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General and Supportive Care

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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ABSTRACT

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 pre-treatment 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.

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Introduction

At the time of diagnosis, up to 2/3 of Head and Neck Cancer Patients (HNCPs) present with dysphagia.[1] Approximately, one third of dysphagic patients develop aspiration pneumonia requiring treatment, with mortality rates ranging between 20% and 65%.[1] Recent studies have shown pre-treatment deficits to be common in advanced stage HNCPs, pointing to a poor correlation between measurable deficits and patients' deficit perception.[2–4] Thus, considering the elevated risk of silent dysphagia/aspiration in this clinical scenario, swallowing function assessment is essential prior to oncologic therapy.[4,5] Pre-treatment aspiration risk determination might be helpful in ensuring optimal intervention by the speech language pathologist (SLP) through application of compensatory manoeuvres, dietary modifications, and rehabilitative interventions. Adjunctively, an appropriate up front evaluation of organ function might drive therapeutic strategies in order to maximize overall organ function and quality of life (QoL) in a post-treatment setting. In recent years, treatment intensification for advanced HNCPs, employing altered fractionated radiotherapy (RT) and/or concomitant chemotherapy (CT), possibly associated with surgery, significantly improved loco-regional control and overall survival.[6–8] However, it supposedly increased toxicity rates with possible detrimental effects on prognosis unless adequate supportive care is administered.[6,9] For instance, dysphagia and oropharyngeal mucositis represent the main obstacles for further treatment intensification and might affect the general dimensions of QoL, even more than radiation-induced xerostomia.[10–13]

The aim of the present work is to provide a detailed overview of the normal swallowing mechanism focusing on anatomical and physiological issues, to review the relevant literature concerning dysphagia mechanisms and causes in HNCPs and to settle clinical recommendations to be adopted in daily clinical practice in HNCPs undergoing RT. The CT and surgical items on dysphagia are reported in the recommendation section only if affecting the aftermath of RT on this clinical issue.

Materials and methods

In July 2011, a comprehensive literature review regarding dysphagia was performed by the supportive care task force within the Head and Neck Group of the Italian Association of Radiation Oncology (AIRO). The electronic databases used were PubMed, The Cochrane Library, Scopus and Embase. The search was time limited from January 1990 to June 2011, with the following keywords: dysphagia, aspiration, swallowing dysfunction, head and neck cancer (HNC), chemo-radiotherapy, deglutition disorders, postoperative radiotherapy. The electronic search results were supplemented by manual examination of reference lists from selected articles and expert consensus meeting notes. The investigation focused on dysphagia in terms of pre-treatment evaluation and the relationship to the tumour itself and/or cancer therapy. Manuscripts were categorized according to three main groups, namely dysphagia assessment and pre- and post-treatment dysphagia in HNCPs. The members of the group discussed the results and elaborated recommendations according to the Oxford CRBM suggestions.[14] The recommendations were revised by external radiation oncologists (J.B. and G.S.), ENT surgeons (F.C.), medical oncologist (M.C.M.) and SLP (V.Z) experts.

Normal swallowing mechanism

The swallowing process can be visualized as a hydrodynamic system in which the bolus of food is transferred through a series of in-line chambers separated by valves (i.e. sphincters)[4]: oral, pharyngeal, and oesophageal chambers (Table 1).

The swallowing process is appropriately coordinated by the main nervous centres set in the cortex[15] and the medulla. Motor impulses activate about 30 pairs of muscles[16] involved in swallowing. The motor fibres pass through V, VII, IX–XII and C1–C3,[17] whereas the mouth and oropharynx sensation pass through V, VII, IX and X cranial nerves (Fig. 1). The dysphagia/aspiration-related structures (DARS) are identified as pharyngeal constrictor muscles (PCMs), the upper oesophageal sphincter (UOES) with the cricopharyngeal muscle and the oesophagus inlet muscle (OEIM), the tongue base, the larynx with vocal cords and arytenoids, velopharyngeal structures, and the posterior pharyngeal wall[18] (Fig. 2). The upper aerodigestive integrity[19–21] is important also for swallowing (Table 1).

An average adult swallows about 35 times per hour while awake and 6 times per hour while asleep.[22]

A "functional swallow" implies no aspiration and minimal residue[23] while a pathologic one is characterized by penetration (bolus entering laryngeal vestibule without passing vocal folds) or aspiration (bolus entering subglottic region). Normally, pathologic swallowing is defined in terms of the amount and incidence of penetration and aspiration[24] and is associated with an increased risk of aspiration pneumonia or airway obstruction.[25]

Aspiration may happen before, during and after swallowing process[26] and may be "silent" (aspiration in the absence of visible response) when laryngeal sensitivity (response to penetration/aspiration) is compromised.

Dysphagia assessment

Assessment of dysphagia includes clinical, instrumental and subjective (QoL impact) evaluations.

Clinical evaluation

The evaluation of "Trigger symptoms" (Table 2) heralding dysphagia is recommended[26] during the first examination by the HNC specialist or trained nurse. In the presence of these symptoms the intervention of an SLP is recommended (level 5 bench search referred to neurologic patients)[26–28] in order (a) to identify swallowing abnormalities, (b) to develop a treatment strategy if indicated, and finally (c) to recommend additional testing to assess aspiration risk.[26]

Several screening tests for silent aspiration and dysphagia derives from neurologic literature[29–37] (Table 3). They employ the cough test (number of coughs during inhalation of a mixture of citric acid-physiologic saline for 1 min with nebulizer), water[32–34] or different viscosity tests (evaluation of swallowing of various aliquots of liquids or semi liquids placed within the mouth)[31,35] with or without oxygen desaturation during swallowing (endpoint: desaturation of >2% compared to baseline).[33,34,36] Although pulse oximetry for screening has been criticized by some authors,[37] it has also been shown to be able to detect silent aspiration,[33,34] which cannot be detected by a swallow test alone. Reports on HNC literature are rare, which weakens the strength of the evidence (level 5: expert opinion based on bench research[14]) of these screening tests.

Objective instrumental evaluation

The most common procedures to evaluate swallowing safety and efficiency from a quantitative and qualitative perspective in HNCPs are video-endoscopy, also known as flexible endoscopic evaluation of swallowing (FEES), and video-fluoroscopy (VFS), also

Table 1
Normal swallow phases.[151]

