

ORIGINAL RESEARCH

Swallowing Function After Chemoradiation for Advanced Stage Oropharyngeal Cancer

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OBJECTIVE: Advanced-stage oropharyngeal cancer may be treated either surgically or nonsurgically. We reported previously functional outcomes after surgical resection with free-tissue transfer. In the present study, we evaluated swallowing function after combined chemoradiation for oropharyngeal cancer.

STUDY DESIGN AND SETTING: Retrospective review of 30 patients treated at a tertiary academic center for Stage III/IV oropharyngeal cancer with sequential or concurrent chemoradiation from 1994 to 2003.

RESULTS: Inclusion criteria were met by 27 of 30 (90%) patients. Most patients had base of tongue lesions (67%) and Stage IV disease (93%). Gastrostomy was carried out in 22 (82%) patients either before or during treatment. Three months after chemoradiation, 33% (9/27) were consuming all nutrition orally, 22% (6 of 27) were NPO, and 45% (12 of 27) had some oral intake but still required tube feeds. One year after treatment, 53% (10 of 19) had an exclusively oral diet whereas 47% still required tube feeds including 1 patient (5%) who was NPO. In patients without recurrence and follow-up length >1 year, 69% (9 of 13) were consuming all nutrition orally whereas 31% still required gastrostomy tube (G-tube) support. A higher rate of G-tube dependence was observed in patients treated for base of tongue lesions vs tonsil lesions (67% vs 25%, $P = 0.049$, χ^2 analysis).

CONCLUSIONS: At this institution, the short-term (3–4 months) rate of G-tube dependence was similar after surgical and non-surgical treatment of oropharyngeal cancer. One year after chemoradiation, 31% of patients without recurrence still required tube feeds.

SIGNIFICANCE: These results suggest that organ-preservation protocols do not reduce the prevalence of chronic dysphagia and G-tube dependence after management of oropharyngeal cancer.

EBM rating: C-4

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Oropharyngeal carcinoma is diagnosed in approximately 4,800 patients each year in the United States.¹ Surgical and nonsurgical treatment strategies are available for advanced stage oropharyngeal cancer. Organ preservation protocols, involving various combinations of chemotherapy and radiotherapy (XRT), have similar efficacy to surgical treatment in terms of locoregional control and survival.^{2–11} Treatment choice should therefore be based largely on functional outcomes after treatment.

Swallowing function may be affected adversely by surgical and nonsurgical treatment of advanced oropharyngeal cancer. Gastrostomy tube (G-tube) dependence 6 to 12 months after surgical management varies in the literature between 6% and 39%.^{12,13} Rates of swallowing dysfunction after chemoradiation for oropharyngeal cancer are less well defined. In a previous report, we evaluated G-tube dependence 4 months after surgical resection, free flap reconstruction, and postoperative radiation for advanced stage (Stage III/IV) oropharyngeal carcinoma.¹⁴ In that study, 50% of patients had an exclusively oral diet at 4 months, 20% had no oral intake, and 30% had some oral intake but still required tube feeds for nutritional support. The objective of the present study was to compare these results with the outcome of patients treated nonsurgically for similar tumors. To achieve this, we retrospectively reviewed swal-

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Table 1
Tumor staging and subsite location

Tumor site	Patients	Percentage
Pharyngeal wall	1	3.7
Tonsil	8	29.6
Base of tongue	18	66.7
Primary tumor		
T1	2	7.4
T2	5	18.5
T3	5	18.5
T4	15	55.6
Stage		
III	2	7.4
IV	25	92.6

lowing function in patients treated with chemoradiation for advanced stage oropharyngeal cancer at Oregon Health and Science University (OHSU).

MATERIAL AND METHODS

The radiation oncology database at OHSU was searched using International Classification of Diseases (ICD-9) codes to identify all patients who received radiation therapy for oropharyngeal cancer between 1994 to 2003. The subset of patients who received sequential or concurrent chemoradiation for Stage III/IV disease was then identified, producing a complete consecutive series of 30 patients. After obtaining IRB approval for a retrospective study, hospital and clinic charts for these patients were retrospectively reviewed, and the following data were recorded: patient gender, age and length of follow-up; tumor histology, stage and subsite; timing of placement and removal of G-tube tube if used; details of chemoradiation protocol including chemotherapy schedule, chemotherapeutic agents used, initiation and completion dates of radiotherapy and total radiation dose administered; requirement for G-tube feeds at 3 months, 6 months; and most recent follow-up after chemoradiation.

