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HEAD & NECK

# Analysis of dysphagia in advanced-stage head-and-neck cancer patients: impact on quality of life and development of a preventive swallowing treatment

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## Abstract

**Objectives** Swallowing and voice dysfunctions are common side effects following head-and-neck squamous-cell carcinoma (HNSCC) treatment. Our aim was to analyze the relationships between quality of life, swallowing, and phonatory problems in patients with an advanced-stage HNSCC and to prospectively evaluate the effects of a prophylactic swallowing program.

**Methods** First, we retrospectively studied 60 advanced HNSCC patients treated with exclusive or adjuvant radiotherapy/chemoradiotherapy (RT/CRT). Subjects were classified according to general and clinical–therapeutic features. Outcome measures included EORTC QLQ-C30, EORTC QLQ-H&N35, Dysphagia Handicap Index (DHI), M.D.Anderson Dysphagia Inventory (MDADI), and Voice Handicap Index (VHI). Then, we conducted a prospective evaluation of a prophylactic swallowing counselling in 12 consecutive advanced-stage HNSCC patients by a two-arm case–control analysis. These patients were treated with exclusive or adjuvant RT/CRT.

**Results** 71% of the retrospective population studied reported swallowing dysfunction as a major side effect. No differences were detected in the severity of dysphagia or dysphonia according to type of treatment or staging of the primary tumour, while hypopharyngeal and laryngeal cancer patients showed significantly better swallowing ability and better QoL compared to oral cavity and oropharyngeal localisation ($p < 0.05$). In addition, a relevant correlation between swallowing and voice problems emerged ($p < 0.05$). In the prospective part, while no statistical correlation was evident before the start of RT/CRT in the experimental group compared to the control one, the former showed better performances at MDADI ($p = 0.006$) and DHI ($p = 0.002$) test 3 months after its end.

**Conclusion** Dysphagia is both an acute-and-long-term side effect which greatly affects QoL of HNSCC patients undergoing multimodality treatment. Our data show that a prophylactic swallowing program could actually produce a beneficial effect on patients' outcomes.

**Level of evidence** 1b and 2b.

**Keywords** Dysphagia · Head-and-neck cancer patients · Swallowing exercises · Swallowing preservation · Quality of life

## Introduction

Advanced head-and-neck squamous-cell carcinoma (HNSCC) and its treatment cause functional, physical, and emotional impairment [1]. Speech disorders, dysphagia,

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pain, and depression are found to be the most common side effects affecting quality of life (QoL) regardless of the treatment modality [2]. Dysphagia is found in up to 50% of head-and-neck cancer survivors, especially those affected by advanced disease, and it results from the sum of multiple factors, such as xerostomia, taste loss, stricture, fibrosis, reduced muscle strength, and trismus [3]. These complications can variably occur and they continue to evolve during the first 12–24 months after the end of therapy because of the delayed effects of radiation therapy (RT) or chemoradiotherapy (CRT) [4]. It has also been shown that any improvement in dysphagia severity cannot be reached after the end of treatment and that it represents an independent risk factor for lower survival rates [5]. In the near future, a greater proportion of patients will experience such issue due to the wider diffusion of organ-preserving strategies for advanced HNSCC and it is still unclear how much new techniques, including intensity-modulated RT, will affect it [6–8]. To date, there are still no definite pharmacological or physical-rehabilitation supports to improve or prevent severe dysphagia in these patients [9].

The present study seeks to determine how the complications of multimodality therapy for advanced HNSCC are related not only to the type of treatment but also to the clinical characteristics of the disease itself. We have studied the relationships between quality of life, swallowing, and vocal disorders with demographic and clinic-therapeutic features of a cohort of advanced-stage HNSCC patients and we have tried to prevent the chronicity of swallowing problems by introducing a prophylactic management program of dysphagia.

## Materials and methods

The study was approved by the local Ethical Committee with the protocol numbers: 11130_oss and 12224_spe. All the participants signed an informed consent agreement before being enrolled in the study.

### Population studied

To verify the impact on QoL of phonatory and swallowing functions in advanced (stage III–IV, TNM, VII edition [10]) HNSCC patients treated with exclusive or adjuvant RT/CRT, we have carried out a preliminary analysis of 60 patients treated at the Otorhinolaryngology Unit of Careggi University Hospital in Florence, from 2010 to 2017.

