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Functional Assessment and Rehabilitation – How to Maximize Outcomes

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INTRODUCTION

The number of oral cavity and oropharyngeal cancer survivors has risen in recent decades owing to the increasing incidence of disease and improved survival rates. By 2030, oropharyngeal cancers are projected to account for almost half of head and neck cancers.¹ The oral cavity and oropharynx are essential to normal speech, swallowing, and respiration. These critical functions can be disrupted by adverse effects of tumor and cancer therapy on the upper aerodigestive tract (UADT). This review will summarize clinically distinct functional outcomes in patients with oral cavity and oropharyngeal cancers, pretreatment functional assessments, strategies to reduce or prevent functional complications, and methods of posttreatment rehabilitation.

OVERVIEW OF FUNCTIONAL OUTCOMES

Oral Cavity Cancer

Surgical resection remains the primary treatment for many cancers of the oral cavity.^{2,3} Surgery disrupts the complex anatomy and functions of the UADT and may lead to lifelong disability, despite advances in minimally invasive approaches and microsurgical reconstruction. Radiotherapy or chemoradiation is often delivered as an adjuvant treatment

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Speech production is dependent on 4 processes: respiration, phonation, resonation, and articulation.⁴ Each process involves precise biomechanical coordination of multiple structures in the oral cavity and UADT. Consequently, the type and degree of speech impairment varies depending on the location and extent of tumor within the oral cavity. In general, speech production is most adversely affected when oral cavity resections involve the mobile tongue or extend to include the soft palate. Resulting defects from lingual and palatal resections impair different speech domains.

Oral cavity cancers involving the tongue most commonly impair articulation. A recent systematic review suggested that speech remains largely intelligible (92–98% intelligible at the sentence level [blinded rating]) for most surgically treated patients with advanced-stage oral cancer (tumor stage 2), including those with tumors involving the tongue. Deviant speech characteristics were commonly reported in published studies despite intelligible speech ratings.⁵ The extent of tongue resection greatly affects the accuracy of articulation and intelligibility. Data suggest that most patients will ultimately acquire good intelligibility after partial or hemiglossectomy procedures that preserve half or more of the native tongue, but outcomes are more variable after subtotal and total glossectomy.⁵

Treatment of oral cavity cancers can also disrupt speech resonance. Resections of cancers involving the maxilla cause significant rhinolalia until the oronasal defect is adequately sealed. Acceptable speech quality is achieved in most patients after successful prosthetic obturation or surgical reconstruction of the oronasal defect,^{6,7} but surveys find that self-reported speech function is still significantly lowered in cancer patients with maxillary defects relative to controls.⁸ In addition, obturation is typically less successful when the defect extends to involve the soft palate because of the soft palate's dynamic involvement in the process of velopharyngeal closure.⁹

Speech and swallowing function are closely related because they rely on common UADT structures. Swallowing occurs in 4 phases: oral preparatory, oral, pharyngeal, and esophageal. Treatment of oral cavity cancers most commonly affects the first 3 phases of swallowing. Oropharyngeal swallowing function can be impaired by the direct effects of oral cavity resection on oral preparatory (i.e., mastication, collecting a bolus in the mouth) and oral transit functions (i.e., posterior propulsion from the mouth to the pharynx). Oral cavity resection can also indirectly affect pharyngeal bolus transit by way of premature spillage that accompanies the loss of oral control, decreased lingual driving pressure on a bolus through the pharynx, or disrupted stabilization of the hyolaryngeal complex required for airway closure and upper esophageal opening. In addition, adverse effects of adjuvant radiotherapy or chemoradiation on pharyngeal swallowing function are well established. Data from a systematic review suggest that swallowing efficiency is commonly impaired after surgical management of advanced-stage oral cancers (i.e., prolonged bolus transit times and incomplete bolus clearance), but chronic aspiration is a less common consequence of surgical management (12-25% prevalence). Therefore, it is not surprising that patients surgically treated for oral cavity cancer perceive the greatest degree of trouble swallowing dry or hard foods when polled about specific dysphagia symptoms.¹⁰

Oropharyngeal Cancer

Survival rates for oropharyngeal cancer have dramatically improved in the past 20 years owing to refinements in and intensification of organ preservation strategies and the rising

