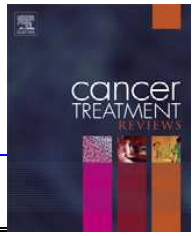

SWALLOWING DYSFUNCTION IN HEAD AND NECK CANCER PATIENTS TREATED BY RADIOTHERAPY: REVIEW AND RECOMMENDATIONS OF THE SUPPORTIVE TASK GROUP OF THE ITALIAN Association of Radiation Oncology

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a b s t r a c t

Purpose: Dysphagia is a debilitating complication in head and neck cancer patients (HNCPs) that may cause a high mortality rate for aspiration pneumonia. The aims of this paper were to summarize the normal swallowing mechanism focusing on its anatomo-physiology, to review the relevant literature in order to identify the main causes of dysphagia in HNCPs and to develop recommendations to be adopted for radiation oncology patients. The chemotherapy and surgery considerations on this topic were reported in recommendations only when they were supposed to increase the adverse effects of radiotherapy on dysphagia.

Materials and methods: The review of literature was focused on studies reporting dysphagia as a pretreatment evaluation and as cancer and cancer therapy related side-effects, respectively. Relevant literature through the primary literature search and by articles identified in references was considered. The members of the group discussed the results and elaborated recommendations according to the Oxford CRBM levels of evidence and recommendations. The recommendations were revised by external Radiation Oncology, Ear Nose and Throat (ENT), Medical Oncology and Speech Language Pathology (SLP) experts.

Results: Recommendations on pre-treatment assessment and on patients submitted to radiotherapy were given. The effects of concurrent therapies (i.e. surgery or chemotherapy) were taken into account.

Conclusions: In HNCPs treatment, disease control has to be considered in tandem with functional impact on swallowing function. SLPs should be included in a multidisciplinary approach to head and neck cancer.

(1) Dysphagia evaluation general recommendation	All patients need to be clinically evaluated for researching signs and symptoms that herald dysphagia. The evaluation of more than one item, as listed in ‘‘Murphy’s trigger symptoms’’ , is recommended (Recommendation D; level 4) (expert opinion based on bench research –neurological patients)
SLP	All patients at risk (based on Murphy’s trigger symptoms) should be referred for a detailed swallowing evaluation to an SLP as soon as possible (Recommendation D; levels 4–5) (expert opinion mainly based on bench research – neurological patients) in order to (1) identify swallowing abnormality, (2) develop a treatment plan when indicated, (3) recommend additional testing to assess aspiration risk
Dysphagia tests	Water tests, with or without oxygen desaturation, with or without cough test29 during swallowing (endpoint: desaturation of >2%), can be performed in order to select patients to be further investigated or treated for dysphagia (Recommendation D) (expert opinion based on bench research – neurologic finding)
FEES vs. VFS/MBS	Both FEES and VFS/MBS are effective in predicting aspiration pneumonia in patients with dysphagia (Recommendation B, level 2b). VFS/MBS permits a superior evaluation of propulsive mechanism (the coordination of all pharyngeal events), velopalatinae closure, the patency of the hypopharyngeal lumen, UOES function, and the distal level of the aspiration26 (Recommendation D; level 5) (expert opinion based on physiology). FEES permits the detection of laryngeal penetration, aspiration, swallowing residue, and pharyngeal pooling in HNCPs. It does not assess UOES, but it permits the sensory deficits in the laryngopharynx to be evaluated (Recommendation B; level 2)

	Even if FEES is less expensive than VFS,189 the choice of examination can be guided by its accessibility (level 5) if the two examinations can give an answer to the specific clinical question. (Recommendation D)
The findings of VFS can be scored with	OPSE (Recommendation B; level 2), Swallowing Performance Status Scale (SPS), (Recommendation C; level 4) and 8-point Penetration–Aspiration scale (Recommendation C; level 4)
QoL	In monitoring the QOL of dysphagic patients, both patient-rated and clinician-rated scales, could be used, considering the given complementary information. (Recommendation B; level 2)54
(2) Pre-treatment recommendations	The TDRS (see the Appendix) can be used in order to predict swallowing dysfunction. If the score is higher than 9, patients may benefit from strategies aiming at the prevention of swallowing dysfunction after curative (CH) RT such as preventative swallowing exercises during treatment and/or emerging IMRT techniques aiming at sparing DARS. (Recommendation B; level 2) At the present time there is no sufficient evidence to determine the optimal timing and method of enteral feeding for HNCPs receiving radiotherapy.129,130 Regardless of when a feeding tube is placed, post tube placement patients should be encouraged to continue to swallow and to wean off the feeding tube as quickly as is feasible26 (Recommendation D; level 5) (expert opinion based)