Subjects were classified retrospectively according to age, gender, smoking, alcohol consumption, tumour site, tumour T stage, and type of treatment. Postoperative complications, use of tracheostomy, nasogastric feeding tube (NGFT), or percutaneous endoscopic gastrostomy (PEG) placement were also retrieved. Concerning RT treatment, the following factors were considered: type of RT/CRT, duration and its possible interruption, elapsed time between the end of RT/CRT treatment and enrolment in this study, and onset of potential complications. Outcomes measures included EORTC QLQ-C30 [11], EORTC QLQ-H&N35 [12], Dysphagia Handicap Index (DHI) [13], M. D. Anderson Dysphagia Inventory (MDADI) [14], and Voice Handicap Index (VHI) [15].

We then conducted the second phase of our study aimed at creating a swallowing counselling service as a resource to improve or prevent the chronicity of severe dysphagia. Twelve patients affected by advanced HNSCC, who were about to be treated at our Institution with exclusive or adjuvant RT/CRT, were included in the study. They were matched by cancer site, stage, treatment type, and chemotherapy regimen. Six patients (experimental group) received standard of care (i.e., diet modifications and use of anti-fungal/hyaluronic acid-based drugs) plus pretreatment swallowing exercises prior to RT/CRT. The remaining six patients (control group) received standard-of-care treatment only. Subjects were randomly allocated to control or experimental groups according to a computer generated randomisation list.

All patients provided their own swallowing outcomes by compiling MDADI and DHI. These tests were administered 2 weeks before the start of RT (time 0), at the first post-treatment week (time 1) and after 3 months from the end of RT/CRT (time 2). Furthermore, each patient was asked to provide information about their diet by self keeping a weekly diary and about their body weight at time 0 and time 2.

### Swallowing exercises

The purpose of the rehabilitation protocol was to maintain the function of the muscular structures involved in swallowing, to increase the accuracy of oropharyngeal movements, and to counter the radiation-induced fibrosis that usually leads to restricted range of muscular motion, leading to dysphagia [16, 17]. Approximately 2 weeks before the beginning of radiotherapy, participants were instructed by one of the authors and given written instructions, so that they could perform the exercises independently and practice them daily at home. Patients were asked to perform all exercises with ten repetitions, twice a day, beginning prior to radiotherapy and onwards. Each training session at home lasted about 10 min; they were encourage to integrate swallowing exercises into their daily activities and to continue oral food intake if considered safe [18]. To increase patients' compliance, the aims of the proposed exercises and the importance of performing them daily had previously been explained to each patient [19]; patients were provided with an exercise diary to record the number of training sessions and to refer

pain related to the exercises [20]. Patients' compliance was evaluated counting the effective days in which exercises were performed, considering as total time of the program about 8 weeks (2 prior to and 6 during RT/CRT).

The swallowing exercises included: tongue resistance exercises, effortful swallow, Masako maneuver, Mendelsohn maneuver, and Shaker Maneuver [21].

For the tongue resistance exercises, the participants were instructed to press with their tongue against the tongue depressor or spoon in different directions: forward, upward, right, and left sides.

In effortful swallow, it must be swallowed by increasing the force and time wherewith the body of the tongue moves in anteroposterior direction, pressing against the palate. In the Masako maneuver, the patients were instructed to swallow while keeping the tip of the tongue pinched lightly between the teeth. For the Mendelsohn maneuver, the participants initiate the swallow, keeping the laryngeal elevation for a few seconds after the swallowing act. Finally, for the Shaker maneuver, the patient was instructed to lie down in a supine position and raise his/her head high enough to be able to see the knees [4, 16].

### Statistical analysis

Categorical variables were calculated in terms of frequencies and percentages for all of the 72 patients. Standard descriptive statistics were used to summarize data, with respect to demographic and clinical characteristics. Wilcoxon and Mann–Whitney tests when appropriate were used. Outcome was analyzed by univariate and multivariate survival analyses for all malignancies, using STATA version 12.1 (StataCorp. 2011. Stata Statistical Software: Release 12. College Station, TX:StataCorp LP). Logistic regression was used to investigate which factors were associated with each response variables. Afterwards, multiple logistic regression analyses were performed to account for several confounding variables simultaneously. Multiple logistic regression included all variables of interest, taking into account multicollinearity and sample size. A two-tailed $p$ value less than 0.05 was considered statistically significant.

