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HEAD AND NECK

Asymptomatic swallowing disorders may be present in individuals with laryngeal and hypopharyngeal cancer treated with chemo-radiotherapy

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Abstract

Purpose Patients with advanced laryngeal and hypopharyngeal cancer are often treated with chemo-radiotherapy to avoid total laryngectomy. Subclinical swallowing disorders could be present in these patients even though patients do not complain of any symptoms. We sought to evaluate the impact of chemoradiation on swallowing and quality of life.

Methods We studied 21 patients undergoing chemo-radiotherapy for advanced laryngeal and hypopharyngeal cancer. All patients were tumor-free and none reported symptoms related to dysphagia during follow-up or showed altered routine screening tests (EAT-10) to detect it. Swallowing functions were assessed using volume–viscosity swallow test (V–VST) and fiberoptic endoscopic evaluation of swallowing (FEES). Quality of life was assessed with the EORT-H&N35, and SWAL-QOL scales.

Results Frequent alterations in swallowing efficacy (100%) and safety (85.5%) were detected with V–VST and FEES. Quality-of-life scales showed a reduction in their scores between 12 and 17%, mainly in the areas of symptoms.

Conclusion Swallowing disorders are common after chemo-radiotherapy, even in patients who do not clinically manifest these disorders, contributing to a decrease in patients' quality of life. FEES and V–VST are useful procedures to detect asymptomatic swallowing disorders.

Keywords Laryngeal and hypopharyngeal cancer · Quality of life · Chemo-radiotherapy · Swallowing

Introduction

Radiotherapy (RT) or chemo-radiotherapy (CRT) is commonly used to treat locally advanced hypopharyngeal and laryngeal cancer [1, 2]. The effects of RT on healthy tissues are enhanced by chemotherapy (CT) causing acute (mucositis, candidiasis, dermatitis) and chronic (xerostomia, fibrosis, atrophy) sequelae [3, 4]. Fibrosis affects the masticatory, pharyngeal and laryngeal muscles, causing trismus, dysphonia and dysphagia [5, 6].

Swallowing disorders are common after CRT, affecting up to 40–80% of head and neck cancer (HNC) patients treated with it, as a single modality or combined with surgery. They vary in intensity and frequency depending if they are evaluated during the CRT or when it is finished [4, 7–9] Dysphagia affects the quality of life (QoL) of the patients [10, 11]. QoL is frequently altered in patients with HNC, even in those who have overcome the disease and have no

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apparent sequelae. QoL is determined by specific questionnaires designed not only for patients with HNC [12, 13], but also for those with swallowing disorders [14].

We hypothesize that some patients treated with CRT, without active cancer disease, do not report swallowing impairment despite showing an altered QoL. The aim of this work is to detect possible subclinical swallowing disorders in patients with advanced tumors of the larynx and hypopharynx treated with CRT, as well as to determine to what extent their QoL is affected.

Methods

Patients

Since 2012, our department has followed an organ preservation protocol with CRT for patients with advanced hypopharyngeal and laryngeal tumors and, until 2017, a total of 80 patients were treated. A cross-sectional observational cohort study was designed. To be included in the study, patients should be tumor-free at the time of the study, without tracheostomy or feeding tube dependence. Patients did not have to have any complaints about their swallowing during follow-up. This condition was assessed by the Eating Assessment Tool (EAT-10) [15]. All patients had EAT-10 score < 3. The minimum time since the end of the treatment had to be 2 years. Patients who had undergone surgery in the head and neck area, those dependent on a feeding tube or percutaneous endoscopic gastrostomy (PEG) for nutritional support, if they had received specific rehabilitation by a speech therapist due to swallowing disorders or if they had stated that they had made some adaptation in their diet, were excluded. All procedures were conducted in accordance to the Declaration of Helsinki and approved by Institutional Ethics Committee of the HUCA (285/18). Written informed consent was obtained from each patient.

The final sample consisted of 21 patients (26,5% of all patients treated with CRT): 16 men (76%) and 5 women (24%), with a mean age of 65 years (range 56–77 years). All patients were or had been smokers and 15 (71%) had a history of alcohol consumption. In 12 patients, the tumor was located in the larynx (8 in stage III and 4 in stage IVa; all in T3) and in 9 patients in the hypopharynx (6 in stage III and 3 in stage IVa; 3 in T2 and 6 in T3). The mean time since CRT was 56.52 months (range 24–96 months).