(3) Recommendations for radiation oncologists in treating postoperative patients	Before postoperative radiotherapy, dysphagia and aspiration signs or symptoms need to be evaluated. If they are present, SLP and swallowing strategies need to be considered (Recommendations C) (extrapolation from level 2 and 3 studies) Edentulous patients with dentures need to keep their dentures in place when eating. If these patients are used to eating without dentures they continue to eat without them. (Recommendation C; extrapolation form level 2). However, dentures and partial prostheses should be left out when oral mucositis is present to avoid trauma • Free and pedicled flap could be acting as an adynamic segment that impairs the swallowing driving force, reducing the swallowing efficiency (level 2 prospective) • Resection of oral tongue slows oral transit, worsening with more viscous bolus (levels 2–4); the resection of more than one half of the mobile tongue can cause serious swallowing disability (level 4) • People (especially older than 60 years) who had wide resection (>50%) of the tongue base might not have an oral diet at all68 (level 4) • While a rim or marginal resection of the mandible has little impact on swallowing function, mandibulotomy can cause damage to genioglossus musculature (as in sagittal mandibulotomy; level 3 case–control), inferior alveolar nerve (as in lateral mandibulotomy) and occlusion (level 5; expert opinion). Furthermore, segmental mandibular resection without reconstruction has a profound negative impact on swallowing function76,192 (level 4) • Surgical extirpation of palate and maxillary sinus leads to surgical

	defects in the hard palate with a large oronasal and oromaxillary communication. Thus, tongue movements are not able to drive the bolus gathered on the dorsal surface of the tongue because of deficient hard palate, so that material might enter the nose through the oronasal fistula during swallowing and may be aspirated after swallowing. Up to 2/3 of all patients submitted to free flap reconstruction are able to return to a normal diet (level 4) with a good swallowing QoL88 (level 4) • Soft palate tumour resection might result in incomplete closure of the nasopharynx with nasal regurgitation at the end of the oral phase. Defects involving the lateral aspect of the soft palate are more likely to result in(4) persistent dysphagia as they are much more difficult to obturate than midline defects (level 5) (level 4) • Dysphagia has been reported to range from 10% to 60% following total laryngectomy80 (level 4), mainly as a result of benign stricture, radiation-induced pseudo-epiglottis formation or PCM coordination loss63 (level 4) • Partial laryngectomy is less problematic than total laryngectomy in terms of dysphagia but aspiration and penetration might represent a serious sequel: patients able to achieve a good functional competence of the neoglottis (correct juxtaposition of tongue base and CAU) will be able to prevent aspiration92–94 (level 4) • Tracheostomy, employed as a short- or long-term solution for airway occlusion due to tumour or laryngeal oedema during chemoradiation, is not protective against aspiration in tracheostomised patients98

	(level 4) • The most common skull base surgical procedures may cause dysphagia due to injuries to the adjoining cranial nerves, but a temporary acute swallowing impairment might be caused by brainstem oedema or cranial nerve trauma. (level 4) • Usually TORS wounds heal by secondary intention without dysphagia69 (level 4)
(4) Recommendation for exclusive radiotherapy	Computed Tomography (CT)-based delineation guidelines for DARS are recommended in order to be able to compare the predictable patients' results with those of literature (Recommendation D; level 5) It is recommended that the volume of the PCM and larynx receiving >60 Gy and, when possible, the volume receiving >50 Gy be minimized. However, multimetric models (more than one parameter: e.g. Dmean, different DVHs) is advised. (Recommendation D; level 5) The medial retropharyngeal nodes, located near the midline and anterior to the prevertebral musculature, are only very rarely involved as metastatic sites and their exclusion from the elective target volume could considerably contribute to sparing the PCM120 (Recommendation B; level 3) However, avoiding under-dosing to the targets in the vicinity should remain the highest priority.(Recommendation D; level 5) Dose distributions through oral mucosa need to be kept under control, preventing, where possible, oral mucosa V9.5–V10 Gy/w exciding 50–60 cm3, anterior oral cavity V30 exciding 65% and anterior oral cavity V35 exciding