## Results

### Retrospective analysis

A total of 60 patients with advanced HNSCC were included. Their features are summarized in Table 1. The most reported complication was dysphagia (71%) followed by dysphonia (53.3%), dysgeusia (33.3%), mucositis (28.3%), xerostomia (25%), and odynophagia (15%). No significant differences were found at the DHI, VHI, and MDADI tests

**Table 1** Description of population studied

| Variables | Total patients (%) |
|---|---|
| Gender | |
| Male | 44 (73.3) |
| Female | 16 (26.7) |
| Age | |
| < 50 years | 7 (11.7) |
| 50–70 years | 36 (60) |
| > 70 years | 17 (28.3) |
| Smoke | |
| < 10 packs/year | 16 (26.7) |
| > 10 packs/year | 44 (73.3) |
| Alcohol | |
| < 1L/die | 52 (86.7) |
| > 1 L/die | 8 (13.3) |
| Tumour site | |
| Oral cavity | 13 (21.7) |
| Oropharynx | 24 (40) |
| Hypopharynx | 5 (8.3) |
| Larynx | 18 (30) |
| pT | |
| 1 | 9 (15) |
| 2 | 5 (8.4) |
| 3 | 23 (38.3) |
| 4 | 23 (38.3) |
| pN | |
| 0 | 19 (31.7) |
| 1 | 9 (15) |
| 2 | 31 (51.7) |
| 3 | 1 (1.6) |
| Stage | |
| III | 18 (30) |
| IV | 42 (70) |
| Treatment | |
| RT/CRT | 26 (43.3) |
| Combined (surgery + RT/CRT) | 34 (56.7) |
| p16+[a] | |
| Yes | 15 (25) |
| No | 45 (75) |
| Interruption of RT | |
| Yes | 17 (28.3) |
| No | 43 (71.7) |
| Complications | |
| Odynophagia | 9 (15) |
| Dysphagia | 43 (71.7) |
| Dysgeusia | 20 (33.3) |
| Xerostomia | 15 (25) |
| Erythema | 14 (23.3) |
| Mucositis | 17 (28.3) |
| Dysphonia | 32 (53.3) |
| Follow-up | |
| < 24 months | 33 (55) |

**Table 1** (continued)

| Variables | Total patients (%) |
|---|---|
| > 24 months | 27 (45) |
| Relapse | |
| Yes | 3 (5) |
| No | 57 (95) |

[a]*p16*+ human papilloma virus, protein 16

considering type of treatment (curative vs. adjuvant RT/CRT; pDHI = 0.181, pVHI = 0.067, pMDADI = 0.233), tumour size (T1–T2 vs. T3–T4; pDHI = 0.727, pVHI = 0.088, pMDADI = 0.241), and clinical regional lymph nodes involvement (N− vs. N+; pDHI = 0.801, pVHI = 0.976, pMDADI = 0.682), respectively. Only considering the emotional scale of VHI test, there was a significantly better result for patients undergoing exclusive RT/CRT ($p = 0.042$). Analysing tumour site (Table 2), we found significant differences between oral cavity/oropharynx HNSCC against hypopharynx/larynx location with a better performance in terms of swallowing ability for the latter. Considering the phonatory impairment, no differences were noted. Based on the time elapsed from the end of the treatment, all the emotional scales of VHI ($p = 0.038$), DHI ($p = 0.015$), and MDADI ($p = 0.002$) showed worse results after 24 months. The MDADI tool also showed significant results for global ($p = 0.005$) and functional scales ($p = 0.001$) (Table 2).

The scores obtained at the EORTC QLQ-C30 and EORTC QLQ-H&N35 were then correlated with some demographic (gender and smoke/alcohol) and clinical (tumour site, pT, pN, stage, and type of treatment) features

**Table 2** Evaluation of VHI, DHI, and MDADI test based on the tumour site and on time elapsed from the end of treatment

