Oral Oncology 61 (2016) 41–46

Contents lists available at ScienceDirect

Oral Oncology

journal homepage: www.elsevier.com/locate/oraloncology

Oncologic outcomes and patient-reported quality of life in patients with oropharyngeal squamous cell carcinoma treated with definitive transoral robotic surgery versus definitive chemoradiation

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ARTICLE INFO

Article history:
Received 9 June 2016
Received in revised form 29 July 2016
Accepted 17 August 2016

Keywords:
Chemoradiotherapy
Head and neck cancer
Robotic surgical procedures
Oropharyngeal cancer
Squamous cell carcinoma
Quality of life
Treatment outcome

SUMMARY

Objective: It has been postulated that treatment outcomes are similar between transoral robotic surgery (TORS) and definitive chemoradiation (CRT) for oropharyngeal squamous cell carcinomas (OPSCC). We compared oncologic and quality of life (QOL) outcomes between definitive CRT and definitive TORS.
Materials and methods: An observational comparison study was performed on 92 patients treated with TORS ± adjuvant therapy and 46 patients treated with definitive CRT between July 2005 and January 2016. The Kaplan Meier method was used for survival analyses, and the Mann-Whitney test was used to compare QOL scores between groups.
Results: All patients had T0-T2 and N0-N2 disease, although CRT patients had higher clinical staging ($p < 0.001$). HPV+ disease was present in 79% (n = 73) of TORS patients and 91% (n = 19) of tested CRT patients. Median follow-up was 22.1 months (range: 0.33–83.4). There were no significant differences in locoregional control or overall survival between CRT and TORS groups. Definitive TORS resulted in better saliva-related QOL than definitive CRT at 1, 6, 12, and 24 months ($p < 0.001$, $p = 0.025$, $p = 0.017$, $p = 0.011$). Among TORS patients, adjuvant therapy was associated with worse QOL in the saliva domain at 6, 12, and 24 months ($p < 0.001$, $p < 0.001$, $p = 0.007$), and taste domain at 6 and 12 months ($p = 0.067$, $p = 0.008$).
Conclusion: Definitive CRT and definitive TORS offer similar rates of locoregional control, overall survival, and disease-free survival in patients with early stage OPSCC. TORS resulted in significantly better short and long-term saliva-related QOL, whereas adjuvant therapy was associated with worse saliva and taste-related QOL compared to TORS alone.

Background

Treatment regimens for oropharyngeal squamous cell carcinoma (OPSCC) have transformed over recent decades due to advancements in all treatment modalities [1–3]. Definitive chemoradiation is now the treatment of choice in most institutions, although this regimen is associated with severe acute and late toxicities which are further exacerbated by chemotherapy [4]. Common toxicities include mucositis, dysgeusia, and xerostomia resulting in increased risk of mucosal trauma and oral infections, all of which limit treatment success and detract from quality of life [5]. Given the increasing incidence of cases in younger patients with oral human papillomavirus (HPV) infection who have much improved long-term prognosis, the optimization of long-term post-treatment quality of life is of paramount significance.

Transoral robotic surgery (TORS) has been increasingly used for OPSCC over the last decade. Prior studies have suggested that TORS offers long-term oncologic and functional outcomes equivalent or superior to those of other surgical and non-surgical options [6–8] with decreased length of hospitalization and requirement for tracheostomy or permanent gastrostomy tube [3]. Patients managed by TORS alone score higher on patient-reported quality of life

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http://dx.doi.org/10.1016/j.oraloncology.2016.08.004
1368-8375/

(PR-QOL) indices in multiple domains compared to patients managed by TORS with adjuvant therapy [9–11]. However, few studies to date have directly compared oncologic outcomes and PR-QOL scores between TORS and definitive chemoradiation (CRT). Herein, we compare oncologic outcomes and PR-QOL scores between early stage OPSCC patients treated with definitive CRT and those treated with TORS ± adjuvant therapy at a single institution. We hypothesize that for select patients, definitive TORS offers non-inferior oncologic outcomes while potentially sparing short and long-term adverse effects on quality of life.

Materials and methods

Patient selection

A retrospective observational comparison cohort study was performed on 92 patients treated with definitive TORS with or without adjuvant therapy and 46 patients treated with definitive CRT between July 2005 and January 2016 at the University of Pittsburgh. Definitive TORS is defined in this paper as curative intent TORS with or without adjuvant therapy. All TORS patients had histology-confirmed OPSCC and T0-T2, N0-N2 disease. Definitive CRT patients were selected on the basis of those who had T0-T2, N0-N2 disease and who had also completed at least one post-treatment QOL survey.