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proportion of human papillomavirus-attributable disease. Options for organ preservation include nonsurgical therapy (i.e., radiotherapy and chemoradiation) and minimally invasive surgery (i.e., transoral robotic surgery [TORS] or transoral laser microsurgery). Organ preservation strategies seek to achieve locoregional control and optimize functional outcomes. Cancers of the oropharynx arise in a region of the UADT critical to swallowing function. Thus, pharyngeal dysphagia is the principal functional toxicity of treatment for oropharyngeal cancer, recognized as a key endpoint measure in contemporary management of the disease. As Weinstein et al noted, "...if it is found that the oncologic outcomes are equivalent...then the most important factor for triaging patients to TORS or chemoradiation will be swallowing outcomes".¹¹

Swallowing is a complex biomechanical process involving 5 cranial nerves and more than 25 muscles in the UADT. Swallowing impairments can occur as the result of surgery alone, radiotherapy alone, or chemoradiation. Data specific to patients with oropharyngeal primary tumors demonstrate a high burden of dysphagia. In a population-based Surveillance, Epidemiology, and End Results–Medicare analysis of more than 8,000 patients with head and neck cancer, patients with cancers of the oropharynx had the second-highest prevalence of dysphagia.¹² In a pooled analysis of 3 Radiation Therapy Oncology Group chemoradiation trials, 35% of 101 oropharyngeal cancer patients with adequate baseline function experienced late grade 3 or 4 laryngeal or pharyngeal toxicity, often including dysphagia.¹³

Even in the era of conformal radiotherapy (i.e., intensity-modulated radiotherapy [IMRT]) for oropharyngeal cancer, 82–85% of patients require feeding tubes during therapy, and authors report 6–31% rates of aspiration 1 year after treatment and 4–8% rates of chronic feeding tube dependence.^{14–16} In a trial evaluating treatment for oropharyngeal cancer with chemoIMRT that was designed to protect dysphagia-organs-at-risk using dysphagia-specific dose constraints, 31% of patients had higher occurrences of aspiration >1 year after treatment relative to baseline, and 22% developed pneumonia.¹⁶ Aspiration was significantly predictive of pneumonia in this trial (p = 0.017, sensitivity = 80%, specificity = 60%), and silent aspiration was evident on modified barium swallow (MBS) studies in 63% of patients who developed pneumonia. In addition, pharyngeal residue on MBS studies was significantly associated with the development of pneumonia after chemoIMRT (p < 0.01).¹⁷

Particularly concerning is the risk of severe, late dysphagia that presents up to decades after radiotherapy in long-term survivors of oropharyngeal cancer. Although the prevalence of severe late dysphagia is not known, data suggest that the level of impairment is profound, often accompanied by a constellation of neuromuscular pathologies, including cranial neuropathies. In addition, late dysphagia is largely refractory to standard, nonsurgical dysphagia therapies and leads to recurrent pneumonias requiring lifelong gastrostomy or elective functional laryngectomy.¹⁸

TORS is emerging as a minimally invasive surgical alternative to nonsurgical organ preservation for oropharyngeal cancer, proposed to offer several functional advantages relative to open surgery or definitive chemoradiation. TORS allows access for resection without pharyngotomy or mandibulotomy, maintaining the critical muscular framework of the laryngopharynx. Tracheostomy, typically required for airway management after open resection, is also not needed for most patients who undergo TORS (70–100%). Furthermore, published series suggest that 9–27% of patients treated with frontline TORS avoid postoperative radiotherapy and 34–45% avoid chemoradiation. Crude endpoints of functional recovery after TORS suggest promising early outcomes relative to radiationbased organ preservation regimens. Rates of percutaneous endoscopic gastrostomy tube placement (18–23%) and chronic dependence (0–7%) after TORS are lower than those

reported for patients receiving definitive chemoradiation.^{19–23} However, patient-reported swallowing outcomes after TORS, according to the MD Anderson Dysphagia Inventory, are fairly similar to those of chemoradiation cohorts,¹⁹ and findings of gold-standard instrumental swallowing assessments are rarely reported after TORS. In addition, functional outcomes have been studied almost exclusively in the first year after TORS. Thus, further comparisons of long-term outcomes and physiologic swallowing outcomes based on instrumental examinations are needed to better understand the functional differences in surgical and nonsurgical organ preservation for oropharyngeal cancer.

