Pharyngeal Transport Dysfunction Consequent to an Organ-Sparing Protocol

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Objective: To investigate the effects of a protocol of concomitant intravenous hydroxyurea and hyperfractionated, accelerated, external-beam radiation therapy on the swallowing mechanism of patients with advanced-stage head and neck cancer.

Design: Posttreatment videofluoroscopic swallow function studies, using images of single-bolus swallows of low-density liquid barium, were analyzed in real time, slow motion, and frame by frame using an integrated system that allows objective analysis of video recordings through image processing and digitization (Kay Elemetrics Computerized Swallowing Station). Radiological descriptors were used for pharyngeal transport abnormalities, and temporal measures were obtained of structural movements.

Setting: Academic, tertiary care, referral medical center.

Patients: Fifteen consecutive patients with previously untreated, stages III and IV, nonmetastatic squamous cell carcinoma of the head and neck who underwent a phase 1 study of prolonged infusion hydroxyurea therapy in combination with hyperfractionated, accelerated external-beam radiation therapy for their disease.

Results: All patients had anterior pharyngeal segment dysfunction, characterized by no epiglottic movement and slowed laryngeal motility (1.011 ± 0.379 seconds [mean ± SD]). Anterior pharyngeal dysfunction was more severe in patients with primary tumors of the hypopharynx than in those with cancer of the oropharynx. Twelve (80%) of our patients demonstrated posterior pharyngeal segment dysfunction characterized by impaired pharyngeal constrictor motility. All 15 patients displayed pharyngeal stage abnormalities that limited bolus transport and clearance.

Conclusions: Severe pharyngeal physiological abnormalities were present that led to impaired bolus transport and that were frequent and debilitating consequences of this organ-sparing protocol. Long-term follow-up of this group will be required to assess the permanence of the abnormalities.


Severe dysphagia is a frequent and debilitating consequence of head and neck cancer resection.1-7 Patients who have undergone major resections for cancer of the oral cavity, oropharynx, hypopharynx, and larynx experience varying degrees of swallowing difficulty. The nature and extent of the swallowing disability are related to the site and size of the tumor and the method of treatment,8 with increasing size of the resection being associated with a greater impairment of swallowing.8,9 The type and method of reconstruction also have a substantial effect on deglutition and associated neurologic deficits.

Although radiation therapy does not result in the removal of structures necessary for effective swallowing, it impairs swallowing ability.10 Specifically, irradiation causes fibrosis of the pharyngeal muscles, with resultant impairment of pharyngeal contraction, and fibrosis of the soft tissues, which impairs laryngeal elevation.11 When the salivary glands are included in the radiation field, the resultant xerostomia and hyposalivation further impair mastication and the initiation of the swallowing reflex.12

The role of combined-modality treatment with chemotherapy and radiation therapy in an organ-sparing context has recently been investigated as an alternative to ablative surgery for advanced-stage disease. The effects of combined-modality therapy on swallowing have not been frequently evaluated.13,17 Among patients with oral and pharyngeal tumors treated with external-beam irradiation and adjuvant chemotherapy, reduced swallowing efficiency and tongue base and laryngeal movement...
disorders have been documented. Among patients with oral, oropharyngeal, and hypopharyngeal carcinomas receiving concurrent chemotherapy and radiation therapy, multiple swallowing deficits were noted, including impairment of laryngeal elevation, epiglottic movement, and pharyngeal stripping. The purpose of our study was to investigate the physiological effects of organ-sparing protocols on swallowing among patients with advanced-stage non–laryngeal head and neck carcinoma who were treated with concomitant hyperfractionated, accelerated, external-beam radiation therapy and intravenous hydroxyurea therapy (XRT-HU).

RESULTS

PHARYNGEAL TRANSPORT

All 15 patients treated with XRT-HU demonstrated abnormal pharyngeal transport for liquid bolus swallows following completion of their therapy. All presented with multiple pharyngeal stage abnormalities affecting bolus transport through, and clearance from, the pharynx. Furthermore, all patients displayed anterior pharyngeal segment dysfunction with impairment of both epiglottic and laryngeal motility. Of the 15 patients, 12 (80%) had posterior pharyngeal segment dysfunction with impairment of pharyngeal constrictor motility.

