



Published in final edited form as:

Curr Opin Otolaryngol Head Neck Surg. 2009 June ; 17(3): 172–178. doi:10.1097/MOO.0b013e32832af12f.

Effects of chemoradiotherapy on voice and swallowing

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Abstract

Purpose of review—Chemotherapy has been found to result in comparable survival rates to surgery for head and neck cancer. However, toxicity can often be worse after chemoradiotherapy, with impairment in voice, swallowing, nutrition, and quality of life. Investigators are attempting to modify radiotherapy treatment regimens to spare organs that have an impact on swallowing. This review will highlight voice and swallowing impairment seen after chemoradiotherapy, as well as treatment for voice and swallowing disorders in this population. Results of newer radiotherapy regimens will also be highlighted.

Recent findings—Specific oropharyngeal swallowing motility disorders after chemoradiotherapy have been identified. Damage to specific structures has been correlated with specific pharyngeal phase swallow impairment. Swallowing function and quality of life have been examined over time, with improvement seen in both. Preventive/prophylactic swallow exercise programs have been encouraging. Chemoradiotherapy effects on voice have been identified in terms of acoustic, aerodynamic, and patient and clinician-rated perception of function. Improvement in voice has also been observed over time after chemoradiotherapy. Voice therapy has been found to have a positive impact on voice and perceptual measures in this population.

Summary—Current studies show some improvement in swallow function after swallow and voice therapy in patients treated with chemoradiotherapy. Further, there is a suggestion of improved swallow function with sparing of organs with specific radiotherapy protocols. Future research needs to focus on specific voice and swallow treatment regimens in the head and neck cancer patient treated with chemoradiotherapy, specifically, timing, frequency, duration, and specific treatment types.

Keywords

chemoradiotherapy; dysphagia; swallowing; voice

Introduction

Radiotherapy alone or in combination with chemotherapy is commonly used to treat cancer of the head and neck. However, dysphagia is a common sequela of treatment and may occur because of a variety of factors. Mucositis, nausea, lack of appetite, fatigue, reduced or altered taste, or tissue fibrosis can contribute to reduced eating ability and impaired quality of life (QoL) [1–3,4•]. Approximately 80% of patients undergoing radiotherapy develop mucositis [5]. Problems with chewing food, meal consumption time, pleasure in eating, xerostomia, trismus, sticky saliva, food sticking in the throat and mouth, and choking result in a major negative impact on QoL [1–3,4•,6].

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Altered fractionation radiotherapy, concurrent chemoradiotherapy, and induction chemotherapy paired with chemoradiotherapy have shown improvement in local control and survival for head and neck cancer patients [7–11]. However, these treatments resulted in increased mucositis and swallowing impairment [12,13].

Radiotherapy may also impact on voice if the larynx is included in the treatment field. Radiotherapy to the larynx has been found to result in muscle atrophy, fibrosis, dryness of the laryngeal mucosa, hyperemia, and erythema [14,15]. Voice changes following radiotherapy may include reduced vocal loudness, low modal speaking pitch, reduced phonic breath support, vocal roughness, breathiness hoarseness, and vocal fatigue [16–18]. Phonatory function testing revealed impairment in acoustic and aerodynamic voice measures [19–21]. Voice variability and unpredictability after radiotherapy is a frequent complaint [22].

Effects of chemoradiotherapy on swallowing

Radiotherapy can have a major impact on oral and pharyngeal phase swallow functioning. Studies [23–25,26•,27•] have found oral phase impairment includes reduced range of lingual motion, reduced lingual strength, impaired bolus formation, impaired bolus transport through the oral cavity, prolonged oral transit times, and increased oral residue percentages. Pharyngeal phase swallow impairment in this population can include impaired tongue base posterior movement, impaired velopharyngeal closure, delayed triggering of the pharyngeal swallow, reduced pharyngeal contraction, reduced hyoid and laryngeal motion, reduced laryngeal vestibule and glottic closure, and reduced opening of the upper esophageal sphincter, resulting in impaired bolus clearance and aspiration [23,24,27•,28–32]. Specifically, the timing, strength, and coordination of pharyngeal structural movement contribute to reduced bolus clearance through the pharynx as well as aspiration, typically after the swallow and often silent [28–37]. Research has shown that the cough reflex is impaired/absent in the irradiated head and neck cancer patient [38]. Reduced tongue base and pharyngeal wall pressures have been found to correlate with impaired bolus clearance and pharyngeal residue that can be aspirated in head and neck cancer patients [39•]. Reduced lingual strength correlates with oral transit times, percentage oral residue, and oropharyngeal swallow efficiency (OPSE) [40], a global measure of swallow safety and efficiency [40], in a group of oral and oropharyngeal cancer patients treated with radio/chemoradiotherapy [25]. A follow-up study [26•] in this population examined the effects of chemoradiotherapy over a 12-month period. Interestingly, tongue strength did not correlate with swallow measures. However, there was a significant correlation between lingual strength and percentage oral intake in these patients. Tongue strength was significantly impaired 1-month postradiotherapy and improved over the course of the year. Diet type also followed this pattern [26•].