PRETREATMENT FUNCTIONAL ASSESSMENT

Pretreatment functional assessment is a critical component of comprehensive care. Baseline functional status has been shown to predict posttreatment functional outcomes, and contributes to clinical decisions about supportive care to optimize treatment tolerance (e.g., pretreatment feeding tube placement, dietary changes to prevent aspiration). Pretreatment functional status is also important to consider when selecting the modality of cancer therapy most likely to maximize functional outcomes, particularly when various modalities offer a similar likelihood of cure. Pretreatment examination by a speech pathologist should include, at a minimum, an oral motor/cranial nerve examination, motor speech evaluation (articulation, resonance, voice quality, intelligibility), and a *clinical swallow evaluation*. An instrumental swallowing examination is indicated in many cases, particularly in patients who present with advanced-stage primary tumors who have an increased risk of baseline aspiration.²⁴ For patients with cancers of the oral cavity and oropharynx, the radiographic MBS study is the instrumental examination of choice because it allows evaluation of both oral and pharyngeal phases of swallowing.²⁵ Laryngeal videostroboscopy is also useful in assessing laryngopharyngeal functioning, particularly in patients with advanced-stage oropharyngeal cancer that extends to involve the larynx.

Instrumental examinations are considered the gold-standard methods of assessment because they objectively assess oropharyngeal swallowing physiology and bolus transit, and predict adverse health outcomes (e.g., pneumonia and malnutrition). Functional outcomes can also be assessed by patient-reported outcome (PRO) measures. Patient-reported outcome measures provide a complementary perspective to instrumental, clinician-rated examinations, mainly regarding the impact of physiologic impairments on daily activities and quality of life. However, there is often a lack of agreement about the severity of impairment between subjective PRO measures and instrumental physiologic examinations, and PRO measures do not fully reflect true swallowing competency. Thus, the consensus is that both metrics should be used for a comprehensive evaluation of functional outcomes.

Standardized functional assessments offer critical data to optimize treatment outcomes, but functional assessments lack uniformity in clinical practice and research. Minimum standards for functional assessment have been suggested on the basis of a recent systematic review to include the following measures, longitudinally assessed at least 3 to 4 times during the treatment trajectory of patients with oral cavity or oropharyngeal cancer: 1) instrumental/ objective swallowing assessment (e.g., MBS study) with supplemental clinical data, 2) assessment of speech intelligibility, 3) supplemental speech assessment of specific impairments relevant to oral cavity and oropharyngeal cancer (e.g., articulation, resonance), and 4) PRO measures related to speech and swallowing.²⁵ Table 1 describes various methods of pretreatment functional assessment.

PREVENTING OR REDUCING FUNCTIONAL PROBLEMS

The severity of functional impairment can be influenced by a number of clinical factors. Current literature indicates that the percentage of oral tongue resection, type of reconstruction, contour of the free flap, and primary tumor stage affect postsurgical speech and swallowing outcomes.^{5,10,26} Functional outcomes also vary depending on the schedule of radiation, radiotherapy dose distribution, and the use of concurrent chemotherapy. Finally, swallowing outcomes can be influenced by supportive care practices, including the timing and type of feeding tube placement and the provision of targeted preventive exercise in patients receiving radiotherapy or chemoradiation. Disease characteristics (i.e., subsite and tumor volume) that influence functional outcomes are unchangeable; thus this section is focused on factors that can potentially be modified to prevent or reduce functional problems after treatment. These include surgical reconstructive factors, radiotherapy techniques, and supportive care/preventive therapy.

Surgical and Reconstructive Factors

Some studies report significantly worse swallowing outcomes in patients who have reconstruction after oral cavity and oropharyngeal resections,²⁶ largely owing to the confounding effects of greater tumor burden and greater surgical defects in patients who require reconstruction rather than primary closure. Reconstructive factors that are associated with functional outcomes include sensory repair and the contour and volume of the flap. In addition, intraoral sensation has been shown to be correlated with UADT function, including pharyngeal swallowing competency,^{27,28} and sensory reinnervation can be performed during microvascular reconstruction.

