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Radiation dose to the floor of mouth muscles predicts swallowing complications following chemoradiation in oropharyngeal squamous cell carcinoma

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SUMMARY

Objectives: While radiation dose to the larynx and pharyngeal constrictors has been the focus of swallowing complications, the suprahyoid muscles, or floor of mouth (FoM) muscles, are critical for hyoid and laryngeal elevation and effective bolus diversion, preventing penetration and aspiration. We hypothesize that radiation dose to these muscles may be important in the development of dysphagia.
Materials and methods: We studied 46 patients with OPSCC treated with CRT and who underwent baseline swallowing evaluations and post-treatment videofluoroscopic swallowing studies (VFSS) from 2007 to 2010. Patients with abnormal penetration aspiration scores (PAS > 2) served as the study population and patients with normal PAS scores ($\leqslant$2) served as the control cohort. Three suprahyoid muscles and two extrinsic tongue muscles were individually delineated and collectively referred to as the FoM muscles. Radiation dose-volume relationships for these muscles were calculated. Univariate logistic regression analysis was used to determine parameters of significance between patients with normal or abnormal PAS scores. A multivariate regression analysis was subsequently performed to isolate the most statistically critical structures associated with abnormal PAS.
Results: Univariate analysis resulted in significance/borderline significance of multiple structures associated with abnormal PAS following irradiation. However, when a multivariate model was applied, only the mean dose to the floor of mouth and minimum dose to the geniohyoid were associated with post-radiation abnormal PAS.
Conclusions: The dose and volume delivered to the collective FoM muscles may be associated with an increased risk of laryngeal penetration/aspiration to a greater degree than previously recognized organs at risk.

Introduction

Over the past 30 years, various treatment intensification strategies to increase local–regional control rates for the management of oropharyngeal squamous cell carcinomas (OPSCC) has led to an increase in dysphagia as a late sequela of treatment of head and neck cancers [1–4]. Severe dysphagia has been well documented to contribute to decreased quality of life expectations for these patients [5]. As such, increasing our understanding of this complication has received significant attention.

The relationship between the dose of radiation to specific sites of the swallowing apparatus and subsequent dysphagia has been well studied. In 2004, Eisbruch et al. were the first to highlight the pharyngeal constrictors and the larynx as critical structures in the development of dysphagia [6]. In a prospective study of 36 patients with Stage III-IV oropharyngeal or nasopharyngeal cancer, Feng et al. found that the mean doses to the pharyngeal constrictors and the supraglottic larynx were significantly higher in patients who reported aspiration compared to those who did not. Additionally, none of the patients that received mean doses <60 Gy aspirated [7]. Levendag et al. reported a 19% increase in the probability of dysphagia for every 10 Gy beyond a dose of 55 Gy to the pharyngeal constrictors [8]. Other studies have found similar relationships between dysphagia and the dose received to the pharyngeal constrictors and supraglottic region [8].

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Although previous dosimetry studies have primarily examined the pharyngeal constrictors and laryngeal structures, the muscles of the floor of the mouth (or suprahyoid muscles) also play a key role in safely transitioning the food bolus from the oral through the pharyngeal phase. To date, limited data exist describing dysphagia as a function of the radiation dose received by the floor of mouth (anterior digastrics [AD], mylohyoid [MH], geniohyoid [GH], and hyoglossus [HG]) and the genioglossus [GG] muscle in the oral tongue. Hirano et al. examined the incidence of postoperative dysphagia and found that removal of the geniohyoid or mylohyoid muscles was significantly associated with poor swallowing function [9]. Contraction strength of the mouth floor muscles determines the upward movement of the larynx, a key determinant of airway protection during swallowing [10]. Laryngeal elevation pulls the larynx away from the posterior pharyngeal wall, diverting the bolus towards the upper esophagus and away from the airway [11]. This function is critical to the prevention of penetration and aspiration of the food bolus into the endolaryngeal space. Despite this critical function, the relationship between the radiation dose to these muscles and its impact on swallowing function has not been evaluated.

As such, we hypothesized that radiation dose to the floor of mouth muscles in patients with OPSCC would be associated with an increased risk of dysphagia including penetration and aspiration of the food bolus given the importance of these muscles in maintaining airway protection.