Other specific swallow motility disorders correlate with oral intake. Pauloski *et al.* [41] examined oral intake over a 12-month period. Swallow motility disorders significantly related to oral intake varied by evaluation point, with reduced tongue base retraction and reduced laryngeal elevation most related to oral intake at 1 month, delayed pharyngeal swallow, incomplete laryngeal vestibule closure, reduced laryngeal elevation and a rating of nonfunctional swallow at 3 months, and reduced cricopharyngeal opening at 6 and 12 months after chemoradiotherapy. This last disorder is not surprising, as cricopharyngeal stricture is frequently seen as a late swallowing impairment after primary chemoradiotherapy [33] as well as postoperative radiotherapy after total laryngectomy [42]. A recent study by Logemann *et al.* [43•] also examined swallow motility disorders in a group of 48 patients treated with radio/chemoradiotherapy over a 12-month period. Results indicated that oral and pharyngeal phase swallow motility disorders increased in frequency over the three time points, with frequency of functional swallow decreased significantly from baseline to 3 months after radiotherapy, with some improvement was seen by 12 months. Interestingly, Salama *et al.* [13] found that

patients with more advanced T stages were less likely to have worsened swallow functioning and more likely to improve in swallow function after concurrent chemoradiotherapy. Additionally, these patients were more likely to demonstrate improvement in swallow functioning following completion of their treatment.

Newer strategies with intensity-modulated radiotherapy (IMRT) have been developed to spare structures related to swallowing. Eisbruch *et al.* [33] identified pharyngeal phase abnormalities that correlated with anatomic changes in pharyngeal structures, as examined by videofluoroscopy, endoscopy, and computed tomography imaging in patients after chemoradiotherapy to the head and neck. Structural damage to the pharyngeal constrictors and larynx was found. In this study, patients having undergone IMRT demonstrated sparing of these structures as compared with standard three-dimensional radiotherapy. Further, dosage of radiotherapy was found to correlate with swallow functioning and aspiration. A follow-up study by Feng *et al.* [44•] revealed similar findings in a group of nasopharyngeal and oropharyngeal cancer patients treated with chemo-IMRT, in which higher doses to the pharyngeal constrictors and glottic/supraglottic regions significantly correlated with impairment in bolus clearance through the pharynx secondary to reduced tongue base, pharyngeal constrictor, and laryngeal elevation for swallowing. This study highlights the need to further modify radiation dosage to spare swallowing structures.

Late effects of radiotherapy on swallowing

Dysphagia can occur long after completion of radiotherapy [30,31,45,46]. Patients with persistent dysphagia at least 1 year after treatment have been rated as having grades 5–7 (moderate-to-severe with aspiration) swallow impairment [46]. Studies have found impairment in swallowing up to 40 years after completion of treatment [47]. It is believed that tissue fibrosis contributes to impaired structural movement, with reduced overall extent (i.e., less than normal excursion/distance) and more sluggish movement [31]. Tongue strength and tongue base function for swallowing are impaired in patients with varied head and neck tumor sites treated with radiotherapy [45] and have been found as early and late impairment. It is clear that regardless of tumor locus, tongue function for swallowing can become impaired if the oropharynx is within the treatment volume due to neck disease. Tongue strengthening exercise programs might reduce the risk of long-term impairment. Advanced T stage has been found to be a risk factor related to severe late toxicity [48].

Malnutrition and weight loss have been found in patients treated with radio/chemoradiotherapy [4•,49,50]. In a retrospective study [49] examining long-term malnutrition and QoL in patients treated for head and neck cancer with surgery and adjuvant chemoradiotherapy, malnutrition rates were highest in patients treated with chemoradiotherapy. Further, QoL was worse in patients treated with chemoradiotherapy [49]. A prospective study [4•] assessing QoL and nutrition over 24 months in patients treated with chemoradiotherapy for nasopharyngeal cancer found a mean weight loss over the 24 months to be 8% (range 3–22%). Despite a significant drop in global health status over the 24-month period, QoL was stable or significantly improved. When examining toxic effects, significant correlations were found between dysphagia and social eating. Thus, nutritional support is critical to maintain adequate nutrition and QoL in these patients.