Oral preparatory phase	Oral chamber[4]	Anatomy[151] (cranial nerve)	Specific function
• Teeth, lips, cheeks, tongue, mandible, and palate grind and manipulate food • Food mixed with saliva • Formation of a bolus consistency appropriate for safe swallow Oral propulsive or transport stage • Lips and cheeks contract • Tongue presses the bolus against the hard palate and soft palate elevates • Bolus is moved backwards by the tongue • A central groove is formed in the tongue for passage of bolus • Bolus is moved to the tonsillar pillars, thus initiating the oral phase of swallowing • The soft palate moves superior and posterior to close off nasopharynx • Piston-like action of tongue to propel food posteriorly • Contraction of mylohyoid muscle causes this movement	Entrance valve	Lips and orbicularis oris (VII)	Seal lips/mouth
	Floor	Intrinsic tongue: longitudinal sup and inf, transversis and vertical (XII)	Bolus preparation, formation, transport
		Extrinsic tongue: Hyoglossus (XII)	Down-retraction of the tongue
		Genioglossus (XII)	Protrude/retract tongue
		Styloglossus(XII)	Raise/retract tongue
		Suprahyoid muscles: Mylohyoid (V3)	Raise/stabilize hyoid, tongue, mouth floor
		Geniohyoid (XII)	Protract/stabilize hyoid
		Anterior (V3) posterior belly digastric (VII)	Raise stabilize hyoid and lower mandible
	Lateral wall	Buccinator (VII)	Push food towards teeth
		Dentition (V2–V3)	Mastication
	Roof	Tensor veli palatinae (V3)	Tense soft palate
		Levator veli palatine (X pharyngeal plexus)	Raise soft palate to seal nasopharynx
		Palatoglossus (X pharyngeal plexus)	Sphincter that seals oral cavity from oropharynx
		Uvular (X pharyngeal plexus)	Brace soft palate
	Exit valve	Base of tongue	Seal oral cavity and push food in oropharynx
		Palatoglossus (X) pharyngeal plexus	Sphincter sealing oral cavity from oropharynx
		Styloglossus (XII)	Raise and retract tongue helping to seal oral cavity
		Palatopharyngeus (X pharyngeal plexus)	Raise pharynx and larynx and lower palate sealing oral cavity
	Supportive structures	Salivary glands: submandibular and sublingual VII; parotid (IX)	Salivation
		Mandibula, teeth and dentures[84]	Stabilize mandible to permit suprahyoid muscles action[84]
		Omohyoid (C1–C2 ansa cervicalis) Sternohyoid (C1–C2) Sternohyoid (C1–C2)	Infrahyoid muscles are activated in oral phase and inhibited (but thyrohyoid) during deglutition
Oropharyngeal phase[26]	**Pharyngeal chamber[4]**	**Anatomy[151] (cranial nerve)**	**Specific function**
• Retroversion of the epiglottis over the laryngeal vestibule • Closure of the larynx to the level of the false and true vocal cords • The larynx is pulled up and forward by pharynx longitudinal muscles and pavement of mouth's muscles • Contraction of the PCM • Relaxation of the cricopharyngeal muscles • Opening of the cricopharyngeal sphincter by upward and forward movement of the larynx • Time: duration approximately 1 s)	Entrance valve	The apposition of the base of the tongue to the velum and palatuspharyngeus muscles	See exit valve of oral chamber
	Laryngeal Valves	Epiglottic swinging	Epiglottis swings down to cover laryngeal vestibule
		Thyroepiglottic (recurrent X)	Approach epiglottis to arytenoids
		Supraglottic adductors Ary-epiglottic muscles in folds (recurrent X)	In continuity with ary-epiglottic m. helps to approach arytenoids to epiglottis and adduct vocal cord
		Oblique arytenoids (recurrent X)	
		Glottic adductor muscles Transverse arytenoid (recurrent X) Thyroarytenoid (recurrent X) Lateral cricoarytenoid (recurrent X)	Adduct vocal cord
		Posterior cricoarytenoid (recurrent X)	Open vocal folds
	Rhino-pharyngeal valve	Tensor veli palatine (V3)	Tense soft palate
		Levator veli palatine (XI pharyngeal plexus)	Raise soft palate to seal nasopharynx
		Superior PCM (X vagus via pharyngeal plexus)	Narrows rhino-pharyngeal volume sealing it
	Pharyngeal wall	Longitudinal group of muscles:	Elevates and shortens pharynx
		Palatopharingeus (X vagus via pharyngeal plexus) Salpingopharingeus (X vagus via pharyngeal plexus) Stylopharingeus (innervated by IX glossopharyngeus)	Raise larynx, shorten pharynx (Stylopharyngeus also widen pharynx)
		Stylohyoid (VII)	It is not strictly part of wall (se supportive structure)
		Circular group of muscles: Superior PCM (X vagus via pharyngeal plexus) Middle PCM (X vagus via pharyngeal plexus) Inferior PCM (X vagus via pharyngeal plexus recurrent and laryngeal nerves)	Peristalsis and bolus transport

(continued on next page)

Table 1 (*continued*)

Oropharyngeal phase[26]	Pharyngeal chamber[4]	Anatomy[151] (cranial nerve)	Specific function
	Exit valve	Cricopharyngeal sphincter (X)	
	Supportive structures	Mylohyoid (V3) Anterior (V3) Posterior belly digastric (VII) Geniohyoid (XII) Thyrohyoid (XII)	Raise and move forward larynx bringing the larynx to a position under the base of the tongue
		Omohyoid (C1–C2 ansa cervicalis) Sternohyoid (C1–C2) Sternohyoid (C1–C2)	Infrahyoid m. are activated in oral phase and inhibited (but thyrohyoid) during deglutition
		Hyoid bone Stylohyoid (VII)	The hyoid has mechanical connections to the cranial base, mandible, sternum, and thyroid cartilage via the suprahyoid and infrahyoid muscles. With those muscle connections, the hyoid plays an important role in controlling the movements of the jaw and tongue
Oesophageal phase[26]	**Oesophageal chamber[4]**	**Anatomy[151] (cranial nerve)**	**Specific function**
• Peristaltic contractions of musculature results in movement of the bolus into the stomach • Time: (duration approximately 3–4 s)	Entrance valveUOES	Inferior PCM (X vagus via pharyngeal plexus recurrent and laryngeal n.) Cricopharyngeal sphincter Oesophagus inlet muscle (OEIM)[132] Suprahyoid muscles and thyrohyoid muscles	Three important factors contribute to the UOES opening: (1) Relaxation of the cricopharyngeus muscle; this relaxation normally precedes opening of the UOES or arrival of the bolus (2) Contraction of the suprahyoid muscles and thyrohyoid muscles. These muscles pull the hyo-laryngeal complex forward, opening the sphincter (3) The pressure of the descending bolus

known as modified barium swallowing (MBS). Both procedures seem to be equivalent in predicting pneumonia outcomes.[38]

Flexible endoscopic evaluation of swallowing

FEES visualizes the pharynx from above by placing an endoscopic tube trans-nasally so that the extremity of the tube hangs over the end of the soft palate. During this examination, the patient is given trials of coloured liquid, semisolid and solid bolus under direct fiberoptic observation.[39] This procedure gives a different view of the pharynx compared to VFS but does not provide information on the oral stages of swallowing. However, it allows for the evaluation of the pharyngeal function, vocal cord dysfunction, intraluminal structural and mucosal abnormalities,[40] possible aspiration, laryngeal penetration, and pooling of secretions. Some authors suggest the addition of sensory tests to FEES.[39,41]

Video-fluoroscopy

VFS allows bolus transit abnormalities to be identified, intra- and extra-luminal structural abnormalities to be detected, abnormal tongue and hyoid–laryngeal motion to be assessed and reduced UOES opening to be identified. It is possible to calibrate VFS by giving the patients different viscosities and volumes of food. The bolus transit time, the quantity and the duration of each physiologic event may be measured and compared with normative data.[42] A standardized protocol for performing a VFS is recommended by the "Larynx preservation consensus panel".[43] Among the main VFS parameters (Table 4)[3,44] the Oropharyngeal Swallow Efficiency (OPSE) is considered a global measure[19,43,44] that describes the interaction of bolus velocity, the safety and efficiency of the mechanism in clearing material from the oropharynx. The OPSE scores typically range from 100 to 140 in normal subjects (meaning that 100% of the bolus is swallowed in 1 s). In HNCPs, OPSE can drop to <50 or even $\leqslant$40, as the percentage of bolus swallowed reduces and the time increases.

The findings of VFS can also be scored with both the "Swallowing Performance Status Scale" (SPS)[45,46] and the "8-point Penetration–Aspiration Scale" (8p-PAS).[47] The SPS provides an accurate assessment of the presence and severity of dysphagia and aspiration risk, while 8p-PAS focuses on penetration and aspiration: a penetration-aspiration score >6 is considered suggestive for aspiration.

Subjective evaluation (QoL)

It is noteworthy that QoL is not usually part of clinical evaluation.[27] In fact, this is a complex and somehow aspecific concept that essentially represents an individual's sense of well-being, fulfilment, or satisfaction with his own life. The evaluation of the "meaningfulness" of a person's life differs from the evaluation of health function. Therefore, this evaluation needs to be described by the individual himself. Indeed, QoL reflects the "gap" between an individual's performance status and the performance status he desires.