The treatment with CRT consisted of a single cycle of induction chemotherapy (cisplatin, 100 mg/m^2 on day 1 plus 5-Fluorouracil, 1,000 mg/m^2, for 5 days) followed by concomitant CRT (70 Gy in 7 weeks plus cisplatin, 75 mg/m^2, every 3 weeks, on days 1, 22, and 43) [16]. All participants were treated with volumetric intensity modulated radiation therapy (IMRT) in volumetric modulated arc therapy (VMAT).

Evaluation of swallowing

Swallowing function was assessed at least 2 years after CRT treatment, using the following procedures: (1) Volume–viscosity swallow test (V–VST). It is a technique for screening of dysphagia. This test identifies patients with oropharyngeal dysphagia [17] V–VST has been previously used in HNC patients treated with CRT to assess the results of rehabilitation [18]. Using V–VST, we can observe alterations in efficacy (lip seal incompetence, oral residues, fractional swallowing) and safety (cough, wet voice and O_2 desaturation). (2) Fiberoptic endoscopic evaluation of swallowing (FEES). This instrumental test is specific to confirm the residues and the risk of penetration (defined as the entry of the bolus into the laryngeal vestibule above the vocal cords) and aspiration (defined as the bolus passing below the vocal cords) with oral feeding [19, 20]. With FEES, we can also observe alterations in efficacy (pharyngeal residues and fractional swallowing). We have not determined the lateralization of the disturbance in the FEES as it would complicate the scoring and would not add value to the significance of the finding. However, these data are important to see the evolution of the disorder and are taken into account during the FEES and recorded in the history. In both V–VST and FEES, xanthan gum-based thickeners are used in liquid viscosities (1–50 centipoise, cP or mPa.s), nectar (51–350 cP), honey (351–1750 cP) and pudding (> 1750 cP). In the FEES, a blue food coloring was also used.

Considering the parameters evaluated in the FESS and in the V–VST, swallowing disorders are classified into alterations in efficacy (if propulsion of the bolus to the esophagus is impaired) and impairment in safety (if the bolus enters the airway). The results obtained by V–VST and FEES were combined according to the number of alterations observed to determine the degree of swallowing disorder [21, 22]. With this score, the volume and viscosity that were considered safer and more effective in swallowing were determined. Patients were given advice with respect to a safe diet, appropriate helpful swallow maneuvers, and the need for further swallow therapy.

Evaluation of quality of life (QoL)

QoL was assessed using 2 instruments: (1) European Organization for Research and Treatment of Cancer—Head and Neck questionnaire 35 (EORTC-H&N35) consists in 7 subscales with 35 items to assess the QoL in HNC. It has been widely used particularly in those patients treated with CRT [12, 13]. The swallowing scale included 4 items (items 35–38) (from 0 to 4; worst-best). Each item has four-point

scale. The scale score is transformed into 0-to-100 scale and a high score on a symptom scale indicates a high symptom level. (2) Swallowing Quality of Life questionnaire (SWAL-QoL) is a specific tool for monitoring the efficacy of rehabilitation and evaluation of swallowing-related QoL. It is a widely used questionnaire to assess QoL in relation to swallowing in patients with HNC [14, 23]. It is a self-administered tool consisting of 44 items divided into 11 domains that assess the impact on the quality of life of patients with swallowing disorders. Each item is given a score from 0 to 4 (worst-best). Scoring in each domain is calculated by the sums of scores for each item expressed as a percentage of the maximum possible domain score. A total SWAL-QoL score is derived by summing each domain score and dividing by 11 giving a total SWAL-QoL score that ranges between 0 and 100 (worst–best).

Statistical analysis

All variables were analyzed with SPSS 22.0 for Windows. Descriptive statistical data were obtained (mean, standard deviation, range, median, interquartile range). Relationships were established between the QoL questionnaires (EORTC-H&N35 and SWAL-QoL) and the score of the degree of alteration of the efficacy and safety of swallowing by means of Spearman's bivariate test, and Kendal's tau-b correlation coefficient. p values < 0.05 were considered statistically significant.