Voice after primary chemoradiotherapy: instrumental and perceptual assessment

Vocal fold lubrication and hydration are important for phonation. Voice problems after radiotherapy may be attributed to observable dryness of the laryngeal mucosa, muscle atrophy, fibrosis, hyperemia, and erythema. A recent study [51] of human laryngeal glands after

radiotherapy found the average size and density of serous and mucous cells within laryngeal glands to be decreased and atrophic in the irradiated larynx. Thus, the quantity and quality of secretions is altered after irradiation, likely contributing to less lubrication of the vocal folds and subsequent voice problems. Several studies have examined QoL, acoustics, and patient and clinician-based perception of voice quality after radiotherapy or chemoradiotherapy. Voice-related QoL has been found to be better in patients after chemoradiotherapy compared with salvage laryngectomy [6,52]. When examining acoustic and perceptual voice measures after primary radiotherapy, several recent studies [23,53•,54•,55,56,57•] have found impairment of function, although severity varied. Electroglottographic (EGG) analyses of voice have revealed superior voice outcomes after primary chemoradiotherapy compared with patients with total laryngectomy and transesophageal puncture (TEP), with improvement over a 12-month period in the chemoradiotherapy group [54•]. In postradiotherapy nasopharyngeal cancer patients, EGG analysis of vocal fold vibratory behavior revealed higher speech quotient, a ratio of glottic opening time to closing time, and lower open quotient, an indication of longer closed phase relative to open phase in the cycle in these patients as compared with healthy controls [58]. Both of these measures reflect increased vocal tension or resistance [58]. These authors also found lower signal-to-noise ratios, indicative of voice abnormality [58]. Others have found abnormal perturbation scores and abnormal perceptual ratings in patients treated with radio/chemoradiotherapy to the larynx [23,53•,55,57•]. Abnormal measures of jitter, shimmer, harmonics-to-noise ratio, and fundamental frequency (i.e., increase in fundamental frequency) have been seen in irradiated laryngeal cancer patients as well [53•]. However, improvement in acoustic measures and QoL have been seen up to 12 months after treatment, though still below normal range [53•]. Patient-rated QoL using the Voice Handicap Index has revealed up to 87.8% with abnormal voice rating after irradiation to the larynx, although with slight-to-moderate dysfunction [56,57•]. Abnormal acoustic and aerodynamic measures are attributed to impairment of vocal fold vibration, as observed stroboscopically, with incomplete closure and reduced mucosal wave, as well as observed ventricular activity, the latter indicative of hyperfunction [57•].

Evaluation and treatment of swallowing problems after chemoradiotherapy

Instrumental examination of swallowing is critical when defining the physiologic swallowing abnormalities and determining whether therapeutic strategies might result in safer and more efficient swallowing in these patients. Instrumental techniques include the modified barium swallow procedure (videofluoroscopy) and flexible endoscopic evaluation of swallowing (FEES) [59–63]. Therapeutic strategies utilized during these instrumental procedures include postures, swallow maneuvers, and sensory enhancements to improve swallow functioning [61,64]. Manometry is useful when examining oral and pharyngeal pressure generation and upper esophageal sphincter function during the swallow, particularly when paired with fluoroscopy to provide information on oral and pharyngeal structural movement simultaneous with pressure information [35,39•,65].

Swallow maneuvers can modify various aspects of the pharyngeal motor response. The Mendelsohn maneuver and Shaker exercise focuses on increasing the extent and duration of hyolaryngeal movement, thereby increasing the width and duration of upper esophageal sphincter opening [66,67]. The super supraglottic swallow maneuver assists in early airway closure (i.e., glottic and supraglottic) for added airway protection [64,68,69]. These maneuvers can not only improve the extent of pharyngeal structural movement but also improve timing and coordination of pharyngeal structural movement during swallowing [70,71]. The tongue-hold maneuver is designed to improve pharyngeal constrictor motion, which is frequently impaired in these patients [72].

Postures may change bolus flow through the oral cavity and pharynx, rather than alter swallow physiology. These include chin tuck, head back, head tilt, head rotation, and lying down to improve bolus flow and clearance through the oral cavity and pharynx [73]. They also afford greater airway protection (i.e., chin tuck and head rotation) as well as improved bolus clearance in unilateral oral and pharyngeal impairment [73]. Effects of postures and maneuvers are determined during the examination, as is specific swallow treatment to address the physiologic swallow disorders defined during the instrumental examination.