Several clinician- and/or patient-rated scales (Table 5) have been developed to assess subjective dysphagia and its impact on QoL. Their subjectivity has created some discrepancy in the literature in terms of correlation between subjective and objective evaluation.[2,48–50] Numerous studies revealed that swallowing dysfunction may impact on the general dimensions of QoL,[12,51,52] even more than radiation-induced xerostomia,[13] but Teguh et al.[53] found a strong correlation between xerostomia and dysphagia-related QoL.

Recently, Christianen et al.[54] in a multicentric prospective cohort study to identify the most important factors to predict radiation-induced dysfunction after CT-RT found that clinician-rated and patient-rated dysphagic endpoints were influenced by different swallowing dysfunction. The authors justified these results by arguing the fact that each objective or subjective issue might be caused by the damage to different specific swallowing structures. Thus, the two perspectives – clinician-rated and patient-rated – are complementary and should be equally reported.[55]

Dysphagia in pre-treatment HNCPs

Dysphagia can pre-exist therapy and can be caused by:

- bulky or infiltrating or ulcerating lesions that disrupt the swallowing structures[3,56] or V or VII or IX–XII cranial nerves;
- damage of laryngeal sphincters due to tumours invading the Suprahyoid muscles, the pre-epiglottic space, or the prevertebral fascia (these clinical situations may inhibit the normal elevation and anterior excursion of the laryngotracheal complex)[4,45,57];
- pain.[56]

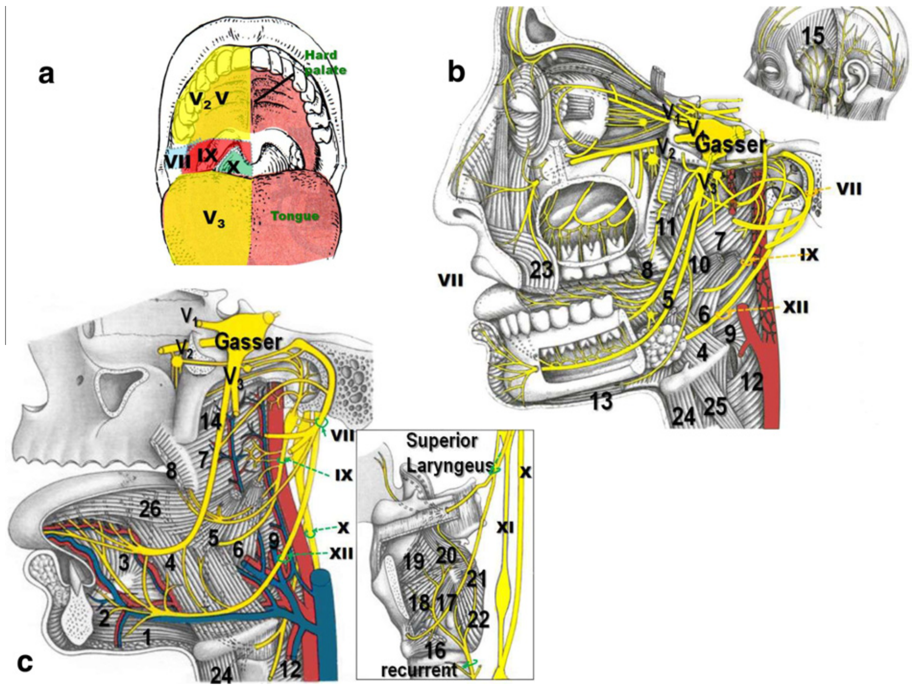

Fig. 1. Sensorial and motorial cranial nerves with main swallowing muscles. (a) Sensory innervations of mouth and oropharynx; (b) innervations of mandible (in the particular temporal muscles); (c) innervations of tongue and mouth (in the particular larynx). V: trigeminal nerve with trigeminal ganglion (Gasser) and its branches; V1: ophthalmic n.; V2: maxillary nerve and V3 mandibular nerve; VII: facial nerve; IX: glossopharyngeal nerve; XII; hypoglossal nerve. In the above frame a particular of the superficial temporal branches of trigeminal nerve (V2). V3: temporalis (15), masseter*, medial (10) and lateral (11) pterygoid; anterior belly digastric (13), mylohyoid (1), tensor veli palatini (14); VII: buccinators (8), orbicularis orbis (23); IX: stylopharyngeus (6), stylohyoid*; X and XI: via pharyngeal plexus: levator veli palatinae*, palatoglossus*, uvular*, palatopharyngeus*, salpingopharyngeus*, superior (7), middle (9) and inferior (12) PCM; via recurrent nerve: thyroarytenoid (18), transverse (21), oblique arytenoid (21), lateral cricoarytenoid (17), posterior cricoarytenoid (22), ary-epiglottic (20), thyroepiglottic (19), inferior PCM; via superior laryngeals nerve: cricothyroid (16); XII: intrinsic tongue (superior (26) and inferior longitudinal*, transverse* and verticalis*) extrinsic tongue: hyoglossus (4), genioglossus (3), styloglossus (5); suprahyoid muscles: geniohyoid (1); C1–C2: infrahyoid muscles (sternohyoid 24; omohyoid 25). *, not shown in the figure.

Swallowing problems at diagnosis are significantly correlated with the presence of late dysphagia.[57]

Pre-treatment dysphagia with silent aspiration is present in 14[24]–18%[2] of HNCPs (Table 6). Recently, Langendijk et al.[58] prospectively studied 529 HNCPs treated with curative RT, either alone or in combination with CT and surgery. The authors identified five independent prognostic factors predicting G2–G4 swallowing dysfunction (RTOG/EORTC) at 6 months after treatment ($\mathrm{SWALL}_{6\,\mathrm{months}}$): i.e. advanced T stage (T3–T4), oropharyngeal and nasopharyngeal tumour site, primary and bilateral neck irradiation, weight loss at baseline, and treatment modality (accelerated RT or concomitant CT-RT). They calculated the Total Dysphagia Risk Score (TDRS) to predict $\mathrm{SWALL}_{6\,\mathrm{months}}$ by using regression coefficients derived from the multivariate model adopted in the study. The TDRS was validated in clinical studies.[58,59] However, the same authors[54] evaluated these five predictive factors together with the dose to DARS in a subsequent study; they found that the dose to DARS hid the predictivity of the other five factors. The authors attributed these results to the fact that probably the predictivity of the five prognostic factors could be related to the high mean dose to DARS that they implied.

Dysphagia after specific therapies: surgery, radio-(chemo)-therapy

Dysphagia after surgery alone

Surgical interventions on HNCPs might cause specific anatomic or neurologic damage conditioning site-specific patterns of dysphagia and aspiration.

Oral and oropharyngeal surgery

Mouth floor resection has an impact on swallowing function when resection involves the geniohyoid or mylohyoid muscles.[60] These muscles are important for the elevation and anteropulsion of the larynx. The swallowing deficits can also vary according to the type of reconstruction[61,62]: i.e. primary closure/secondary intention, split-thickness skin grafts, local (tongue, pharyngeal and palatal) or regional (e.g. pectoralis major, latissimus dorsi, trapezius, etc.) flaps, free microvascular flaps (fasciocutaneous forearm, lateral thigh, lateral arm, and scapular), and prosthetics.

McConnel et al.[62] in a multicentre prospective study compared (with case control matching) the swallowing function before and after oral/oropharyngeal surgery in patients treated with primary closure, distal myocutaneous flap and microvascular free flap reconstruction: primary closure led to less pharyngeal residue than free flaps and distal flap, while free flaps had less residue than distal flap. The authors concluded that the oropharyngeal swallowing mechanism could be conceptualized as a pump, with the tongue being the piston and the pharynx being the dynamic chamber. In this model, free and pedicled flap could be acting as an adynamic segment that impairs the swallowing driving force, reducing swallowing efficiency (level 2 prospective).[62]

Oral tongue resection slows oral transit, which is worsened with more viscous bolus.[63,64] The probability of aspiration increases as the percentage of resected tongue increases (Table 7). In small resections of the oral tongue (<30%) and of the tongue base (<15[65]–60%[66]), primary defect closure gives equal or better functional results than flap reconstruction.[67] However, Kimata et al.[68] suggest that wider and thicker flaps (i.e. rectus abdominis musculo-cutaneous flaps) should be used for a good functional tongue reconstruction.