Results

Swallowing evaluation results

Alterations in swallowing efficiency and safety observed with V–VST and FEES are shown in Tables 1 and 2. The evaluation of the V–VST protocol showed that most of the participants had swallowing disorders (90.4% efficacy and 66.6% safety). All patients showed signs of impaired efficacy using the FEES and 52% presented signs of impaired safety. By combining the results of the V–VST protocol and FESS, all patients presented 2 signs of impaired efficacy, while safety was altered in 18 (85.5%). The best tolerated viscosity was liquid, and the worst one pudding. The mean number of alterations in swallowing (efficacy plus safety) with each viscosity was 2.61 for pudding, 2.19 for honey, 1.71 for nectar and 1 for liquid.

Table 1 Alterations in efficacy and safety swallowing assessed with V–VST and FEES ($n = 21$)

	Impaired efficacy		Impaired safety	
V–VST	Incompetent labial seal	0	Cough	14 (66.6%)
	Oral residues	0	Wet voice	0
	Fractional swallowing	19 (90.4%)	O_2 desaturation	1 (4.8%)
FEES	Pharyngeal residues	21 (100%)	Aspiration	2 (9.6%)
	Fractional swallowing	21 (100%)	Penetration	11 (52.3%)

V–VST volume–viscosity swallow test, *FEES* fiberoptic endoscopic evaluation of swallowing

Table 2 Swallowing efficiency and safety as measured by the score obtained by combining the FEES and the V–VST results

Number of alterations	Impaired efficacy	Impaired safety
0	0 (0%)	3 (14.2%)
1	0 (0%)	8 (38.1%)
2	21 (100%)	8 (38.1%)
3	0 (0%)	2 (9.6%)

V–VST volume–viscosity swallow test, *FEES* fiberoptic endoscopic evaluation of swallowing

QoL results

Tables 3 and 4 present summary data for the swallowing EORTC-H&N35 scale and the SWAL-QoL domains, respectively.

The data indicated that swallow-specific QoL was mild involved with a mean EORTC-H&N35 scale domain of 15.3. However, the degree of impaired safety obtained with V–VST and FEES was significantly related to the EORTC-H&N35 ($p < 0.001$).

Patients reported higher scores across all SWAL-QoL domains. The mean SWAL-QoL domain scores were 81.9, ranging between 27.8 and 100. There was a significant relationship between all SWAL-QoL domains, and the degree of impaired safety obtained with V–VST and FEES ($p < 0.001$). The greater the degree of deterioration in safety, the lower the score on the QoL scales. However, the degree of deterioration in swallowing efficacy does not show a significant relationship with the scores on the QoL scales and their different areas.

SWAL-QOL is not related to any of the EORT-H&N35 symptom areas ($r = 0.240$ $p = 0.294$) ($r = 0.252$ $p = 0.270$).

Discussion

As CRT becomes more widely used for treatment of HNC, it is imperative to appreciate, prevent, and optimally manage treatment-related side effects. Swallowing disorders are common sequelae after treatment with CRT in HNC [4].

Table 3 Comparison of the mean value of the items valued according to the EORTC-H&N35 with the mean value of the number of alterations observed when combining the FEES and the V–VST

Symptom scale	Mean	Median	Standard deviation	Range	Impaired efficacy	Impaired safety
Swallowing (items)						
35. Problems swallowing liquid	12.7	0.5	26	0–100	NS	NS
36. Problems swallowing pureed food	6.3	0.2	22.2	0–100	NS	$p < 0.001$ tau = – 0.104
37. Problems swallowing solid food	25.3	1	33.2	0–100	NS	$p < 0.001$ tau = – 0.193
38. Choked when swallowing	17.4	3	28.3	0–100	NS	$p < 0.001$ tau = 0.146
All items 35–38	15.3	6.5	24.8	0–100	NS	$p < 0.001$ tau = – 0.104

EORTC-H&N35 European Organization for Research and Treatment of Cancer—Head and Neck questionnaire 35, *FEES* fiberoptic endoscopic evaluation of swallowing, *NS* no significant association, *V–VST* volume–viscosity swallow test

Table 4 Comparison of the mean value of the items valued according to the SWAL-QoL with the mean value of the number of alterations observed when combining the FEES and the V–VST