	35%. (Recommendation B; level 3)
(5) Recommendations for chemo radio-treated patients	Patients submitted to chemo-radiotherapy need to be monitored for aspiration, history of recurrent pneumonia, and pulmonary function tests both during therapy and during follow up. (Recommendation C; extrapolation from level 2 and 3) If pneumonia or sepsis is suspected the search for Systemic inflammatory Reaction Syndrome (SIRS) is recommended (Recommendation D; level 5) (expert opinion based on physiology and bench research)

Appendix

Raccomandazioni AIRO sulla valutazione e gestione della DISFAGIA

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Table 1 Murphy's trigger for dysphagia evaluation (Murphy and Gilbert 2009)

● Inability to control food, liquids, or saliva in the oral cavity
● Pocketing of food in cheek
● Excessive chewing
● Drooling
● Coughing, choking, or throat clearing before, during, or after swallowing
● Abnormal vocal quality after swallowing; “wet” or “gurgly” voice
● Build-up or congestion after a meal
● Complaint of difficulty swallowing
● Complaint of food “sticking” in throat
● Nasal regurgitation

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Water tests

Table 2 Patterson's test *(Hughes and Wiles 1996; Patterson et al. 2009)*

Validated on 167 head and neck cancer patients.

The patient was seated in an upright position.

- Tap water (100 mL) was measured into a plastic breaker. The patient was instructed to drink the water 'as quickly as is comfortably possible'.
- The amount of liquid swallowed was recorded. If the patient was unable to complete the task, the residual water was measured by syringe, using a minimum scale of 1 mL.
- The number of swallows taken was counted simultaneously by the researcher (by feeling the thyroid cartilage for laryngeal elevation). Timing started from when the water first touched the bottom lip to when the larynx came to rest after the last swallow (this was usually accompanied by other signals e.g. exhalation, phonation or opening of the mouth).

From these measurements, three swallowing performance parameters were calculated:

1. swallow volume (millilitres per swallow = mL swallowed divided by number of swallows taken)
   Normal median value per age:

Age	Head & neck cancer group	Control
35-55	25 ml	30 ml
56-74	20 ml	26 ml
75-88	15.5 ml	20 ml

2. swallow capacity (millilitres per second = mL swallowed divided by time taken)
   Normal mean value per age:

Age	Head & neck cancer group	Control
35-55	20.2 ml	24 ml
56-74	16.8 ml	18.7 ml
75-88	13.1 ml	14.6 ml

3. Swallow speed (time per swallow = time taken divided by number of swallows).

The baseline test can be used to monitor patient dysphagia during follow up.

Table 3 Modified water swallowing test (MWST) ***(Wakasugi et al. 2008)***

Patient is invited to swallow cold water (3 ml) placed on the floor then to swallow saliva. Placement on the floor of the mouth prevented premature spillage of test water into the pharynx.
The patient was then instructed to swallow.

Item	Score	Comment
Cold water (3 ml) was placed on the floor of the mouth using a 5-ml syringe		
• If the patient was unable to swallow	1	Dysphagia
• If the patient was able to swallow but experienced dyspnoea (difficulty breathing) after swallowing	2	
• If the patient was able to swallow and experienced coughing or wet-hoarseness after swallowing	3	Indicate "aspiration"
The patient was asked to perform two dry (saliva) swallows.		
• If the patient was able to swallow the water but unable to perform either of the two dry swallows	4	Normal
• If the patient was able to complete the water and both dry swallows	5	

The entire procedure was repeated twice more and the final score was defined as the lowest score on any trial.

Table 4 - Recommendation of Larynx Preservation Consensus Panel: "Swallowing and voice evaluations modified barium Swallowing (from Lefebvre and Ang Int. J. Radiat Oncol 2009) (see also (Martin-Harris and Jones 2008)

1. Studies are performed using standard radiographic systems with video fluoroscopic capabilities and the image is stored on digital videodisc (DVD).
2. A video counter imprints a time code (accurate to 0.001 s) on the DVD.
3. Video fluoroscopic imaging is completed in the lateral and anterior–posterior (AP) planes.
4. The fluoroscopic camera is focused on the patient's lips anteriorly, the posterior pharyngeal wall posteriorly, the hard palate superiorly, and the upper oesophageal segment inferiorly.
5. Fluoroscopy continues for 3 s after each swallow to allow observation of penetration or aspiration after the swallow and the patient's reaction to it.
6. The order of bolus presentation is as follows:
a. two 5-ml Varibar thin liquid boluses, b. two 10-ml Varibar thin liquid boluses, c. two 20-ml Varibar thin liquid boluses, d. two cup sips of Varibar thin liquid, e. two pureed/Varibar pudding boluses, f. two solid boluses consisting of one fourth of a shortbread cookie or cracker coated with Varibar pudding, and two trials of the most difficult consistency in the A-P plane.