| | Oral cavity/oropharynx (mean ± SD) | Hypopharynx/larynx (mean ± SD) | *p* value |
|---|---|---|---|
| VHI | | | |
| Global score | 35.08 ± 24.05 | 32.61 ± 22.36 | 0.692 |
| Emotional | 9.27 ± 8.58 | 7.22 ± 6.32 | 0.325 |
| Functional | 12.11 ± 9.22 | 12.00 ± 9.84 | 0.965 |
| Physical | 13.70 ± 7.81 | 13.39 ± 8.28 | 0.883 |
| DHI | | | |
| Global score | 37.84 ± 21.07 | 22.17 ± 15.55 | **0.003** |
| Emotional | 8.27 ± 7.15 | 3.13 ± 4.51 | **0.003** |
| Functional | 14.32 ± 8.53 | 9.13 ± 6.90 | **0.016** |
| Physical | 15.24 ± 7.06 | 9.91 ± 6.25 | **0.004** |
| MDADI | | | |
| Global score | 64.84 ± 14.21 | 72.30 ± 13.45 | **0.048** |
| Emotional | 20.84 ± 4.37 | 23.09 ± 3.75 | **0.045** |
| Functional | 17.54 ± 4.59 | 19.61 ± 3.74 | 0.074 |
| Physical | 23.86 ± 6.11 | 26.52 ± 6.35 | 0.112 |
| | < 24 months (mean ± SD) | > 24 months (mean ± SD) | *p* value |
| VHI | | | |
| Global score | 29.15 ± 19.58 | 40.22 ± 26.17 | 0.066 |
| Emotional | 6.61 ± 5.95 | 10.78 ± 9.20 | **0.038** |
| Functional | 10.15 ± 8.56 | 14.04 ± 10.12 | 0.142 |
| Physical | 12.09 ± 7.08 | 15.41 ± 8.64 | 0.107 |
| DHI | | | |
| Global score | 27.64 ± 15.55 | 36.96 ± 24.62 | 0.079 |
| Emotional | 4.42 ± 4.71 | 8.59 ± 8.07 | **0.015** |
| Functional | 11.09 ± 6.62 | 13.85 ± 9.88 | 0.201 |
| Physical | 12.12 ± 6.36 | 14.52 ± 8.03 | 0.202 |
| MDADI | | | |
| Global score | 72.21 ± 13.86 | 62.19 ± 13.01 | **0.005** |
| Emotional | 23.15 ± 3.81 | 19.93 ± 4.17 | **0.002** |
| Functional | 19.91 ± 3.99 | 16.41 ± 4.10 | **0.001** |
| Physical | 26.27 ± 6.29 | 23.19 ± 5.96 | 0.057 |

Significant values are in bold

of our study population. In a multivariate statistical analysis, higher scores were significantly related to female gender and larynx/hypopharynx site (all $p=0.04$). Finally, when treatment strategy was considered, worse results were detected in those undergoing combined treatment (surgery + RT/CRT) than the group undergoing exclusive RT/CRT ($p=0.04$).

Furthermore, our population was divided into two groups based on whether they had voice problems or not. Patients who reported a VHI score in the "mild", "moderate", and "severe" level were considered patients with voice problems, while those who reported normal VHI scores were considered as patients without voice problems [15]. In these two groups, we compared the scores obtained from the MDADI and DHI tests (total, functional, physical, and emotional) and, in all scales, those without voice problems showed a better swallowing function (Table 3).

## Preventive swallowing program

Description of the 12 patients recruited is given in Table 4. They reported a strikingly high mean compliance of 70%. To confirm the potential benefit of our swallowing rehabilitation method, we analyzed the scores acquired by the two groups: at time 1, the physical scale of the DHI test proved to be better in the experimental group ($p=0.039$), and, at time 2, the physical scales of MDADI ($p=0.006$) and global ($p=0.032$) and physical ($p=0.003$) scale of DHI test were statistically significant in comparison to the control group. In addition, the MDADI composite score was calculated as the sum of the functional, physical, and emotional scale in the three different times. At time 0, the two studied groups had the same score on average. At time 1, though a difference of 10 points was apparent, and at time 2, the experimental group showed an average difference of more than 15 points better than the control group. This difference in points emerged even if statistical significance emerged only for the physical scale of the MDADI test at time 2.

Figure 1 represents the average of the scores obtained by experimental and control groups at the two tests administered.

