3)	1 (16.7)	0.841
	Mild/Minimum	34 (58.6)	13 (22.4)	11 (19.0)	
Physical - MDADI	Severe/Moderate	14 (50.0)	7 (25.0)	7 (25.0)	0.476
	Mild/Minimum	23 (63.9)	8 (22.2)	5 (13.9)	
Final score- MDADI	Severe/Moderate	6 (37.5)	6 (37.5)	4 (25.0)	0.149
	Mild/Minimum	31 (64.6)	9 (18.8)	8 (16.7)	

reflex was fully absent in all of the participants in the present study who exhibited aspiration (silent aspiration). This finding might be accounted for by the large number of participants who exhibited reduction or absence of laryngeal sensation and agrees with the results of other studies, which not only detected this association but also noted the increased risk of aspiration pneumonia (Madden et al., 2000). Although the tactile test performed in the present study is a non-quantitative and poorly reproducible method of assessing laryngeal sensitivity, it is easy to apply and has been widely used in other studies (Madden et al., 2000; Gomes et al., 2004).

The results did not observe any association between the severity of dysphagia and clinical-demographic data. Some studies that assessed dysphagia after radiotherapy and chemotherapy for head and neck tumours reported associations between severe dysphagia and the more advanced stages, the site of the primary tumour (oropharynx or hypopharynx) and the extension of the radiation field (Koiwai et al., 2009). One study that

compared clinical variables and the degree of dysphagia in individuals with oropharyngeal cancer found that the severity of dysphagia was greater in the cancers of the base of the tongue, although without a significant difference, and that the severity of dysphagia was significantly greater in stage T3 and T4 tumours (Nguyen et al., 2009; Dysphagia Section et al., 2012). In our study we included a quite homogeneous population relative to the risk factors reported in the literature, e.g., all of the participants exhibited oropharyngeal tumours, were classified as T3 or T4, were subjected to the same radiotherapy technique, similar fields and doses and all had received concomitant chemotherapy; this is more likely the reason we did not identify risk factors for dysphagia.

Self-assessment is an individual's unique and personal perception of his health status and social, functional and psychological aspects (Speyer, 2013). The MDADI is a quality-of-life questionnaire that evaluates four domains relative to the self-assessment performed by patients. The global domain consists of a general question regarding

the patient's routine. The emotional domain encompasses affective statements, such as lack of confidence, shame and self-esteem. The functional domain assesses the impact of dysphagia on the activities of daily living, such as isolation, loss of income and the difficulty other people experience in cooking for the patient. The physical domain corresponds to the individual's self-perception of his difficulty in swallowing, such as increased time to eat, differences relative to the consistency of food, effort to swallow and weight loss (Chen et al., 2001; RLV, 2010).

The participants in the present study reported personal issues in all of the MDADI domains. We could not observe any association with the MDADI domains and the presence of penetration/aspiration. However, the severity of dysphagia showed a significant association with the MDADI physical domain. One study that compared the MDADI scores before and two years after concomitant chemoradiation also found that only the results relative to the physical domain were significantly worse (Cartmill et al., 2012).

In conclusion, a large fraction of the individuals with advanced oropharyngeal cancer subjected to an organ preservation protocol based on concomitant chemoradiation exhibit impaired deglutition. One out of every five such individuals also exhibits aspiration, which is particularly important because aspiration is practically always silent in this patient population and a risk factor for pneumonia. Moreover, almost half of such patients exhibit moderate or severe dysphagia. The socio-demographic and clinical variables analysed in this study did not show association with the severity of dysphagia or with the occurrence of penetration/aspiration. The assessment of the participant's quality of life by MDADI revealed an association between the physical domain scores and the severity of dysphagia. The participants with the most severe degrees of dysphagia more often exhibited severe/moderate limitations in the MDADI physical domain.

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