Patients after chemoradiotherapy often need to be followed for extended periods with the goal of return to optimal/normal diet, G-tube removal, or both. It is critical that patients are followed long after chemoradiotherapy to ensure adequate oral nutrition. Adding oral nutritional supplementation with weekly counseling by a registered dietician has had a positive impact on outcomes regarding weight loss and rate of percutaneous endoscopic gastrostomy (PEG) tube placement [74]. Nutritional supplement was associated with a 37% relative reduction in weight loss in patients treated with chemoradiotherapy. Weight loss has been found to correlate significantly with treatment interruption, early mortality, infection, hospital readmission, and survival in noncompliant patients [75]. Thus, it is critical that health professionals work as a team to achieve optimal nutritional status, swallow rehabilitation, and QoL.

Once patients have returned to optimal oral diet intake, it has become common practice to recommend continued daily practice of swallow exercises [45]. This is based on the current data regarding effects of radiotherapy on swallowing long after completion of treatment, as discussed previously. Unfortunately, patients are often reticent to practice if they feel their swallowing has improved or normalized and, therefore, need strong encouragement to practice to reduce the risk of swallowing problems at a later date.

Treatment of voice after chemoradiotherapy

Voice therapy following chemoradiotherapy focuses on vocal hygiene, direct voice therapy, and helping the patient to produce voice without using inefficient compensatory behaviors such as increased laryngeal strain and supraglottic constriction [22]. Few studies have examined outcome of voice therapy in irradiated patients. One recent study by van Gogh *et al.* [76••] examined the effect of voice therapy in patients treated with radiation for early glottic cancer. These authors examined a variety of measures and found voice therapy to be effective in a voice-therapy group as compared with randomly assigned control (no therapy) group. Patient self-rating with the Voice Handicap Index, clinician perceptual rating, as well as acoustic and videostroboscopic assessment were shown to improve after voice therapy [76••]. Perceptual ratings of vocal fry significantly decreased in the experimental group, as did jitter and harmonics-to-noise measures. Interestingly, there were no changes in vibratory function after therapy for either group, as observed stroboscopically. Clearly, there is a need for more studies examining the efficacy of voice therapy in the irradiated head and neck cancer patient.

Prevention of swallowing problems in patients undergoing chemoradiotherapy

Because approximately 44% of patients experience difficulty swallowing following chemoradiotherapy [77], it has become fairly common practice to provide preradiotherapy instruction in swallow exercises designed to preserve range, rate, coordination, and flexibility of the vocal tract musculature involved in swallowing [73]. These exercises focus on maintaining tongue, jaw, pharyngeal constrictor, hyolaryngeal elevation and anterior motion, airway closure, and upper esophageal sphincter opening. This treatment regimen typically includes tongue range of motion, tongue strengthening, tongue base range of motion [i.e., effortful swallow, tongue-hold maneuver, and tongue base retraction exercise (gargle)], jaw

range of motion (as indicated), pharyngeal constrictor exercise (tongue-hold maneuver), hyolaryngeal elevation/upper esophageal sphincter opening exercises (Mendelsohn maneuver and Shaker exercise), and airway closure exercises (i.e., super supraglottic swallow). Patients are instructed to perform these exercises on a daily basis during chemoradiotherapy.

Data are emerging that support the efficacy of swallow exercise programs during radio/chemoradiotherapy. Two studies [78,79] have shown potential benefit to patients undergoing primary radio/chemoradiotherapy, with improvement in both QoL and pharyngeal phase swallow functioning as compared with control (no exercise) groups. Unfortunately, in one of these studies, PEG tube removal did not differ between groups, with no significant difference in ability to maintain oral nutrition. A recent randomized, controlled study [80] examined two types of swallow exercise programs (standard vs. standard and tongue strengthening exercises) in oral/oropharyngeal cancer patients administered 1 month after chemoradiotherapy. Results revealed no change in tongue strength between or across groups. However, improved QoL was seen in the treatment group as compared with controls [81].

Conclusion

The effects of chemoradiotherapy can have a major impact on swallowing, voice, and QoL. Dysphagia is only one of many variables that may have an impact on swallowing. Future studies are needed to determine optimal radiotherapy regimens to minimize oral, pharyngeal, and laryngeal structural damage that impacts voice and swallowing, as well as minimize side effects of chemoradiotherapy that impact oral intake such as mucositis, taste alterations, and appetite loss. Studies examining the utility of exercise programs during chemoradiotherapy on maintenance of swallowing are somewhat encouraging. However, future studies need to examine other swallow treatment paradigms, examining variables, including specific swallow exercise protocols, with focus on timing, frequency, and duration of exercise programs to optimize function for swallowing. Further, future studies should examine utility of swallow exercise programs on a long-term basis, for up to 5–10 years to determine whether swallow function and oral intake are maintained over time. Finally, additional studies examining the effects of specific voice therapy regimens in this population are needed, as are studies examining timing, frequency, and duration of treatment.

Acknowledgments

The author's work was supported by a grant from NIDCD R03 DC007497-02.

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Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 000–000).

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