**Table 3** Correlation between swallowing and voice problems

| | Patients with voice disorders ($n=31$) (mean ± SD) | Patients without voice disorders ($n=29$) (mean ± SD) | $p$ value |
|---|---|---|---|
| MDADI | | | |
| Total score | 61.42 ± 12.41 | 74.41 ± 13.22 | **< 0.01** |
| Functional scale | 16.68 ± 4.34 | 20.10 ± 3.72 | **< 0.01** |
| Physical scale | 22.23 ± 5.18 | 27.72 ± 6.19 | **< 0.01** |
| Emotional scale | 20.23 ± 4.25 | 23.28 ± 3.73 | **< 0.01** |
| DHI | | | |
| Total score | 38.26 ± 21.13 | 24.97 ± 17.67 | **< 0.01** |
| Functional scale | 14.90 ± 8.18 | 9.59 ± 7.60 | **0.011** |
| Physical scale | 15.03 ± 7.36 | 11.24 ± 6.60 | **0.040** |
| Emotional scale | 8.32 ± 7.43 | 4.14 ± 5.15 | **0.014** |

Significant values are in bold

**Table 4** Description of the cohort involved in the perspective part of our study

| Variables | Experimental group $n$ (%) | Control group $n$ (%) |
|---|---|---|
| Gender | | |
| Male | 4 (33.3) | 3 (25) |
| Female | 2 (16.7) | 3 (25) |
| Age | | |
| 50–70 years | 4 (33.3) | 3 (25) |
| > 70 years | 2 (16.7) | 3 (25) |
| Smoke | | |
| < 10 packs/year | 2 (16.7) | 4 (33.3) |
| > 10 packs/year | 4 (33.3) | 2 (16.7) |
| Alcohol | | |
| < 1L/die | 6 (50) | 4 (33.3) |
| > 1 L/die | 0 | 2 (16.7) |
| Co-morbidities | | |
| Yes | 2 (16.7) | 4 (33.3) |
| No | 4 (33.3) | 2 (16.7) |
| Subsites | | |
| Oral cavity | 2 (16.7) | 3 (25) |
| Oropharynx | 2 (16.7) | 1 (8.3) |
| Hypopharynx | 0 | 1 (8.3) |
| Larynx | 2 (16.7) | 1 (8.3) |
| pT | | |
| 1 | 2 (16.7) | 1 (8.3) |
| 2 | 1 (8.3) | 1 (8.3) |
| 3 | 1 (8.3) | 2 (16.7) |
| 4 | 2 (16.7) | 2 (16.7) |
| pN | | |
| 0 | 3 (25) | 2 (16.7) |
| 1 | 0 | 2 (16.7) |
| 2 | 3 (25) | 1 (8.3) |
| 3 | 0 | 1 (8.3) |
| Stage | | |
| III | 2 (16.7) | 2 (16.7) |
| IV | 4 (33.3) | 4 (33.3) |
| Treatment | | |
| RT/CRT | 2 (16.7) | 1 (8.3) |
| Combined (surgery + RT/CRT) | 4 (33.3) | 5 (41.7) |
| p16+[a] | | |
| Yes | 2 (16.7) | 1 (8.3) |
| No | 4 (33.3) | 5 (41.7) |

*Co-morbidities* included were: hypertension, diabetes mellitus, hypercholesterolemia, hypothyroidism, or hyperthyroidism

[a]*p16+* human papilloma virus, protein 16

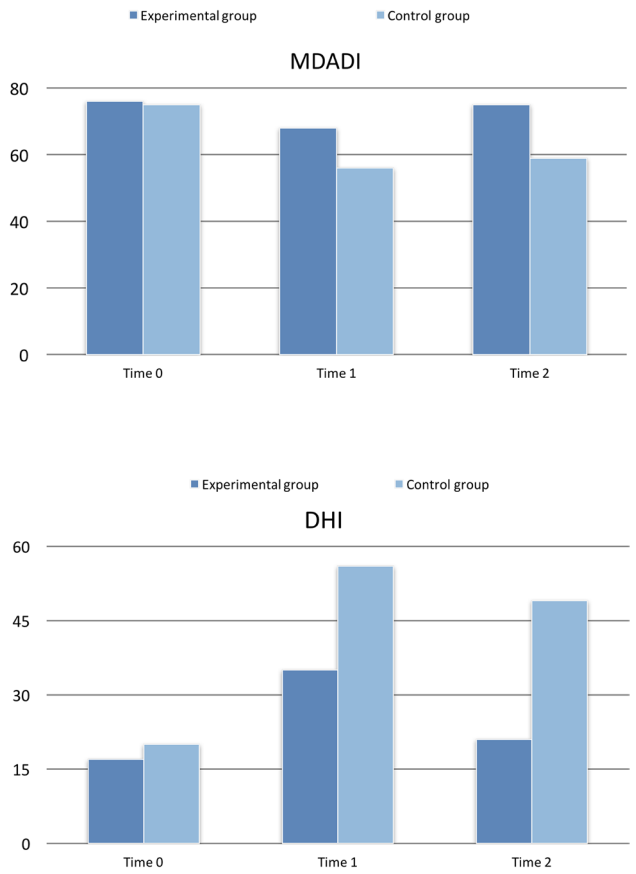


**Fig. 1** Histograms represent the average of the scores obtained by experimental and control groups at the two tests administered: MDADI and DHI