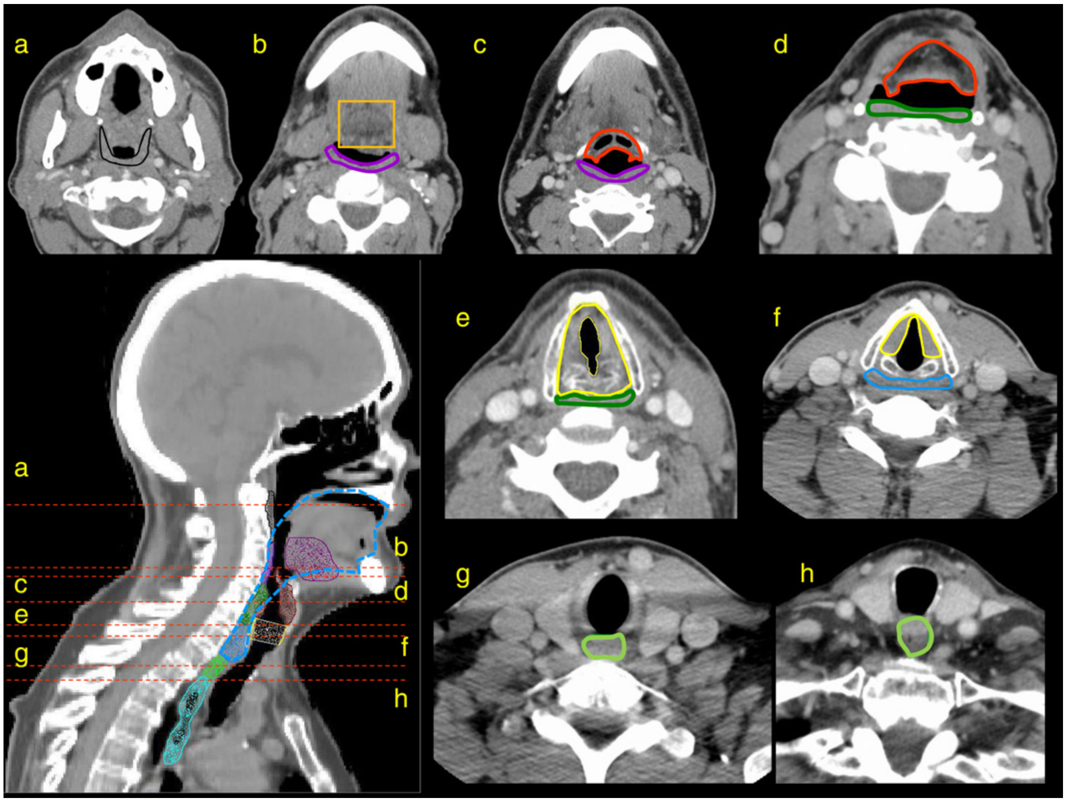

Fig. 2. CT images reproducing DARS delineation according to Groningen University recommendations[18] and upper aerodigestive tract mucosa.[20] DARS delineation. Superior pharyngeal constrictor muscle (black); middle pharyngeal constrictor muscle (violet); inferior pharyngeal constrictor muscle (thyropharyngeal part) (dark green); cricopharyngeus (blue); oesophagus inlet muscle OEIM (green); cervical oesophagus (COE) (light blue); base of tongue (orange) and supraglottic (red) and glottic larynx (yellow). Upper aerodigestive tract mucosa (dotted light blue). The level of each CT-slice is dotted on digitally reconstructed image. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 2
Triggers for dysphagia evaluation.[26]

Inability to control food liquids or saliva within 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
Weight loss

In recent years, transoral laser microsurgery has been introduced in clinical practice.[69,70] The robot application to this approach, used to control endoscopic instruments during surgical procedures, has been implemented to extend transoral robotic surgery (TORS) to various HNCP sites.[71,72] This strategy allows for the transformation of open surgical management to transoral minimally invasive surgery, limiting DARS damage. Presently, wounds are left to heal by secondary intention. This is an advantage for saving the swallowing process, but limits TORS adoption in larger resections. However, preclinical investigation and case-reports, using free-flap reconstruction of the TORS defects, have only recently been reported in literature.[73,74]

Mandibular resection: some tumours may infiltrate the alveolar ridge and mandible, requiring resection. A rim or marginal resection of the mandible will not disrupt the continuity of the mandibular arch and has little impact on swallowing function.[75]

Mandibulotomy can cause damage to genioglossus muscles (as in sagittal mandibulotomy[77,84]), the inferior alveolar nerve (as in lateral mandibulotomy) and occlusion. The loss of occlusion causes dysphagia because of loss of stability during deglutition and loss of correct larynx elevator muscle action.[75] Thus, in the case of mandibulectomy the reconstruction of the mandible at the time of initial surgical resection[76] is recommended in patients with large mandibular defects (i.e. larger than 5 cm), in patients undergoing mandibular resection for malignancy in which there is an associated large soft tissue deficit, and in patients for whom RT is planned.[76–82]

Teeth and dentures are important[75] for jaw stabilization by occlusion of the posterior teeth or dental prosthetics. Indeed, suprahyoid musculatures pivoting on the immobilized mandible can pull forward the larynx and permit the tongue base to cover it.[83] In a case–control study,[84] edentulous older people with dentures were asked to swallow a 10-mL barium sulphate solution three times both with and without dentures. In this study, the functional swallowing was recorded on cine-film. The occurrence of laryngeal penetration was nearly three times more likely ($P < .05$) for patients swallowing without dentures. Probably the swallowing process becomes anti-ergonomic with no dentures and without a sufficient time to develop compensation mechanisms. However, no participants exhibited aspiration. Yet, patients with laryngeal penetration are approximately four times ($P = .0008$) more likely to develop pneumonia than patients with normal swallowing.[1] Thus edentulous patients with dentures need to keep them in place when eating. If these patients are used to eating without dentures they should continue to eat without them. However, dentures and partial prostheses should be left out when oral mucositis is present to avoid trauma.

Table 3
Diagnostic performance of the screening methods to detect dysphagia.

Bedside test	Endpoint of index text	Endpoint of reference test	Sensitivity (%)	Specificity (%)
Trial swallowing using water test[32–34]	Coughing, choking or voice change, wet voice	Aspiration and penetration	47–85	63–88
Trial swallow using different viscosity[31,35]	Cough and throat clear	Aspiration	78	58
	Gurgly voice		41	76
	Wet voice		50	63
	Reduced laryngeal elevation		66	57
	Multiple swallows		58	57
	Spontaneous cough		68	82
	Subjective estimate of aspiration[32]		78[35]–88[32]	63[35]–30[32]
Oxygen desaturation[33,34,36]	>2% desaturation	Aspiration (or penetration[33,152])	56–87	39–97
Swallow test combining water test with oxygen desaturation[33,34]	Coughing, voice change or >2% desaturation	Aspiration (or penetration)	94 and 98	63–70
Combination of clinical conditions[35]	Spontaneous cough, subjective estimate of aspiration, wet voice	Aspiration	91	47

Table 4
Main parameters of VFSS – MBS.[44]

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
ORES	Oral residue	Approximate percentage of oral residue after first swallow on a bolus
PRES	Pharyngeal residue	Approximate percentage of pharyngeal residue after first swallow on a bolus
ASP	Percentage of aspirated bolus	Approximate per cent aspirated
OPSE	Oropharyngeal swallow efficiency	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

Surgical extirpation of *palate and maxillary sinus* leads to surgical defects in the hard palate with a large oronasal and oromaxillary communication.[85] Thus, tongue movements are not able to drive the bolus gathered on the dorsal surface of the tongue because of a deficient hard palate, thus material might enter the nose through the oronasal fistula during swallowing and may be aspirated after it. However the rigid, static nature of the hard palate adapts well to prosthetic implants.[86] Up to 2/3 of all patients undergoing free flap reconstruction are able to return to a normal diet[87] with good swallowing QoL.[88]

In contrast, soft palate tumour resection might result in incomplete closure of the nasopharynx with nasal regurgitation at the end of the oral phase. The soft palate is very adaptive to structural changes with sufficient recovery time and intensive speech therapy, but dysphagia strongly depends on the degree of tissue loss. Defects involving the lateral aspect of the soft palate are more likely to result in persistent dysphagia as they are much more difficult to fill in than midline defects.[89,90]

Laryngeal surgery

The larynx fulfil two main functions: voice production and sphincter function during swallowing. Schematically, while endolaryngeal soft tissue is important for voice production, the laryngeal framework (cartilage structures and neuromuscular complex) is important for sphincter function during swallowing.