Definitive TORS

Patients underwent definitive TORS with unilateral or bilateral neck dissection, depending on the extent of disease. Patients with N0 or N1 disease without extracapsular extension were managed with TORS alone. Patients were recommended adjuvant radiation therapy for adverse prognostic features such as $\geqslant$N2 disease, angiolymphatic or perineural invasion, and close (<3 mm) margins. Adjuvant CRT was offered for extracapsular extension or positive margins. Our institution defines close margins as <3 mm, consistent with the definition used in ECOG 3311 and supported by a recent study which reported an average closest margin of 2.82 mm among patients treated with transoral laser microsurgery [12].

Radiation therapy

All patients who underwent radiation therapy were treated with intensity-modulated radiotherapy (IMRT). Patients underwent a computed tomography (CT)-based planning scan on either a combined positron emission tomography-computed tomography (PET-CT) or helical CT scanner (GE Medical Systems, Milwaukee, WI, USA) with intravenous contrast. A custom relocatable thermoplastic mask was fabricated for each patient on the CT simulation table. All radiation treatments were delivered via 6 MV photons. Treatments for all patients were planned using either ADAC™ (Siemens Medical Solutions, Milpitas, CA, USA) or Eclipse™ (Varian Medical Systems, Palo Alto, CA, USA).

Follow-up

Patients were typically seen 2–4 weeks following radiation therapy or TORS depending on the severity of toxicities during treatment. Beyond 1 month, patients underwent follow-up by members of the multidisciplinary team at regular intervals. Selected low-risk TORS patients who had negative margins, N0 disease, no extracapsular extension, and no perineural or angiolymphatic invasion were managed without adjuvant therapy and did not receive follow-up imaging. For all others, treatment response was assessed using contrast-enhanced CT scans or PET-CT obtained 2–3 months after treatment completion. When local progression was suspected but questionable based on available imaging or clinical examination, biopsy was performed. University of Washington Quality of Life-Revised, Version 4 (UW-QOL V4) questionnaire scores were obtained at 1, 6, 12, and 24 months from the date of TORS or completion of definitive CRT. Surveys were pooled by time point into 4 categories (1 month, 6 months, 12 months, and 24 months after TORS or definitive CRT) for analysis.

Statistics

The chi-square test was used to assess for differences in baseline characteristics. Our primary oncologic endpoints were local and regional control. Local failure was defined as failure within the primary site, and regional failure was defined as failure within the cervical nodes. Secondary endpoints were distant control, disease-free survival, disease-specific survival, and overall survival. The log rank test was used to evaluate for significant differences in these endpoints between the definitive TORS and definitive CRT groups. For the survival analyses, patients were censured at death or last follow-up, whichever was latest. Our PR-QOL endpoints were the mean UW-QOL V4 scores at 1 month, 6 months, 12 months, and 24 months after treatment. The Mann-Whitney test was used to compare scores between groups. Patients who did not complete UW-QOL V4 forms at any given time point were excluded from this analysis. No adjustments were made for multiple testing. Because the most consistent finding was a difference in saliva-related QOL between CRT and TORS groups, we conducted a univariate linear regression analysis to investigate whether other factors such as age, gender, smoking history, HPV status, T classification, or N classification were potentially associated with this difference in QOL. We then performed a multivariate analysis using the factors identified as significant on univariate analysis. A p-value of <0.05 was considered statistically significant.

Results

Patient and treatment characteristics

A flow chart demonstrating our selection of definitive TORS patients for inclusion in this study is outlined in Fig. 1. See Table 1 for patient and tumor characteristics. Median age was 57 (range: 31–85) years, median Karnofsky Performance Status was 90 (range: 80–100), and 83% of patients were male, which was similar between groups. However, definitive CRT patients had significantly higher N classification and clinical staging ($p < 0.001$, $p < 0.001$) than definitive TORS patients. HPV+ disease was present in 79% (n = 73) of TORS patients and 91% (n = 19) of tested CRT patients, although HPV status was not tested in 54% of the CRT patients.

Definitive CRT patients received IMRT to a median dose of 72 Gy (range: 66–75.6 Gy). Of 92 patients who underwent TORS, 29 (32%) were not recommended to have adjuvant therapy because of low-risk features. Of the 63 (70%) who were recommended adjuvant therapy, 11 patients refused for personal reasons. Of the 52 (57%) TORS patients who underwent adjuvant therapy, 37 (71%) received CRT and 15 (29%) underwent RT alone. Eighty-two out of 92 TORS patients (89%) underwent selective neck dissections.

Oncologic outcomes

At a median follow-up of 22.1 months (range: 0.33–83.4), the local failure rate for the entire cohort was 4.3% (6.5% for definitive CRT, 3.3% for definitive TORS, $p = 0.48$). Overall regional failure rate was 4.3% (2.2% for definitive CRT, 5.4% for definitive TORS,