By performing a multivariate analysis, a significant trend emerged between tumour size and functional ($p=0.05$), emotional ($p=0.05$) and total scale ($p=0.05$) in comparison to the DHI test and global scale ($p=0.05$) of MDADI test. Curiously, this event only emerged at time 0. Considering weight and diet type, making a comparison between weight at time 0 (before the start of RT/CRT) and at time 2 (after 3 months from the end of the treatment), there was a significant weight loss for the control group ($p=0.032$) but not for the experimental group ($p=0.258$). In terms of diet, the following types have been considered: free, semi-solid, and liquid diets. Before the beginning of the treatment, the diffusion of the typologies of diet was homogenous between experimental and control groups ($p=1.000$), while, after 3 months from the end of treatment, the experimental group showed a trend towards solid foods ($p=0.030$).

## Discussion

Dysphagia in advanced HNSCC is a frequent and devastating consequence of the disease and the treatments themselves [22, 23]. Despite recent publications have demonstrated the progressive attention from several experts towards this problem [3, 4, 18], there is still no quick and clear way against it, and usually, common practice provides only a palliative support often at distance from the end of the treatment, due to the lack of both robust clinical evidences and shared standardised dysphagia management guidelines in head-and-neck cancer patients. For instance, patients are often destined to feed themselves with semi-solid and homogeneous consistency food or they are given oral supplements based on hyaluronic acid or aqueous gels to facilitate the preparation of the food bolus and the pharyngeal phase of the swallowing. In situations in which dysphagia is so severe as to determine the onset of malnutrition, the only measures adopted are often the insertion of NGFTor PEG placement [9].

We have divided our analysis into two steps, allowing us to reach a complete picture of the problem. The first one shows that swallowing dysfunction does actually affect the quality of life of patients with advanced HNSCCs. In fact, more of two-thirds of them considered dysphagia as the predominant side effect of the treatment received. Interestingly, dysphagia and xerostomia were not reported in the same proportion, thus showing that they are not necessarily related. Many authors keep still erroneously consider oropharyngeal dysphagia as a direct consequence of a reduction in salivation [24]. Instead, it has been proved that post-actinic dysphagia is caused primarily by the effect of radiation-induced fibrosis, which decreases the excursion and the strength of the movements involved in swallowing [25, 26].

Based on the tumour site, patients affected by carcinoma of the hypopharynx/larynx showed a better swallowing function in comparison to those affected by oral/oropharyngeal cancers, while other authors have found the opposite [27]. No significant differences were found through the VHI test, but this can be clarified, because, in the hypopharynx/larynx group, there was a greater percentage of patients undergoing combined treatment instead of exclusive RT/CRT. On the other hand, those who underwent combined therapy showed worse QoL score compared to those patients who had exclusive RT/CRT, whereas other studies found no differences between treatment modalities [28, 29]. In this regard, we can suppose that there are other elements, such as disfiguring wounds, that might undermine the quality of life in such patients.

Considering the long-term impact of dysphagia on patients' life, it is interesting to highlight that dysphagia

and dysphagia-related QoL were better preserved in patients who had received curative treatment in the past 24 months, than who have already passed this temporal limit. In fact, the performance obtained in the MDADI test was significantly better for those who had finished the radiation treatment for less than 24 months (Table 2). This could be explained by the fact that, initially, patients justified their swallowing difficulty as a temporary complication following treatment; however, once this problem shows no improvement over the following months, this complication reveals itself as really disabling and it does negatively affect quality of life [30].

To find a possible correlation between dysphagia and dysphonia, we stratified our population by phonatory problems shown at the VHI test. The group with voice problems showed a more deficient swallowing ability and, in particular, the total score of the MDADI test showed the greatest difference between the two groups; thus, those who had voice problems had worse swallowing ability and dysphagia-related QoL than those who were normal at VHI. Such association is in line with the hypothesis proposed by Kraaijenga et al. [31], for whom swallowing and voice impairment could be commonly explained based on changes in saliva production which can lead to insufficient lubrication of the vocal folds. However, the complex connections between voice and swallowing dysfunction need to be further clarified in future studies.