Total laryngectomy (TL) causes the loss of voice, laryngeal sphincter function and disfigurement of the body image. Although, the loss of the sphincter function is supposed to be irrelevant to the swallowing process, considering the separation of the air-ways from the digestive tract, dysphagia has been reported to range from 10–60% following total laryngectomy,[80] mainly as a result of pharyngeal constrictor muscle (PCM) coordination loss.[63]

Partial laryngectomy (PL) procedures were introduced to decrease the functional impact of TL on speech and body image disfigurement. In PL, the entire thyroid cartilage (rather than the upper half described in standard supraglottic laryngectomy), the paraglottic spaces are removed, while the hyoid bone and one or both correctly-functioning cricoid–arytenoid units (CAUs) need to be preserved in order to create a neoglottis which retains the sphincter function. The neoglottis is a circular structure schematically resembling a ring whose anterior 180° is represented by the base of the tongue,[91,92] overlapped, when applicable, with the residual suprahyoid epiglottis,[93] while its rear 180° part is represented by at least one efficient CAU. An efficient CAU is formed by its crycoarytenoid joint, its muscular apparatus and sensory-motor innervations, and mucosal coating (Fig. 3a).

Table 5
Patient- and clinician-rated scales evaluating subjective dysphagia and its impact on QOL.

Scale denomination	Acronyms	Definition	Bibliography
The Swallowing Questionnaire QoL Questionnaire	SWAL-QOL and SWAL-CARE	44-item QOL assesses 10 quality of life domains, including: food selection (two items); eating duration (2); eating desire (3); fear (4); burden (2); mental health (5); social functioning (5); communication (2); sleep (2); and fatigue (3). It defines cut-off scores aimed to identify patients with dysphagia Patient-rated	153
MD Anderson Dysphagia Inventory	MDADI	Validated dysphagia specific QOL instrument consisting of 20 questions with global, emotional, functional, and physical subscales	154
European Organization for Research and Treatment of Cancer (Global QoL Scale	EORTC (QLQ C-30)	The QLQ-C30 incorporates nine multi-item scales: five functional scales (physical, role, cognitive, emotional, and social); three symptom scales (fatigue, pain, and nausea and vomiting); and a global health and quality-of-life scale. Several single-item symptom measures are also included Patient-rated	155,156
European Organization for Research and Treatment of Cancer (Head and Neck Module)	EORTC (QLQ H&N35)	It is designed to be used together with the core QLQ-C30. Seven scales were constructed (pain, swallowing, senses, speech, social eating, social contact, sexuality) Patient-rated	157–159
European Organization for Research and Treatment of CancerPerformance Status Scale for HNC patients	EORTC (PSS-H&N)	It is a clinician-rated instrument consisting of three subscales: Normalcy of diet, Understandability of Speech, and Eating in Public (some patient input incorporated in ratings of eating and diet). Each is rated from 0 to 100, with higher scores indicating better performance Patient rated	155
Functional Assessment of Cancer Therapy	FACT –G	The 39-item FACT-HN module. It consists of two subscales: 27 items that assess the patient's general QOL issues in the physical, social/ family, emotional, and functional domains (G subscale) and 12 items that assess HNC-specific QOL issues (HN subscale). Patients rate each item according to how true the statement was during the past 7 days	160
Functional Assessment of Cancer Therapy Head and Neck Module	FACT-H&N		160
University of Washington QoL Revised	UW-QOL-R	Ten individual domain scores: 1. Pain; 2. Appearance; 3. Activity; 4. Recreation; 5. Swallowing; 6. Chewing; 7. Speech; 8. Shoulder; 9. Taste;10. Saliva	161
The Head and Neck Cancer Inventory	HNCI	Five individual domains: Speech, Eating, Aesthetics, Social disruption, Overall QOL Patient rated	162
University of Michigan Head and Neck QoL Survey	HNQOL	Four relevant domains: Eating, Communication, Pain, and Emotion Patient rated	163
The Oral Mucositis Daily Questionnaire	OMDQ	Validated scales that have been developed to assess mucositis-associated mouth and throat pain, as well as its impact on function (including swallowing) and overall well being	164
The Oral Mucositis Weekly Questionnaire	OMWQ-HN		165
The Vanderbilt Head and Neck Symptom Survey	VHNSS	Validated to screen for symptoms, including swallowing in HNC patients treated with chemoradiation	166
The Sydney Swallow Questionnaire	SSQ	Self-reported physiological oral and pharyngeal swallowing function. Patient-rated	167
Common Terminology Criteria for Adverse Events (CTCAE) v. 3 and v. 4 and the Radiation Therapy Oncology Group/ European Organization for Research and Treatment of Cancer's (RTOG/EORTC) Acute and Late Radiation Morbidity Scoring System	RTOG/EORTC	Clinical rated scales of adverse events. In v. 4, more credits is given to Activities of Daily Living (ADL): "Instrumental ADL" refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money); "Self care ADL" refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden	168–170
The Therapy Outcome Measure (TOM)	TOM	Clinician rated instrument that comprises ten scales relating to communication and swallowing disorders	171
Head and Neck Performance Status Scale	HNPS	Clinician rated instrument evaluating speech, normalcy of diet and eating in public	172

The functional competence of the neoglottis depends on the anatomical–functional integrity and juxtaposition of the front half with the back half of the ring.[94–96] This neoglottis permits speech, respiration and swallowing to be preserved. However, aspiration and penetration might represent serious sequelae.[94]

The names of PLs are derived from the most caudal anatomic element above which the neolarynx is reconstructed and from the reconstructive technique utilized (Fig. 3b–d), hence the definition of supraglottic horizontal laryngectomy (SHL), supracricoid laryngectomy (SCL) with cricohyoidopexy[97] (CHP) or cricohyoidoepiglottopexy (CHEP)[91] and supratracheal or subtotal laryngectomy (STL) with tracheohyoidopexy (THP) or tracheohyoido epiglottopexy (THEP).[92]

Tracheotomy, employed as a short- or long-term solution for airway occlusion due to tumour or laryngeal oedema during CT-RT, does not seem to be protective against aspiration in tracheotomised patients.[98]

The causes of the aspiration after tracheotomy are influenced by:

- Mechanical factors characterized by decreased laryngeal elevation due to suturing of the trachea to the skin and secretion stasis in the upper airways caused by local compressive forces exerted by the inflated cuff on the cricopharyngeal opening.[99]
- Neurophysiologic factors including desensitization of the protective cough reflex and loss of co-ordination of the laryngeal closure.[100]

High volume, low pressure cuffs significantly decrease this risk of aspiration.

Table 6
Aspiration in relation to anatomical site and tumour stage.