Published studies report conflicting results regarding the functional outcomes of sensory reinnervation in oral cavity reconstructions. For instance, objective swallowing ratings according to MBS studies did not differ between patients with reinnervated flaps and those with noninnervated flaps in a prospective functional analysis of 44 patients.²⁹ In contrast, Yu et al³⁰ found significantly higher diet levels in patients with reinnervated ALT flaps compared with those with noninnervated flaps after near-total or total glossectomy. Nonetheless, authors have advocated that a relatively simple reinnervation procedure improves intraoral sensation and should be attempted when possible.³¹

In addition, the shape and volume of the reconstructed tongue has been shown to affect postoperative speech and swallowing outcomes. Reconstructed flaps that are protuberant or semi-protuberant and those with greater volume are associated with significantly better speech intelligibility and dietary outcomes.^{32,33} On the basis of these findings, authors have suggested overcorrection of the defect to account for volume loss that occurs with atrophy and postoperative radiotherapy.^{32,33} Finally, the utility of laryngeal suspension in patients requiring total or subtotal glossectomy has been demonstrated both to help protect the airway from aspiration and prevent prolapse of the flap.^{32,34}

Radiotherapy Techniques

Radiotherapy techniques can vary greatly, particularly the conformal methods used to spare normal tissue. Normal tissue constraints using IMRT have historically limited the dose to the salivary glands to reduce xerostomia. Swallowing-specific dose-constraints using IMRT have only recently been explored¹⁶ after a number of studies (most commonly in oropharyngeal cancer) elucidated the core swallowing-related organs at risk.³⁵ The anterior oral cavity, superior pharyngeal musculature, and inferior larynx/esophageal inlet have been identified as swallowing-specific organs at risk, for which dose-volume coverage is correlated with short-term and long-term swallowing outcomes after IMRT. Data suggest

that integrating swallowing-specific organ dose constraints into IMRT plans may reduce gastrostomy dependence, improve oropharyngeal swallowing efficiency, minimize aspiration, and optimize swallowing-related quality of life.^{14,16,36–39}

Pharyngeal and oral cavity constraints can be integrated into IMRT plans, and laryngeal dose sparing constraints can be included in full-field IMRT plans or accomplished using a split-field technique. A split-field laryngeal block technique matches IMRT fields at the level of the arytenoid cartilages with a conventional supraclavicular laryngeal block (3×3 cm) using anteroposterior bilateral low neck fields. The split-field technique has been shown to achieve a lower laryngeal and esophageal inlet dose compared with full IMRT fields in patients with oropharyngeal cancer.^{14,37} Thus, current evidence supports the potential for laryngeal shielding and dysphagia-specific dose constraints to reduce or prevent dysphagia after radiotherapy.

Preventive Therapy

Preventive swallowing therapy encourages ongoing use of the swallowing musculature during radiotherapy under the "Use it or lose it" paradigm. In preventive swallowing therapy, speech pathologists train patients to perform targeted swallowing exercises before and during radiotherapy and prescribe compensatory swallowing techniques or dietary modifications to discourage even brief NPO periods. Three randomized clinical trials have shown a benefit of early exercise during chemoradiation;^{40–42} one found a 36% absolute risk reduction for loss of functional swallowing ability among patients randomized to receive swallowing exercises during chemoradiation.⁴¹ Favorable outcomes reported with preventive swallowing exercises include superior swallowing-related quality of life scores;^{43,44} better base of tongue retraction and epiglottic inversion;⁴⁵ larger postradiotherapy muscle mass and T2 signal intensity of the genioglossus, mylohyoid, and hyoglossus muscles;⁴¹ more normal oral diet levels after chemoradiation;⁴⁰ and shorter duration of gastrostomy dependence.^{46,49}

In addition, maintenance of *any* oral intake during radiotherapy (i.e., avoidance of NPO intervals) has been found to independently predict long-term swallowing-related quality of life outcomes according to the MD Anderson Dysphagia Inventory and was associated with superior diet levels up to 1 year after radiotherapy.^{47,48} Multidisciplinary management of acute radiation toxicities, including odynophagia, dysgeusia, weight loss, and dysphagia, is necessary to help patients safely maintain oral intake during therapy. The evidence in favor of proactive swallowing therapy with radiotherapy in patients with head and neck cancer is summarized in Table 2.