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Table 5 Main parameters of VFSS - MBS (Rademaker et al. 1994)

Acronyms	Index	Definition
OTT :	Oral transit time	the time it takes the bolus to move through the oral cavity, measured from the first backward movement of the bolus until the head of the bolus passes the point where the ramus of the mandible crosses the tongue base. (usually < 1 s.)
PTT:	Pharyngeal Transit Time	the time required for the bolus to move through the pharynx, measured from the time the head of the bolus passes the ramus of the mandible until the tail of the bolus leaves cricopharyngeal region (usually < 1 s.)
DLC :	Duration of Laryngeal closure	The length of time the laryngeal between the arytenoid and base of epiglottis is closed during swallow
PDT:	Pharyngeal Delay time	the time required to trigger the pharyngeal swallow, measured from the time the head of the bolus passes the ramus of the mandible until the onset of laryngeal elevation
DCO:	Duration of cricopharyngeal opening	the length of time the cricopharyngeal region is open during the swallow
O.RES	Oral Residue:	Approximate percent oral residue after first swallow on a bolus
P.RES:	Pharyngeal Residue	Approximate percent pharyngeal residue after first swallow on a bolus
ASP:	Percentage of Aspirated bolus	Approximate percent aspirated
OPSE	Oropharyngeal Swallow Efficiency	is defined as the percentage of the bolus swallowed divided by the bolus transit time, from the oral cavity through the cricopharyngeus: [100-(PRES+ ORES+ ASP)]/(OTT+PTT). In the calculation of OPSE, the amount aspirated and the amount left unswallowed in the mouth or pharynx is subtracted from the percentage swallowed.

Table 6 The Swallowing Performance Status Scale (SPS) (Karnell and E. MacCracken 1994; Stenson et al. 2000)

Score	Description
1	Normal
2	Within functional limits: abnormal oral or pharyngeal stage; able to eat regular diet without modifications or swallowing precautions
3	Mild impairment: mild dysfunction in oral or pharyngeal stage; requires modified diet without need for therapeutic swallowing precautions
4	Mild-moderate impairment with need for therapeutic precautions: mild dysfunction in oral and pharyngeal stage; requires modified diet and therapeutic precautions to minimize aspiration risk
5	Moderate impairment: moderate dysfunction in oral or pharyngeal stage: aspiration noted on examination; requires modified diet and swallowing precautions to minimize risk of aspiration
6	Moderate-severe dysfunction and requires supplemental enteral feeding support: moderate dysfunction in oral or pharyngeal stage, aspiration noted on examination; requires modified diet and swallowing precautions to minimize risk of aspiration: needs supplemental feeding support
7	Severe impairment: severe dysfunction with significant aspiration or inadequate oropharyngeal transit to esophagus; requires primary enteral feeding support

Table 7 Penetration- Aspiration Scale (8-point interval scale)(Rosenbek et al. 1996)

1. Material does not enter the airway
2. Material enters the airway, remains above the vocal folds, and is ejected from the airway
3. Material enters the airway, remains above the vocal folds, and is not ejected from the airway
4. Material enters the airway, contacts the vocal folds, and is ejected from the airway
5. Material enters the airway, contacts the vocal folds, and is not ejected from the airway
6. Material enters the airway, passes below the vocal folds and is ejected into the larynx or out of the airway
7. Material enters the airway, passes below the vocal folds, and is not ejected from the trachea despite effort
8. Material enters the airway, passes below the vocal folds, and no effort is made to eject

Table 8 Total Dysphagia Risk Score- Predictive model for swallowing dysfunction after curative Radiotherapy((Langendijk et al. 2009))

Independent Predictive factors	β	Risk points (β*5)	Risk category	Total Dysphagia Risk Score (TDRS)	NTCP (Grade >2 swallowing dysfunction RTOG/EORTC)
T-classification (T3 or T4)	0.868	4	Low Risk	0-9	<10%
Weight loss Baseline 1-10%	1.053	5			
Concomitant chemoradiation	0.975	5	Intermediate Risk	10-18	10-30%
Accelerated radiotherapy	1.170	6			
Weight loss Baseline >10%	1.324	7	High risk	>18	>30%
Primary tumour site: Oropharynx	1.376	7			
Bilateral neck irradiation	1.715	9			
Primary tumour site: Nasopharynx	1.816	9			