Authors	Year	Pts	Anatomical site	Stage	Aspiration at diagnosis [***silent***]	After [***silent***][*]
Stenson et al.[45]	2000	79	Oral cavity Oropharynx Larynx Hypopharynx	III–IV	43% (34/78)[†]	
Wu et al.[118]	2000	31	Nasopharynx	Dysphagia		93.5% (29/31) ***[41.9% (13/31)]***
Hughes et al.[173]	2000	49	Nasopharynx	Treated pts		***[22% [11/49)]***
Rosen et al.[174]	2001	27	Oral cavity Oropharynx Larynx Hypopharynx	III–IV	41% (11/27) ***[18.5%(5/27)]***	
Eisbruch et al.[24]	2002	22	Not specified	Non resectable	14% (3/22) ***[9% (2/22)]***	62% (8/13) ***[38% (5/13)]***
Carrara-de Angelis et al.[175]	2003	19	Larynx Hypopharynx	II–IV		26% (5/19) ***[26%(5/19)]***
Graner et al.[176]	2003	11	Oropharynx Larynx Hypopharynx	III–IV	18% (2/11)	54% (6/11)
Smith et al.[177]	2004	29	Oropharynx Hypopharynx	III–IV	n.r.	81% (13/16 → 74 Gy) 11% (1/9 → 60 Gy)
Kotz et al.[178]	2004	12	Oral cavity Oropharynx Larynx Unknown	III–IV	0%	41% (5/12)
Nguyen et al.[179]	2006	63	All[§]	II–IV	17% (10/63)[‡]	59% (37/63)
Langerman et al.[56]	2007	130	All[§] and unknown	II–IV	53% (33/62) (15% frank[**])	62% (81/130) (23.1% frank aspiration)
van der Molen et al.[2]	2009	55	All[§]	III–IV	18% (10/55) ***[13% (7/55)]***	
Dirix et al.[57]	2009	53	All[§]	III–IV	32.1% (17/53)	26.4% (14/53)
Feng et al.[180]	2010	73	Oropharynx	III–IV	11% (8/73)	26% (18/73) ***[60% (12/18)]***

[*] Numbers and percentages of silent aspirator are in bold italics and square brackets.
[†] 1 missed.
[‡] All patients who had grade 6–7 aspiration at diagnosis continued to have aspiration following treatment.
[§] All: Nasopharynx, Oropharynx, Hypopharynx, Oral cavity, Larynx.
[**] Frank aspiration $\geqslant$ 5% of swallowed material; track if less than 5%.

However, some authors[101] did not find a causal relationship between tracheotomy and aspiration status.

Skull base surgery

Patients with extensive skull base tumours do not usually present significant dysphagia as the swallowing mechanism adapts to the slow onset of the cranial nerve paresis, but in the case of skull base surgical procedures, dysphagia is due to injuries to the adjoining cranial nerves.[102] Furthermore, the anterior approach involving maxillectomies may cause palatal defects and nasal reflux. The presence of dysphagia and aspiration is well-established in literature,[103] but a temporary swallowing impairment might be caused by brainstem oedema or cranial nerve trauma.

Conclusions after surgery

Swallowing impairment after HNC surgery strongly depends on the extent of resection, particularly for tongue base; less important seems to be the nature of reconstruction. Although primary or post-TORS secondary intention closure appears to provide a better swallowing function, this type of reconstruction cannot be used with large resection volumes.

A larger extent of resection is associated with a worse swallowing function since larger pedicles and free flaps are necessary for the consequent reconstruction. Thus, flap adynamia increases oral or pharyngeal bolus residue and the probability of aspiration.

Dysphagia after radiotherapy

Conventionally fractionated (1.8–2 Gy/day) RT with curative intent for HNCPs usually delivers total doses up to 66–70 Gy (6–7 weeks). Altered fractionation schedules as well as concomitant CT may significantly improve tumour response.[9,104] However, these aggressive treatment regimens might also contribute to significant functional impairment in swallowing function leading to dysphagia.[16]

Physiopathology and risk factors

Radiation-induced dysphagia has a complex etio-pathogenesis involving acute inflammation, oedema and fibrosis with consequent neurological and/or muscular injury.[26,105] In early radio-induced dysphagia, oedema causes the obliteration of normal pockets (e.g. vallecula) and channels (e.g. pyriform sinus) for the bolus to flow down. Thus, the bolus can be directed into the airway instead of beyond. In late dysphagia, fibrosis prevails over oedema and fibrotic tissue accumulates diffusely: below the skin, within the connective tissue layers, around muscles, and even between muscle fibres. Moreover, some preliminary research suggests that certain molecular fibrosis mediators may also directly damage skeletal muscles.[106] Fibrotic evolution of damaged tissue seems to depend on "Transforming Growth Factor beta" (TGF-β) and "Connective Tissue Growth Factor" (CTGF).[107] These mediators instruct cells involved in the wound healing process to fix damaged tissue. CTGF prolongs scar tissue production and down-regulates degradation. This process usually stops when appropriate, driven by several check-points and homoeostatic regulators.[107–110] Considering radiation induced fibrosis, the normal wound healing process is deregulated: to much TGF-β is produced, CTGF is not deactivated, and homoeostasis is disrupted. Thereby, fibrosis spreads within specific anatomical structure.[105,107,111–113] This issue is noteworthy for peri-mucosal structures since fibrosis sec-

Table 7
Aspiration in tongue resected patients.

Authors	Year	Note	Percentage of base of tongue resected	Aspiration	Swallowing efficiency
Logemannet al.[65]	1993	Closed primarily after resection	<15	No	Reduced
Zuydam et al.[181]	2000		>25	Yes	Reduced
Fujimoto et al.[182]	1998		>50	Severe	Reduced
Barbosa Furia et al.[183]	2000	Analyzing patients with total glossectomy included base of tongue	>90	20% severe	Reduced
Kimata et al.[68]	2003	Total or subtotal glossectomy with reconstruction (preservated larynx)	Near 100		Deglutition was significantly poorer in patients with flat or depressed tongues in comparison to patients with protuberant or semi-protuberant tongues ($P < 0.003$)

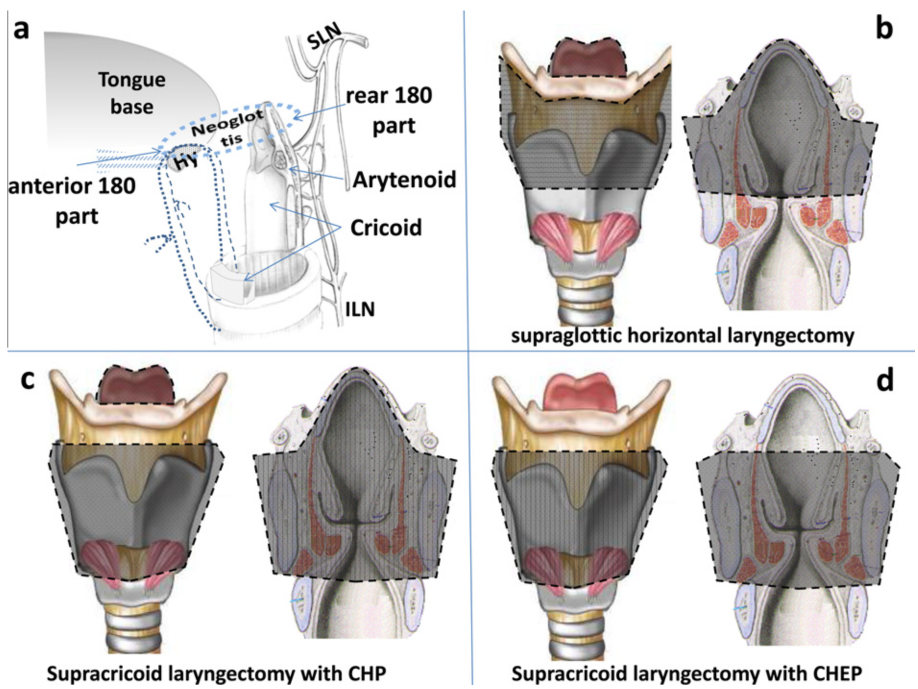

Fig. 3. Partial laryngectomy and cricoarytenoid unit (CAU) description: (a) cricoarytenoid unit (CAU): articular, neuromuscular, vascular and mucosal integrity of the crycoarytenoid complex is essential. The continuity of the cricoid cartilage is not essential. SLN = superior laryngeal nerve; ILN = inferior laryngeal nerve; Hy = hyoid bone (b) supraglottic horizontal laryngectomy. (c) Supracrycoid laryngectomy with cricohyoidopexy (CHP) (sec. Labayle). (d) Supracrycoid laryngectomy with cricohyoidoepiglottopexy (CHEP) (sec. Piquet and Mayer).

ondary to acute intense mucositis might spread to the underlying PCMs, laryngeal muscles and parapharyngeal and paraglottic spaces. This effect, also known as Denham's "bystander effect",[114] can justify long-term oedema and inflammatory changes reported by Popovtzer's RMI study[115] in DARS, but not in sternocleidomastoid (dose being equal).