POSTTREATMENT REHABILITATION

Functional rehabilitation after cancer therapy is individualized to meet the unique needs of each patient. In general, patients with oral cavity cancers who have had surgery (and often postoperative radiotherapy or chemoradiation) require both speech and swallowing therapy, whereas patients who receive radiotherapy or chemoradiation for oropharyngeal cancers are most likely to require dysphagia therapy. In either case, rehabilitation should be planned to target physiologic and functional impairments identified on standardized, instrumental assessments. That is, effective rehabilitation begins with comprehensive and standardized functional assessment. Functional assessment includes, for all cases, oral motor/cranial nerve examination and motor speech assessment. In addition, standardized articulation and intelligibility batteries are available to identify goals for speech intervention, and swallowing therapy goals should be determined on the basis of instrumental examinations (e.g., the MBS study or fiberoptic endoscopic evaluation of swallowing).

Patients with postoperative dysarthria can be taught compensatory mechanisms of articulation that rely on exaggeration of the remaining labial, mandibular, pharyngeal, and laryngeal structures. Glossectomy-specific compensatory phonetic strategies pioneered by the work of Skelly et al in the 1970s remain useful in contemporary practice.^{51,52} Articulation targets are selected on the basis of standardized batteries such as the Fisher-Logemann Test of Articulation. Speech pathologists also use findings of articulation testing to collaborate with maxillofacial prosthodontists in the process of designing palatal augmentation prostheses. Palatal augmentation prostheses improve the accuracy of consonant production and can normalize yowel production by reshaning the contour of the

augmentation prostheses. Palatal augmentation prostheses improve the accuracy of consonant production and can normalize vowel production by reshaping the contour of the hard palate for better contact by the surgically altered tongue.⁵³ A systematic review that evaluated studies over more than 35 years found that palatal prostheses improve objective ratings of both speech and swallowing function in roughly 85% of patients. Published data also suggested an inverse relationship between the efficacy of a palatal prosthesis and mobility of the residual tongue. That is, the prognosis for improving speech with a palatal prosthesis is less favorable as the mobility of the residual tongue increases.⁵⁴

Evidence-based compensatory swallowing techniques have been shown to improve airway protection and bolus clearance in patients with oropharyngeal dysphagia after cancer therapy.⁵⁵ Compensatory techniques may include postures such as a chin tuck or head rotation, strategies such as the supraglottic swallow, and/or dietary modifications such as thickening liquids or blending foods. Instrumental examination is critical to match appropriate compensations with the specific swallowing impairment and to test the efficacy of compensations in individual patients. In some cases, compensations are used for a short interval to ensure safe oral intake during acute periods of recovery whereas patients with chronic dysphagia may adopt swallowing compensations as a lifelong tool to prevent aspiration compromise.

Evidence-based swallowing exercises are also selected on the basis of the pathophysiology of dysphagia identified during instrumental examinations.^{56–63} Exercise therapy is maximized by attending to defined principles of strength training and neuroplasticity. Exercises must challenge the system beyond its normal capacity in a systematic fashion, and skills-training encourages re-learning and neuroplasticity through direct swallowing activities. Adjunctive biofeedback measures such as surface electromyography or endoscopic monitoring, coupled with swallowing therapy, can help the patient examine, modify, and challenge the therapeutic task.^{64,65} In addition, investigations are ongoing to determine the efficacy of transcutaneous neuromuscular electrical stimulation (NMES) as a treatment for dysphagia after cancer therapy. Current evidence suggests that NMES often lowers the hyolaryngeal complex because the superficial infrahyoid strap muscles receive more intense levels of stimulation than the deeper laryngeal elevators.⁶⁶ This finding suggests that transcutaneous NMES may benefit only patients who are able to sufficiently elevate the larynx during swallowing against the resistance (i.e., downward pull) induced by the stimulation. This premise requires further investigation; if confirmed, it indicates that the physiologic effect of NMES on hyolaryngeal movement must be examined under videofluoroscopy in each patient before applying this therapy to avoid potential harm or unintended physiologic effects. Finally, the intensity of swallowing therapy matters. Doseresponse data are lacking for most swallowing therapies, but intensive "boot-camp" paradigms show promise to improve swallowing outcomes in patients with chronic or severe dysphagia.57