Domain	Item	Mean	Median	Standard deviation	Range	Impaired efficacy	Impaired safety
Burden	1–2	78.5	100	34.5	0–100	NS	$p < 0.001$ tau = 0.267
Eating desire	5–7	89.3	100	17.3	0–100	NS	$p < 0.001$ tau = – 0.087
Feending duration	3–4	68.5	100	42.5	50.0–100	NS	$p < 0.001$ tau = 0.158
Symptom frequency	8–21	74.3	82.1	20.7	23.2–100	NS	$p < 0.001$ tau = – 0.095
Food selection	22–23	85.7	100	28.1	0–100	NS	$p < 0.001$ tau = 0.064
Communication	24–25	85,1	100	24.6	0–100	NS	$p < 0.001$ tau = 0.466
Fear	26–29	82.4	87.5	20.1	25–100	NS	$p < 0.001$ tau = 0.267
Mental health	30–34	93.6	100	18.4	20–100	NS	$p < 0.001$ tau = – 0.031
Social function	35–39	84.7	100	28.8	10–66.6	NS	$p < 0.001$ tau = 0.125
Sleep	43–44	83.9	100	31.9	0–88.9	NS	$p < 0.001$ tau = – 0.279
Fatigue	40–42	89.7	100	13.7	66.6–100	NS	$p < 0.001$ tau = – 0.143
Total		81.9	89.2	18.1	27.8–100	NS	$p < 0.001$ tau = 0.073

NS no significant association, *SWAL-QoL:* wallowing Quality of Life Questionnaire

Our study shows that, although patients consider their swallowing normal, it is affected, mainly on the safety scale, which can generate a significant degree of preventable morbidity. Almost a third of the patients who have received CRT do not show complaints about their swallowing and, nevertheless, they present swallowing disorders, when performing specific tests for their detection. We use a selected and homogeneous sample of patients. Only advanced tumors of larynx and hypopharynx were included unlike other series that also include the oropharynx, oral cavity and nasopharynx, with expected swallowing sequelae of different severity and significance [4, 7]. Moreover, in our sample, there were no patients with previous surgery in the upper aerodigestive tract, including tracheostomy, which could lead to swallowing disorders. Other criteria that limited the sample size were the exclusion of patients with EAT-10 ≥ 3, those with known swallowing disorders before and after treatment with CRT, those who required a feeding tube or PEG, patients with the diagnosis of malnutrition or pneumonia and those who received a specific rehabilitation by a speech therapist or adapted their diet.

Some authors [24] propose the EAT-10 questionnaire as an indicator of the presence of post-swallowing pharyngeal residues in patients with HNC. However, this test has several limitations because it has been used in heterogeneous series of patients according to tumor subsites, stage, cancer treatment modalities and post-treatment time. Arrese et al. [25] in a series of 44 patients with HNC, compared EAT-10 with

a penetration-aspiration scale assessed by modified barium videofluoroscopy to detect oropharyngeal dysphagia after treatment. The results showed a significant relationship between the EAT-10 score and the presence of oropharyngeal dysphagia in the group of patients in the pre-treatment period up to 1 year after treatment with HNC. However, no significant relationship was found in groups of patients one year after CRT.

We interpret that although the EAT-10 is a valid tool as a screening for oropharyngeal dysphagia, it does not discriminate against all patients with HNC treated with CRT. Our findings confirm the high prevalence of asymptomatic swallowing disorders after CRT that can be suspected with V–VST and confirmed with FEES. Thus, with V–VST alterations in efficacy and safety were diagnosed in 90% and 66% of patients, respectively. With FEES, these alterations were confirmed in 100% and 52%. The presence of alterations in efficacy in all patients must be taken into account. These alterations without being corrected can lead to potentially more serious safety problems. Variations between V–VST and FEES may be because V–VST is, like EAT-10, a screening test, while FEES is a confirmatory instrumental test, therefore more specific when it comes to objectifying penetration-aspiration and residues and it does not assess fewer specific symptoms, such as cough or wet voice.