The variability of the timing and intensity of radio-induced swallowing defects depends on the intensity of acute reactions as well as intrinsic radiosensitivity in terms of fibrosis, based on genetics and co-morbidities.[110] Certain patients can experience a progressive onset of fibrosis soon after radiation therapy, some a delayed one while others need to undergo a further event (trauma-surgery, addition of co-morbidity, exhaustion of compensatory mechanisms with age) to experience fibrosis.[116]

Thus, radio-induced fibrosis may cause: atrophic changes in the tongue with or without fasciculation, vocal cord palsy, velopharyngeal incompetence with premature leakage, and poor pharyngeal constriction.[117,118] These events may cause oropharyngeal motility disorders with reduced tongue-base contact to the posterior pharyngeal wall, decreased laryngeal elevation, reduced vestibule and true vocal cord closure during swallowing, prolonged duration of oropharyngeal transit and swallowing uncoordination with delayed ary-epiglottic fold closure. A consequence of these dysfunctions may be pharyngeal residue aspiration[117,118] after swallowing. These etio-pathogenetic aspects may explain the most important difference between neurologic patients[105] (from which most dysphagia information is obtained) and HNCPs: the former usually aspirate before or during swallowing, whereas the later aspirate after swallowing. Moreover, HNCPs often experience radio-induced xerostomia increasing swallowing issues. Adjunctively, radiation-induced sensory and motor modifications[119] may also occur within the airways. This fact may explain post-radiation vocal cord palsy[118] and the high percentage of silent aspiration/asymptomatic abnormal swallowing[120–124] occurring in post-radiation patients.

The variables negatively influencing radio-induced acute and late dysphagia are: smoking status during and after RT, old age,[125] total radiation dose, fraction size, interfraction interval,

Table 8
Chemo radiotherapy in head and neck cancer toxicity.

Authors	Year	Study design	Methodology	Pathological damages	Dysfunction parameters	Major events
Lazarus et al.[96]	1996	9 pts vs. 9 (age-matched normal subjects)	VFS	Reduced posterior tongue base movement toward the posterior pharyngeal wall reduced laryngeal elevation during swallow	Eight patients required an average of three swallows to clear a single bolus compared with the one swallow required by normal subjects The OPSE was significantly lower in the irradiated patients Eight patients aspirated on liquids	
Lazarus et al.[148]	2000	13 pts vs. 13 (age- and sex-matched control subjects).	VFS before and 2 months after chemoradiation	Higher tongue (statistically significant) strength was observed in the control group than in the patients with head-and-neck cancer, both before and after treatment		
Eisbruch et al.[24]	2002	29 pts (Phase I) Gem + RT	VFS	Base-of-the tongue weakness, reduced hyoid/laryngeal movement, reduced epiglottic inversion, swallow reflex delay, velopharyngeal incompetence, and upper oesophageal stricture was observed in a number of patients	Pharyngeal residue Aspiration was observed in 65% of patients (13) early after treatment and in 62% (several months after treatment aspiration rates post-therapy vs. pretherapy: $P = 0.0002$)	Six patients had pneumonia requiring hospitalization 1–14 months after therapy (median: 2.5 months), being the likely cause of death in 2 patients Five cases of pneumonia occurred among 17 patients who had demonstrated aspiration compared with no cases of pneumonia among 8 patients who had not demonstrated aspiration ($P = 0.1$)
Hanna et al.[149]	2004	One hundred and twenty-seven consecutive advanced HNCPs treated with primary concurrent chemo radiotherapy • oropharynx in 46%, • larynx in 28%, • hypopharynx in 16%, • oral cavity in 8% • and oesophageal and sinonasal in 3%	Toxic effect data included the rate and grade of treatment-related complications and the rate of unscheduled hospital admissions for managing treatment-related toxic effects	The authors felt that the cause of dysphagia may be due to stricture formation as a consequence of ulcerative mucositis	Dysphagia was the most common long-term complication and 40% of the patients required a change from their pre-treatment diet	Neutropenia was seen in 50% of the patients and of these 50% had grade 3–4 neutropenia Mucositis was seen in 64% of the patients of which 33% were severe Nausea was seen in 44% of patients and severe nausea in 15% and vomiting was seen in 11% of the patients Gastrostomy tubes were placed in 73% of the patients
Nguyen et al.[131]	2004	Fifty-five consecutive pts HNCPs	Modified barium swallow (MBS) studies were performed if the patients complained of dysphagia or if there was clinical suspicion of aspiration	Severe dysfunction of:the base of the tongue, larynx with epiglottic dysmotility pharyngeal muscles	Stasis of the bolus, vallecular residue, and, in severe cases, aspiration	The combination of aspiration with neutropenia arising from chemotherapy, may lead to aspiration pneumonia, sepsis and respiratory failure[56]
Gillespie et al.[145]	2004	Cross sectional study 22 Ct + RT (CTRT)18 S → RT (SRT) stage III and stage IV patients with oropharynx, larynx and hypopharynx	The MD Anderson Dysphagia Inventory (MDADI), and the Short-Form 36 (SF-36)		The swallowing outcome was better in patients with chemoradiation for oropharyngeal primaries then in patients with surgery and RT	
Gillespie et al.[146]	2005	Cross sectional study 10 Ct + RT (CTRT) 11 S→RT (SRT) stage III and stage IV patients with oropharynx, larynx and hypopharynx	Penetration–Aspiration Scale and the MDADI		8/10 SRT were able to consume a complex diet of all solids and liquids after treatment in comparison to 2/11 CRT	

Table 9
Summary of recommendations.