About 10 years ago, two American studies have shown that performing pretreatment swallowing exercises could produce functional improvements in terms of videofluoroscopic parameters [21] or MDADI score [23]. Both studies, however, only involved patients undergoing organ-preservation CRT. Our study, on the other hand, aimed to evaluate the benefits of prophylactic treatment even in those patients who underwent surgery plus adjuvant RT/CRT. A statistically significant trend was found between the tumour size (cT) and the functional, total, and emotional scale of the DHI test and the global scale of the MDADI test at time 0, but not later. The data obtained are very important, because they showed that cancer size could affect swallowing ability only before RT, while, at the end of the treatment, this element is no longer relevant, since side effects affected all patients indiscriminately. Contrary to the results obtained by a recent trial [32], a clear improvement of the physical scale for the DHI test emerged ($p = 0.03$) at the end of the RT for the experimental group and even better scores were shown at time 2, where the physical scales of both MDADI and DHI were statistically significant. Regarding the composite MDADI test, it was recently shown that a 10-point between-group difference in composite MDADI score was associated with a clinically relevant difference in head-and-neck cancer patients [33]. In our series, although statistical significance emerged only for the physical scale of the MDADI test at time 2, such difference was spotted at time 1 and time 2.

Given the difficulty in establishing the benefits and drawbacks of RT/CRT, as side effects are not objectively detectable as survival or local control rates [25], we have also considered weight loss of patients during treatment and diet type. Such endpoints have been already used in a larger American trial in which patients undergoing prophylactic swallowing treatment did show a lower deterioration in diet compared to the control group, though no differences in weight loss were registered [34]. In our series, the difference between the weight of time 0 and time 2 was significant for the control group but no for experimental group, but data could be explained by an impressively high compliance of 70%. Adherence to such home-based exercises is one of the critical aspects of this kind of investigations and we would like to recall that compliance almost invariably decreases towards half of the radiation treatment [20, 35].

In the end, a recent meta-analysis has shown that prophylactic exercises before, during, and/or immediately after advanced HNSCC treatment do not lead to any improvement in swallowing function, and the authors conclude highlighting some weak points which their study partially suffer from [36].

Regarding the perspective part of the present study, we had a limited sample size, a short longitudinal follow-up period, and the lack of instrumental evaluation such as videofluoroscopy.

## Conclusion

Based on the results obtained in the present study, 71% of our population treated for advanced-stage HNSCCs referred swallowing problem as the predominant and most disabling treatment side effect, especially in oral cavity and oropharyngeal cancer. Dysphagia, therefore, represents an acute-and-late complication that greatly affects the quality of life of such patients, and it correlates significantly with voice problems, accordingly to our results of MDADI and VHI ($p < 0.01$) [Table 3]. For such reason, here, we have proposed a novel swallowing exercise protocol with the aim of reducing dysphagia claims and improving the QoL of these patients. Our results suggest that, if swallowing exercises are begun before the beginning of the exclusive/adjuvant RT treatment, they could significantly improve post-treatment swallowing ability and this can have a positive impact on their quality of life. Obviously, other studies are needed to gain a full understanding of the benefits of the preventive swallowing protocol and to strengthen the evidence on the field. In the future, we believe that further studies should introduce a more tailored swallowing rehabilitation protocol

diversified according to the type of dysphagia, because not all the exercises can actually fit the single patient's situation.

**Funding** None to declare.

## Compliance with Ethical Standards

**Conflict of interest** Each author has participated actively in designing and writing this article: Giuditta Mannelli is the main creator of the work and critically discussed the final manuscript. Ilaria Carmignani assisted in conception of the study, which gave her important help by providing patient questionnaires and subjecting patients in the study group to speech therapy sessions; Luca Giovanni Locatello assisted in data collection, manuscript preparation, discussion, and statistical analysis; Odile Le Saec helped with the speech therapy sessions; Isacco Desideri, Pierluigi Bonomo, Emanuela Olmetto, and Lorenzo Livi assisted in following patients during the radiotherapy treatment; Salvatore Coscarelli assisted in reviewing the manuscript and gave his final approval for this version of the manuscript.

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