Several studies in the literature suggest alterations in the biomechanics of swallowing in subjects after CRT. In most cases, dysphagia is mild to moderate, although some cases evolve to more severe grades of dysphagia where oral feeding is not possible [4, 26]. In our study, we obtain a scoring system considering the results of V–VST and FEES that assesses the efficacy and safety of swallowing. We think, as other authors, that the use of these scales allows a numerical quantification of dysphagia, facilitating accurate communication between clinicians [26]. According to this combined scale, 86% of the patients presented some type of alteration that compromises the safety of swallowing. The swallowing disorders that we observed with V–VST and FEES correspond to the alteration of the pharyngeal phase of swallowing: cough, pharyngeal residuals (remaining in the vallecula and/or pyriform sinuses after spontaneous clearing swallows), fractional swallowing, penetration and aspiration, as demonstrated by other authors who also find more alterations in the pharyngeal phase [4, 27–29]. This fact is relevant since many studies on HNC do not take into account the swallowing phase that is altered, and this may serve to achieve a better planning of rehabilitative therapy as other authors have also suggested, who even propose exercising the pharyngeal phase even before starting CRT [10, 26, 30].

We also observed that liquid consistency causes the fewer swallowing alterations, followed by nectar. On the other hand, the consistencies honey and pudding cause more alterations in the efficacy and safety. This observation is also important since the use of thickeners could increase the swallowing disorders. In addition, the single intake of foods with nectar and liquid consistencies can lead to malnutrition, in which case nutritional supplements should be used [6, 26, 31, 32]. Pudding and honey are normally considered the safest viscosities in cancer patients and liquid consistency has a higher risk of aspiration and entry into the airway. However, in our work, the opposite is observed: nectar and liquids are the viscosities with the least number of alterations. Something similar has been observed by us in previous work on neurodegenerative diseases [21, 22]. In these pathologies, there is an incoordination of the swallowing muscles that cause a lack of propulsion of the food bolus. Thus, the lower viscosities (nectar and pudding) are easier to propel and are more efficient as they have a higher transit speed; however, they would also be more unsafe as they pass more easily into the respiratory tract. Likewise, after CRT, muscle fibrosis, mucositis, xerostomia would occur, and bolus propulsion would be affected, with altered swallowing efficacy, making fluid progression easier. However, this observation cannot be generalised, and it would be very important to make an individual diagnosis with objective procedures (V–VST, FEES or videofluoroscopy) in each patient, as individual circumstances may concur.

Because the EORTC-H&N35 includes multiple dimensions, if we only analyze swallowing scale, the results do not show an impairment in quality of life as a function of swallowing. Some authors observed that patients treated with RT obtained better scores in EORTC-H&N35 than those treated with surgery [33]. Using the SWAL-QoL questionnaire, QoL is also reduced in our study with respect to normal values. Other studies also observed a high prevalence of swallowing disorders (79%) after CRT for advanced HNC using this questionnaire [14, 31]. Moreover, the degree of impairment in swallowing safety is significantly related to the EORTC-H&N35 and SWAL-QoL. No significant relationships were observed between the test results and the impairment in efficacy since alterations in swallowing safety are more serious and have a greater impact on patients [11].

One aspect to note is that in our study a considerable time has elapsed from the end of CRT to the completion of the QOL questionnaires, favoring adaptation to the after-effects of treatment and the tendency to better judge their overall condition. The greatest effect of CRT in relation to the severity of dysphagia has been reported to be during its administration or just at the end of treatment [13, 31, 34, 35], but our results confirm that silent swallowing disorders are common even after of several years. Some authors propose reducing these sequelae through preventive exercises, planning rehabilitation earlier and for a longer time, observing the benefits 6 months after the end of therapy [10, 31, 35].

Among the limitations of the study, we note the sample size, which has been greatly reduced to represent a uniform

series of tumor-free patients treated exclusively with CRT with a minimum follow-up of 2 years and who have not been diagnosed or treated due to swallowing disorders.

Conclusion

Patients with locally advanced tumors of the larynx and hypopharynx treated with CRT have frequent asymptomatic swallowing disorders that alter their QoL. These disorders can be diagnosed with V–VST and on FEES, so they should be used routinely in the follow-up and control of these patients.

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Declarations

Conflicts of interest/Competing interests The authors have no conflicts of interest to disclose.

Ethics approval All procedures were conducted in accordance to the Declaration of Helsinki and approved by Institutional Ethics Committee of the HUCA (285/18).

Consent to participate Written informed consent was obtained from each patient.

Consent for publication This manuscript, or any part of it, has not been previously published; nor is it under consideration for publication elsewhere. I would be most appreciative if you would consider this paper for publication in EAOHNS.

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