SUMMARY

In summary, the number of long-term oral cavity and oropharyngeal cancer survivors is rising, and speech and swallowing outcomes are principal determinants of quality of life

during cancer survivorship. Thus, maximizing long-term functional outcomes is a priority of contemporary multidisciplinary head and neck cancer care. Optimizing functional outcomes begins with a standardized, comprehensive baseline assessment. Pretreatment functional assessment should combine complementary instrumental, clinician-rated examinations with PRO measures. Functional analysis before treatment is critical to plan rehabilitation and supportive care, predict outcomes, and select the optimal cancer therapy. A number of strategies can be targeted to prevent or reduce the burden of functional problems. Therapeutic techniques that can maximize function include attention to flap volume and contour and consideration of sensory reinnervation in surgical cases requiring reconstruction. Current evidence also supports the potential for larvngeal shielding and dysphagia-specific IMRT dose constraints to diminish pharyngeal dysphagia after radiotherapy. Finally, preventive swallowing therapy that couples targeted swallowing exercises with avoidance of NPO intervals has been shown to positively affect a number of important functional endpoints. Functional rehabilitation after treatment requires individualized planning and should be guided by physiologic findings of instrumental examinations. Functional success is best achieved with a multidisciplinary team that includes speech pathologists specialized in assessment and management of head and neck cancer.

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KEY POINTS

- The number of long-term oral cavity and oropharyngeal cancer survivors is increasing. Speech and swallowing outcomes are critical survivorship endpoints.
- Pretreatment functional assessment is essential to plan rehabilitation and supportive care, to predict functional outcomes, and to select the modality of therapy most likely to maximize functional outcomes.
- Refinements in surgical reconstruction, conformal radiotherapy techniques, and preventive therapy can be used to reduce functional problems after treatment.
- Posttreatment rehabilitation requires individualized planning on the basis of standardized, instrumental assessments.

Table 1

Pretreatment functional assessment methods

Pretreatment functional assessment	Domains assessed	
Clinical examinations		
Cranial nerve/oral motor examination	Symmetry/range of motion oral musculature	
	Oral opening	
Motor speech examination	Articulation	
	Resonance	
	Voice quality	
	Subjective intelligibility rating	
Clinical swallowing evaluation	Oral preparatory functions: mastication, oral containment, bolus consolidation	
	Oral phase functions: oral control, oral clearance	
	Pharyngeal phase functions (inferred): airway protection, pharyngeal transit	
Instrumental examinations		
Modified barium swallow	Oral and pharyngeal physiology	
	Airway protection: laryngeal penetration, aspiration	
	Pharyngeal transit: residue	
Fiberoptic endoscopic evaluation of swallowing	Laryngeal and pharyngeal physiology	
	Airway protection: laryngeal penetration, aspiration	
	Pharyngeal transit: residue	
	No direct observation of oral phase	
Laryngeal videostroboscopy	Vocal fold mobility	
	Symmetry, amplitude, periodicity	
	Mucosal wave	
	Laryngeal pathology	

Table 2

Evidence for preventive "Use it or lose it" swallowing therapy in irradiated head and neck cancer patients

Institution	Study design	Comparison	Outcomes	
"Use it or lose it" principal: early swallowing exercises				
University of Alabama–Birmingham	Retrospective*	Pretreatment exercise vs standard care †	Superior MDADI scores ^{43,‡} Better base of tongue and epiglottic movement ⁴⁵	
The University of Texas MD Anderson Cancer Center	Retrospective*	Adherent to pretreatment exercise vs not adherent	Shorter duration of percutaneous endoscopic gastrostomy ^{46,49} Superior MDADI scores ⁴⁴	
University of Florida	Randomized controlled trial	Pretreatment exercise vs pretreatment sham exercise vs standard care †	Significant preservation of muscle mass according to magnetic resonance imaging ⁴¹	
Netherlands Cancer Institute	Randomized clinical trial	Pretreatment exercise vs pretreatment exercise + Therabite	Improved mouth opening ⁵⁰	
Mount Sinai	Randomized controlled trial	Pretreatment exercise vs standard care †	Superior diet levels (3–6 months after conformal radiotherapy) ⁴⁰	
"Use it or lose it" principal: avoid NPO				
Medical University of South Carolina	Retrospective with cross- sectional survey*	Prolonged NPO (>2 weeks) vs no prolonged NPO interval	Significantly lower MDADI scores with prolonged NPO ⁴⁷	
Boston University	Retrospective*	Partial or fully PO at end of radiotherapy vs 100% NPO	Partial or fully PO led to significantly better diet levels (through 12 months) after radiotherapy ⁴⁸	

*Observational between-group comparisons; not randomized.

 † Standard care = no pretreatment exercise, posttreatment exercise provided as indicated.

^{\ddagger}MDADI, MD Anderson Dysphagia Inventory.