(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" (Table 2), is recommended[26,30,184,185] (*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[26,28,30,184,186] (*Recommendation D*; levels 4–5) (expert opinion mainly based on bench research – neurological patients)[26–28] in order to (1) identify swallowing abnormality, (2) develop a treatment plan when indicated, (3) recommend additional testing to assess aspiration risk[26]
• Dysphagia tests	Water[29,187,188] tests, with or without oxygen desaturation, with or without cough test[29] 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)[38,174] 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 aspiration[26] (*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)[39,41] Even if FEES is less expensive than VFS,[189] the choice of examination can be guided by its accessibility (level 5)[27] if the two examinations can give an answer to the specific clinical question. (*Recommendation D*)
• The findings of VFS can be scored with	OPSE (tab 4) (*Recommendation B*; level 2)[19,44] Swallowing Performance Status Scale[45,46] (SPS), (*Recommendation C*; level 4) and 8-point Penetration–Aspiration scale[47] (*Recommendation C*; level 4)
• QoL	In monitoring the QOL of dysphagic patients, both patient-rated and clinician-rated scales Table 5, could be used, considering the given complementary information. (*Recommendation B*; level 2)[54]
(2) Pre-treatment recommendations	The TDRS 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.[54] (*Recommendation B*; level 2[54,58]) 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 feasible[26] (*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 form level 2 and 3 studies)[190,191] 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 from level 2 studies).[84,125] 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)[62] Resection of oral tongue slows oral transit, worsening with more viscous bolus[63,64] (levels 2–4); the resection of more than one half of the mobile tongue can cause serious swallowing disability (level 4)[60,75] People (especially older than 60 years) who had wide resection (>50%) of the tongue base might not have an oral diet at all[68] (level 4) While a rim or marginal resection of the mandible has little impact on swallowing function,[75] mandibulotomy can cause damage to genioglossus musculature (as in sagittal mandibulotomy[77,84]; level 3 case–control), inferior alveolar nerve (as in lateral mandibulotomy) and occlusion[75] (level 5; expert opinion). Furthermore, segmental mandibular resection without reconstruction has a profound negative impact on swallowing function[76,192] (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[87] (level 4) with a good swallowing QoL[88] (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 persistent dysphagia as they are much more difficult to obturate than midline defects (level 5)[90] (level 4) Dysphagia has been reported to range from 10% to 60% following total laryngectomy[80] (level 4), mainly as a result of benign stricture, radiation-induced pseudo-epiglottis formation or PCM coordination loss[63] (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 aspiration[92–94] (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 patients[98] (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.[102] (level 4) Usually TORS wounds heal by secondary intention without dysphagia[69] (level 4)

Table 9 (*continued*)

(4) Recommendation for exclusive radiotherapy	Computed Tomography (CT)-based delineation guidelines for DARS[18,20,193] 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[139] 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 PCM[120] (*Recommendation B*; level 3) However, avoiding under-dosing to the targets in the vicinity should remain the highest priority.[193–195] (*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 cm[321], anterior oral cavity[19] 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)[24,96,131,145–149] If pneumonia or sepsis is suspected the search for Systemic inflammatory Reaction Syndrome (SIRS) is recommended[196] (*Recommendation D*; level 5) (expert opinion based on physiology and bench research)

extension of treatment volume, treatment techniques, weight loss at baseline, and site and size of the primary tumour.[58,126] Patients using PEG tubes are reported to have persistent dysphagia, requiring more pharyngoesophageal dilation.[127] Inactivity of the muscles involved with swallowing may lead to atrophy and future inability to consume food orally.[16] Thus, although substantial data clearly demonstrate that the use of prophylactic feeding tubes reduces weight loss during and immediately after RT,[128] there is concern that feeding tubes result in disuse atrophy and late effect dysphagia.[16,127] Presently, 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 feasible.[26]

Researchers at the University of Groningen[18] have recently shown that the dose given to DARS is the most predictive factor of $SWALL_{6\,months}$. Indeed, DARS radio-injury is directly related to radiation dose parameters (i.e. total dose, fraction size, and duration of treatment).[131] However, available data[10,19,21,119,120,132–137] on this topic are mostly based on retrospective analyses of small patient datasets with differences in study design, eligibility criteria, analyzed endpoints and systems to detect dysphagia (clinician-rated, patient-rated and instrumental assessment).[138] The numerous biases make the knowledge of DARS dose constraints unclear.

Recently, the panel of "Quantitative Analysis of Normal Tissue Effects in the Clinic (QUANTEC)"[139] provided focused summaries of the dose/volume/outcome information for many organs inferred from literature data. A single dose–volume histogram (DVH) point is not an ideal representation of the 3D doses: e.g. the same $V_{20\,Gy}$ can be obtained with an infinite number of highly differing dose distributions.[140] Thus, it is prudentially advisable to adopt the multimetric models (more than one parameter: e.g. Dmean, different DVHs) in clinical practice. In general, the dose/volume/outcome data provided in the Quantec summary table[140] are associated with generally acceptable clinical injury rates. Yet, prudence is recommended, before adopting a predictive parameter in clinical practice, to assess if its prediction capability fits into each specific centre experience. The conclusive dysphagia recommendation is that "the limited available data suggested that minimizing the volume of the pharyngeal constrictors and larynx receiving <60 Gy and reducing, when possible, the volume receiving <50 Gy is associated with reduced dysphagia/aspiration".[139]

Considering the DARS definition, a panel of Dutch experts[18] drew up guidelines in order to reduce the variability among centres on this topic.

Scant data are available[19–21] regarding the role of mucosa sparing in order to prevent swallowing dysfunction. Schwarts[19] identified dose–volume constraints predictive as objective swallowing dysfunction (V30 < 65% and V35 < 35% for anterior oral cavity and V55 < 80% and V65 < 30% for high superior PCM), while Sanguineti et al.[21] found that the risk of PEG use was drastically reduced when the weekly DVH of oral mucosa was V9.5 Gy/week < 64 cm^3. These results need to be validated.

Dysphagia in post-surgical radiotherapy

HNCPs, treated with post-operative RT, experience both post-surgical and radiation induced swallowing dysfunction. In one study, non-irradiated patients demonstrated a steady improvement in swallowing efficiency between 3 and 12 months after surgery; while postoperatively irradiated patients did not show any functional improvement.[141]

The effect of postoperative RT[142] on HNCPs is characterized by significantly decreased OPSE and shorter duration of cricopharyngeal opening. These dysfunctions are probably due to xerostomia and radiation-induced fibrosis of the oropharyngeal musculature,[142] especially of the tongue base. In these patients the preservation of the tongue base in the swallowing mechanism is very important.[96,142]

While surgery-induced swallowing dysfunction occurs during the first few months after excision, the additional effects of RT generally occur 6 months later. In these patients the summing effect of both therapies worsens swallowing uncoordination and may cause severe dysphagia and aspiration (if the larynx is preserved).

Dysphagia after chemo radiotherapy

CT *per se* might cause mucositis often resulting in swallowing difficulty (Table 8). Furthermore, side-effects like nausea, vomiting, infection, and fatigue can concur to acute dysphagia and malnutrition. Approximately 40% of patients undergoing CT are reported to have mucositis while almost 100% of patients receiving CT-RT report some grade of mucositis.[80] The anti-metabolites such as methotrexate and 5-fluorouracil seem to be the drugs most associated with the oral, pharyngeal, and oesophageal symptoms of dysphagia.[143]

Even though combined modality treatment significantly increased late toxicity,[58,144] when both chemoradiation and DARS-dose were studied together as predictive variables of $SWALL_{6\,months}$, the effect of CT was hidden by DARS-dose.[54]

Eisbruch et al.[24] observed aspiration in 65% of patients soon after treatment and in 62% several months later. The aspiration was often silent and the main cause of delayed pneumonia (median: 2.5 months after the end of RT) and septic deaths (6.8% of patients). Conversely, Gillespie[145,146] observed better swallowing outcome in patients who underwent CT-RT for oropharyngeal primaries than in those treated with surgery plus RT.

The causes of dysphagia[24,96,131,145–149] after CT-RT might be predominantly due to generalized weakness and un-coordination in deglutition. This could be due to the enhancement of radio-induced fibrosis of the musculature or added toxic effects on the neuromuscular junctions.[150]

However, the individual role of CT and RT in swallowing disorders is difficult to distinguish.

Conclusions

The conclusions are summarized in Table 9.

In HNCP treatment, disease control has to be considered *in tandem* with the functional impact on swallowing function. A thorough knowledge of the anatomy and physiology of the swallowing mechanism are essential for optimal dysphagia/aspiration management. SLPs should be included in a multidisciplinary approach to HNC. However, signs and symptoms of dysphagia/aspiration have to be actively searched by each specialist that has the patient in charge in each phase of therapy.

Further prospective studies are advocated to better develop preventive and therapeutical strategies by optimizing the aggressiveness of the treatment according to the therapeutic sensitivity of the tumour, utilizing information obtained from tumour biomarkers (dose de-intensification whenever recommendable) and by developing our knowledge about the effects of the different specific treatments on each different structure involved in swallowing.

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Conflict of interest statement

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