Methods

Patient selection

Eligible patients were identified in our institutional database (Oncospace) for our analysis treated with definitive doses of radiation between 2007 and 2011. Inclusion criteria included patients treated with a definitive course of chemoradiation to an oropharyngeal primary site having both a complete pre- and post-treatment swallow study with a retrievable treatment plan for data-analysis. Intensity modulated radiation therapy was used in the treatment of all patients on this analysis. Prescribed dose to the tumor volume and involved nodes was 70 Gy in 1.8–2 Gy fractions, with standard dose to high risk (63 Gy) and low risk (57 Gy) nodal volumes. Patients with pre-radiation dysphagia were excluded from analysis.

Critical structure delination and dosimetric analysis

Contouring was performed on the Pinnacle planning software (Philips Healthcare, Andover, MA) version 9.0. The patient's treatment plan was utilized for normal structure delineation. The treatment plan, including treatment beams, dose, and isocenter placement, were not altered. Standard normal structures, including the larynx, pharyngeal constrictors, oral mucosa, and parotid glands, were delineated on the patient's planning CT scan as directed by the senior investigator (HQ).

Delineation of the FoM muscles was completed by two independent investigators with the oversight of both the senior investigator and expert anatomist (EM) on the planning CT scan, all of whom were blinded to the patient's swallowing outcome (Fig. 1). The methodology for the identification and contouring of these structures is provided in the submitted supplementary material (Appendix e1). The radiation treatment plan was recomputed with the additional critical structures (GH, GG, MH, AD, HG, FoM) and the resulting dose was calculated and recorded. The FoM composite contour included the GH, MH, AD, and HG. The GG was not included as a FoM muscle as laryngeal elevation is not its direct function.

Specific dosimetric values of interest in this analysis included minimum, maximum, mean, and volumetric dose to the previously noted muscles and muscle groups. The minimum dose represents the minimum measurable dose to the muscle, the maximum dose represents the maximum measurable dose to the muscle, the mean dose represents the average dose to the muscle (total dose divided by volume), and the volumetric dose (V40, etc.) represents the percent volume of a muscle receiving *at least* the specified dose. For example, a V40 of 95.2 indicates that 95.2 percent of the muscle received at least 40 Gy. V50 for the larynx and constrictor

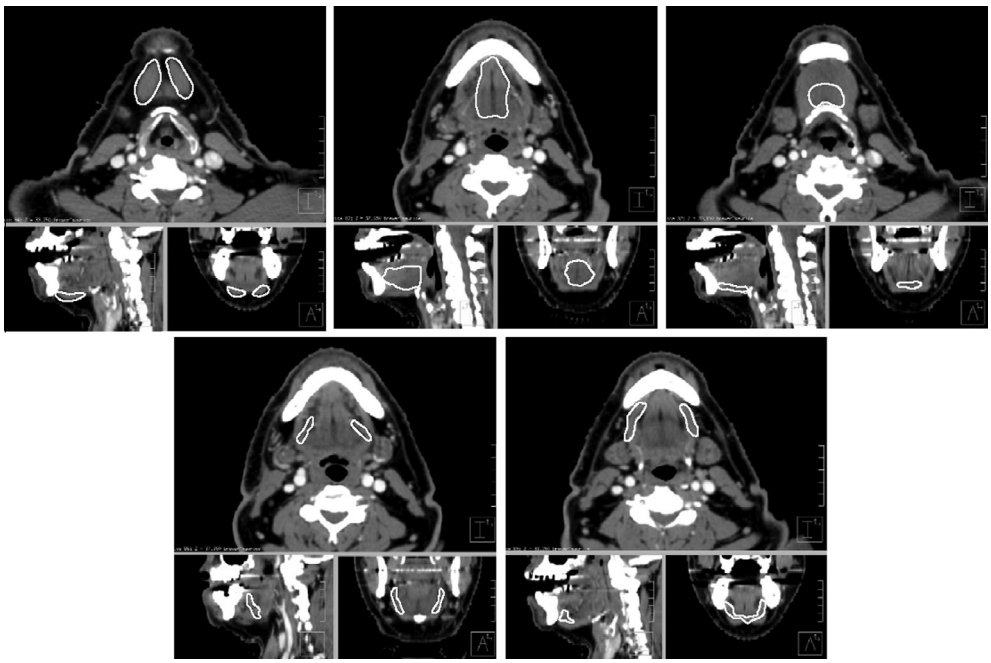

Figure 1. Representative contours of the muscles of the floor of mouth including (from left to right) anterior digastric, genioglossus, geniohyoid, hyoglossus, and mylohyoid.