All 15 patients had anterior segment dysfunction. All of the study patients demonstrated epiglottic dysmotility, defined as restricted or limited range of motion. Fourteen (93%) patients had normal vertical positioning of the epiglottis at rest, and 1 had horizontal epiglottic malpositioning at rest. No epiglottic movement from a vertical or horizontal resting position to partial or complete inversion was evidenced during the swallows in all 15 patients. Twelve (80%) of the 15 patients treated with XRT-HU had vallecular residua after the swallow study, and this was in concordance with supraglottic laryngeal stasis (χ² = 12.86; p < 0.001).
An evaluation of laryngeal motility demonstrated adequate timing of the start of laryngeal elevation associated with the swallow response. In contrast, the speed of laryngeal motion during swallowing was impaired, with a mean (SD) onset time of laryngeal elevation of 0.146 (0.169) seconds and a range of 0.033 to 0.528 seconds. The patients’ onset times of laryngeal elevation were within the temporal standards reported by Logemann \(^{21}\) for normal adult subjects (up to 0.2 seconds) and for adults older than 60 years (0.5 seconds). The mean (SD) duration of laryngeal motion from the start of superior movement of the larynx to its return to rest was 1.011 (0.379) seconds, with a range of 0.429 to 1.792 seconds. Using Logemann’s standard of 0.32 seconds for pharyngeal transport of small-volume bolus swallows, \(^{21}\) all patients had an increased duration of laryngeal motion during the swallow study. Patient subgrouping was then performed according to the site of tumor and a maximum pharyngeal transport time of 1 second. \(^{21}\) Wilcoxon signed rank testing revealed significant differences in duration between tumor site subgroups, with patients with hypopharyngeal cancer having a significantly longer duration of laryngeal motion during the swallow study than those with oropharyngeal cancer (\(P = .03\)).

**LARYNGEAL MOTILITY**

The surgical approach to the treatment of advanced-stage head and neck cancer can be influenced by the resultant severe impairments of swallowing function. Investigation of combined-modality chemoradiation and radiation therapy is based on the premise that the preservation of structure will result in the preservation of function. Our experience with radiation treatment alone reveals that serious functional consequences may arise following nonoperative therapy. The xerostomia, fibrosis, edema, and mucositis caused by radiation treatment all have an adverse effect on swallowing function. With concomitant chemotherapy, the detrimental effect on swallowing function may be even greater and must be closely examined.

Studies by Lazarus et al \(^{13}\) and Koch et al \(^{14}\) have shown severely impaired swallowing function in patients with oral and pharyngeal cancers that were treated using chemotheraphy and radiation therapy for organ preservation. The use of XRT-HU produced similar results of debilitating pharyngeal dysphagia, characterized by the inability to successfully transport a small-volume liquid bolus through the pharynx into the esophagus due to multiple pharyngeal stage abnormalities. Specifically, epiglottic dysmo-
sity was seen in all patients, with all but 1 patient showing epiglottic enlargement. The duration of laryngeal motion on bolus swallows was increased for all patients, but those with hypopharyngeal tumors showed substantially longer durations of laryngeal motion during the swallow than patients with oropharyngeal tumors. Consistent with patients' increased laryngeal motion time was delayed closure of the laryngeal vestibule, resulting in supraglottic penetration. Glottic aspiration, however, was observed in only 4 (27%) study patients and was not responsible for the patients' inability to tolerate oral feeding. Most of the patients showed dysfunction of the pharyngeal constrictors, the muscles primarily responsible for moving a bolus through the pharynx and clearing it. Ideally, all patients would have been analyzed within the first 3 to 4 months following therapy, to identify the short-term effects of the treatment regimen. In some patients, however, the dysphagia was so pronounced that an earlier evaluation could not be performed, and patient compliance issues required delay in others. Swallowing often improves over time, or stabilizes rather than worsens, and our data show no association between the timing of the study and the severity of abnormalities.

An objective and standardized evaluation of the swallowing function is necessary not only to clearly describe the effects of combined-modality treatment but also to provide as a basis for appropriate comparison with other treatment modalities, including conventional surgical resections. This has become even more important as recent investigations of the chemoradiotherapy approach to the treatment of head and neck cancer have not consistently demonstrated increased survival rates. Quality-of-life issues will play an even greater role in determining treatment. In a study to assess patients' perceptions of the changes in swallowing function after undergoing concurrent chemoradiotherapy and irradiation for the treatment of head and neck cancer, Murry et al. noted that a treatment-related decline in quality of life was observed that varied according to disease site (oropharynx, hypopharynx, and larynx), with the greatest decline observed in patients with hypopharyngeal carcinoma. This is consistent with our finding of a greater impairment of laryngeal motion among patients with hypopharyngeal primary tumors and validates the relationship between impairment of swallowing function and the perception of swallowing dysfunction.

The physiological abnormalities demonstrated in this study, both anterior and posterior segment, were marked when compared with previously published norms and were, though more pronounced, than those observed with radiation therapy alone. The prior studies of swallowing abnormalities following organ-sparing chemoradiotherapy have been limited by small numbers or a lack of objective findings and a reliance on subjective patient-based questionnaires, and these studies have demonstrated less severe abnormalities than those described in the present study. This may be due to the different treatment regimen used, both in the type of chemotherapy and the more aggressive radiation therapy regimen used or to the bulky tumors present in these patients. The conclusions that can be drawn from this study are limited by the lack of pretreatment swallowing studies; however, all patients were swallowing before their therapy. Increased abnormalities were seen in those patients with hypopharyngeal carcinomas, which may have long-term quality-of-life effects in these patients. These findings suggest that the preservation of structure by itself does not guarantee the preservation of function and that further studies on these important quality-of-life issues are clearly indicated. A randomized trial would eliminate any patient selection factors.

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REFERENCES