Raccomandazioni AIRO sulla valutazione e gestione della DISFAGIA

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Table 9 QUANTEC Summary: Approximate Dose/Volume/Outcome Data for Main DARS Following Conventional Fractionation (From (Marks et al. 2010)

Organ	Volume segmented	Irradiation type (partial organ unless otherwise stated)†	Endpoint	Dose (Gy), or dose/volume parameters†	Rate (%)	Notes on dose/volume parameters
Pharynx	Pharyngeal constrictors	Whole organ	Symptomatic dysphagia and aspiration	Mean dose <50	<20	Based on Section B4 in paper
Larynx	Whole organ	3D-CRT	Vocal dysfunction	Dmax <66	<20	With chemotherapy, based on single study (see Section A4.2 in paper)
	Whole organ	3D-CRT	Aspiration	Mean dose <50	<30	With chemotherapy, based on single study (see Fig. 1 in paper)
	Whole organ	3D-CRT	Edema	Mean dose <44	<20	Without chemotherapy, based on single study in patients without larynx cancer**
	Whole organ	3D-CRT	Edema	V50 <27%	<20	
Parotid	Bilateral whole parotid glands	3D-CRT	Long term parotid salivary function reduced to <25% of pre-RT level	Mean dose <25	<20	For combined parotid glands¶
	Unilateral whole parotid gland	3D-CRT	Long term parotid salivary function reduced to <25% of pre-RT level	Mean dose <20	<20	For single parotid gland. At least one parotid gland spared to <20 Gy¶
	Bilateral whole parotid glands	3D-CRT	Long term parotid salivary function reduced to <25% of pre-RT level	Mean dose <39	<50	For combined parotid glands (per Fig. 3 in paper) ¶

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Table 10 The Netherlands guideline for contouring DARS(Christianen et al. 2011)

Netherlands guideline	Pharyngeal constrictor muscles			Cricopharyngeus	Oesophagus inlet muscle (EIM)	Cervical oesophagus CE	Base of tongue	Larynx	
	Superior PCM (fig 1 a)	Middle PCM (fig 1 b)	Inferior (fig 1 c)	Fig 1 f	Fig 1 h		Fig 1b	Supraglottic Fig. 1 e	Glottic Fig. 1f
Cranial	Caudal tip of the pterygoid plates (hamulus)	Upper edge of C3	First slice caudal to the lower edge of hyoid bone	First slice caudal to the arytenoid cartilages	First slice caudal to lower edge of the cricoid cartilage	1 cm caudal to the lower edge of the cricoid cartilage	Lower edge of anterior tubercle of atlas	Tip of epiglottis	Upper edge of the arythenoid cartilages
Caudal	Lower edge of C2	Lower edge of hyoid bone	Lower edge of the arytenoid cartilages	Lower edge of the cricoid cartilages	1 cm caudal to the superior border	Sternal notch	Upper edge of hyoid bone	First slice cranial to the upper edge of the arytenoid cartilages	Lower edge of cricoid cartilage (if soft tissue is present)
Anterior	Hamulus of pterygoid plate; mandible; base of tongue; pharyngeal lumen	Base of tongue; hyoid	Soft tissue of supraglottic/ glottic larynx	Posterior edge of cricoid cartilage	Tracheal lumen		Posterior one third from mandibular bone to pharyngeal lumen	Hyoid bone, pre-epiglottic space, thyroid cartilage	Thyroid cartilage
Posterior	Prevertebral muscle	Prevertebral muscle	Prevertebral muscle	Prevertebral muscle	Prevertebral muscle		Pharyngeal lumen	Pharyngeal lumen, inferior PCM	Inferior PCM, pharyngeal lumen/ cricoid cartilage
Lateral	Medial pterygoid muscle	Greater horn of hyoid bone	Superior horn of thyroid cartilage	Thyroid cartilage, fatty tissue, thyroid gland	Fatty tissue, thyroid gland		Width of the pharyngeal lumen	Thyroid cartilage	Thyroid cartilage
Medial	Pharyngeal lumen	Pharyngeal lumen						Pharyngeal Lumen (lumen excluded)	Pharyngeal Lumen (lumen excluded)