Advances in Radiation Oncology (2018) ■■, ■■–■■

advances
in radiation oncology

www.advancesradonc.org

Scientific Article

Preservation of swallowing function with de-intensified chemoradiation therapy for HPV-associated oropharyngeal squamous cell carcinoma

Greg D. Judy MD [a,b,*], Rebecca Green MSW [a], Shannon L. Aumer MA [c], Robert J. Amdur MD [d,e], Xianming Tan PhD [b], Nathan Sheets MD [f], Mark Weissler MD [c], Adam Zanation MD [c], Samip Patel MD [c], Trevor Hackman MD [c], William M. Mendenhall MD [d,e], Bhishamjit S. Chera MD [a,b]

[a] *Department of Radiation Oncology, University of North Carolina School of Medicine, Chapel Hill, North Carolina*
[b] *Lineberger Comprehensive Cancer Center, University of North Carolina Hospitals, Chapel Hill, North Carolina*
[c] *Department of Otolaryngology/Head and Neck Surgery, University of North Carolina School of Medicine, Chapel Hill, North Carolina*
[d] *Department of Radiation Oncology, University of Florida Hospitals, Gainesville, Florida*
[e] *Shands Cancer Center, University of Florida Hospitals, Gainesville, Florida*
[f] *REX/UNC Healthcare, Raleigh, North Carolina*

Received 24 December 2017; received in revised form 7 March 2018; accepted 9 March 2018

Abstract

Purpose: This study aimed to compare the swallowing function in patients with human papillomavirus–associated oropharyngeal squamous cell carcinoma treated with de-intensified chemoradiation therapy (6 weeks, 60 Gy) versus those receiving standard-of-care chemoradiation therapy (7 weeks, 70 Gy).

Methods and materials: A retrospective review was conducted of 78 patients with human papillomavirus–associated oropharyngeal squamous cell carcinoma with modified barium swallow studies pretreatment and 6 to 8 weeks posttreatment. The swallowing function was objectively scored for penetration, aspiration, and pharyngeal residue. Forty patients received de-intensified chemoradiation therapy (60 Gy image guided radiation therapy with weekly cisplatin 30 mg/m^2) and 38 patients received standard-of-care chemoradiation therapy (70 Gy image guided radiation therapy with chemotherapy of the medical oncologist's choosing). Univariate and multivariate analyses were performed to detect differences between the cohorts with regard to laryngeal penetration, aspiration, and pharyngeal residue. A multivariate logistic regression was used to determine the overall effect of treatment

Conflicts of interest: There are no known conflicts of interest for any of the authors.

* Corresponding author. University of North Carolina Hospitals, 101 Manning Drive, CB #7512, Chapel Hill, NC 27599.
E-mail address: Gregory.judy@unchealth.unc.edu (G.D. Judy).

https://doi.org/10.1016/j.adro.2018.03.002

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on the swallowing function. Patient-reported swallowing outcomes in de-intensified cohort were assessed with the European Organisation for Research and Treatment of Cancer Quality of Life Module for Head and Neck Cancer and the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events questionnaires.

Results: Patients treated with de-intensified chemoradiation therapy were associated with a suggestion of lower risk of developing overall swallowing dysfunction (odds ratio [OR], 0.62; $P = .07$), laryngeal penetration (OR, 0.63; $P = .12$), and pharyngeal residue (OR, 0.61; $P = .08$). The mean pre- and 2-year post-European Organisation for Research and Treatment of Cancer Quality of Life scores pertaining to swallowing (1-4 scale, higher worse) in the de-intensified cohort were 1.4 and 1.2 for liquids; 1.2 and 1.1 for purees; 1.5 and 1.7 for solids, 1.0 and 1.3 for choked when swallowing; and 9.0 and 10.8 for composite score, respectively. The mean pre- and 2-year post-Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events swallowing difficulty scores (1-5 scale, with higher scores being worse) were 1.5 and 1.8, respectively.

Conclusions: Compared with 7 weeks of 70 Gy, 6 weeks of 60 Gy de-intensified chemoradiation therapy appears to better preserve the baseline swallowing function (per objective modified barium swallow assessment). Patients treated with de-intensified chemoradiation therapy reported minimal changes in swallowing function.

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Introduction

Definitive chemoradiation therapy is a standard organ preservation treatment option for patients with human papillomavirus (HPV)-associated oropharyngeal squamous cell carcinoma (OPSCC). The standard chemoradiation therapy regimen has been a 7-week course of 70 Gy of radiation with concurrent high-dose cisplatin (100 mg/m^2) for 3 cycles. Dysphagia is a common long-term complication of chemoradiation therapy. Patient-reported rates of late (≥3 months) grade ≥2 dysphagia after chemoradiation therapy have been reported to be 12% to 21%, with rates declining with increasing time from completion of therapy.[1,2] Patients are also at risk for potential aspiration, permanent feeding tube dependence, and impairment in their overall quality of life (QoL).[1,3-8]

Improvements in radiation delivery with the use of intensity modulated radiation therapy (IMRT) have been shown to improve sparing of the pharyngeal constrictors and reduce radiation-related dysphagia when compared with conventional radiation therapy in treatment of head and neck cancers.[1,9,10] A dose-response effect has also been seen, with mean dose to the pharyngeal constrictor muscles, glottic, and supraglottic larynx correlating with aspiration, stricture formation, and reduced laryngeal elevation and being predictive of long-term swallow function.[9,11-13] Common dose constraints for pharyngeal constrictor muscles include a mean total dose 58 Gy, V40 85%, V50 76%, V60 61%, and V70 33%. For the larynx, dose constraints include mean total dose 48 Gy, V40 64%, V50 48%, V60 32%, and V70 13%.[9] Additional studies have shown slight variations in these constraints.[12]

In addition to improvements in radiation delivery, de-intensified treatment for HPV-associated OPSCC is currently being studied in an effort to further improve the treatment toxicity profile without a decrement in tumor response. At our institution, the de-intensification paradigm has been to reduce both radiation and chemotherapy.[14] Patients with favorable-risk HPV-associated OPSCC are treated on trial with a 6-week course of 60 Gy of IMRT with 6 concurrent weekly low doses of cisplatin 30 mg/m^2 (without induction chemotherapy or upfront surgery). We have conducted several prospective clinical trials to evaluate this regimen and carefully collected prospective objective (modified barium swallow [MBS] studies) and subjective (patient-reported outcomes [PRO] of symptoms and QoL) assessments of dysphagia from our trial patients. Also, as a standard practice at our institution, all patients with OPSCC regardless of receipt of de-intensified or standard-of-care chemoradiation therapy (ie, on/off protocol) are assessed with pre- and posttreatment MBS studies.

We hypothesize that swallowing function is better preserved in patients who receive de-intensified chemoradiation therapy. The primary aim of the current study is to compare objective swallowing function (using MBS results) in patients with HPV-associated OPSCC treated with de-intensified chemoradiation therapy (6 weeks, 60 Gy) versus those receiving standard-of-care chemoradiation therapy (7 weeks, 70 Gy). The secondary aim was to report on patient-reported swallowing outcomes for patients enrolled on our de-intensified chemoradiation therapy regimen.

Methods and materials

Study design and subjects

This is a single-institution, retrospective analysis that was performed on patients who underwent MBS studies pre- and post-chemoradiation therapy for pathologically confirmed

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