Only patients who received all treatment at OHSU and had a minimum of 3 months of post-treatment follow-up were included. Patients with any history of prior surgery, radiation, or chemotherapy to the head and neck were excluded. Patients with pre-existing neurologic or gastroenterologic disease affecting swallowing function were also excluded.

Swallowing outcomes were based on G-tube dependence, and patients were categorized into three groups: no oral intake; some oral intake but still requiring tube feeds; 100% oral intake with no tube feed requirement. Statistical analysis was carried out to determine whether patient age, tumor stage, tumor subsite or chemoradiation protocol affected swallowing outcome in terms of G-tube dependence. The χ^2 test was used for statistical analysis with significance set at the $P = 0.05$ level.

RESULTS

Thirty patients were identified that received chemoradiation for treatment of advanced-stage (Stage III/IV) oropharyngeal cancer. Tumor histology was squamous cell carcinoma in all patients. Three patients were excluded, including 2 who died during treatment from chemotherapy-related toxicity and had <3 months of post-treatment follow-up. The other excluded patient had undergone previous surgical resection and received chemoradiation as salvage treatment. Of the remaining 27 patients, 26 were male, mean age at time of treatment was 57 (range = 45-80 years) and mean length of follow-up was 23.2 months (range = 3.2-72.8 months). Tumor subsite and staging data is detailed in Table 1.

Eight patients (30%) received induction chemotherapy followed by radiotherapy, 4 (15%) received induction chemotherapy followed by concurrent chemoradiation, and 15 (55%) received concurrent chemoradiation alone. Total radiation dose received was 7,100 cGy on average (range = 6,600-7,700 cGy). Twelve patients (44%) underwent post-treatment neck dissection, either for residual adenopathy or as a planned operation for bulky adenopathy at presentation. As indicated in Table 2, 22 of 27 (81%) of patients underwent G-tube placement, either before or during chemoradiation.

Table 3 details swallowing outcome at 3 months, 6 months, and most recent follow-up for all patients after chemoradiation. At 3 months after treatment, 33% of patients had an exclusively oral diet and this improved to 50% at 6 months. Only 22% of patients had no oral intake at 3 months. Of 13 patients with no recurrence and at least 1 year of follow-up, all were able to eat orally. Nine of these (69%) had an exclusively oral diet and 4 of 13 (31%) had some oral intake but still required tube feeds for nutritional support.

Table 4 details the relationship between swallowing outcome and patient characteristics such as age, tumor stage, and subsite. As indicated, there was no apparent association between age or tumor stage and the rate of G-tube dependence. There was a significantly higher rate of G-tube dependence in patients treated for base of tongue primaries when compared to patients treated for tonsil primaries (67%

Table 2
G-tube status

	Patients	Percentage
No G-tube	5	19
G-tube placed, removed*	9	33
G-tube placed, not removed†	13	48

G-tube, gastrostomy tube.

*Mean duration of tube placement before removal = 6.2 (\pm 5.7) months.

†G-tube still in place after mean follow-up of 17.7 (\pm 11.4) months.

Table 3
Swallowing outcomes

Swallow outcome	3 months (%)	6 months (%)*	Last follow-up (%)†
Tube feeds only	6 (22.2)	5 (20.8)	4 (14.8)
Tube feeds + oral intake	12 (44.5)	7 (29.2)	10 (37.0)
Oral intake only	9 (33.3)	12 (50.0)	13 (48.2)

*Three patients did not have 6-month follow-up.

†Length of follow-up = 23.1 ± 18.5 months.

vs 25%, $P = 0.049$, χ^2 analysis). This was no longer statistically significant when patients with recurrent disease after chemoradiation were excluded (50% vs 17%, $P = 0.18$, χ^2 analysis).

DISCUSSION

The concept of organ preservation therapy for resectable head and neck cancer gained widespread attention with the publication the Veterans Affairs Laryngeal Cancer Study Group data in 1991.¹⁵ In that study, patients treated with induction chemotherapy followed by radiation for advanced-stage resectable laryngeal cancer had a 2-year survival approximately equal to that of patients treated surgically. Over the subsequent decade, several studies evaluated the use of combined chemotherapy and radiation for resectable cancer in other subsites of the head and neck. Comparison of studies is complicated by several factors such as the inclusion of patients with unresectable tumors, variability in chemoradiation protocol and variable representation of different tumor subsites. Nevertheless, outcomes seem similar to the surgical series, with disease-free survival at 3 years ranging from 61% to 73% after chemoradiation.^{3,5,9} Machtay et al¹⁰ prospectively evaluated chemoradiation given specifically for resectable Stage III/IV oropharyngeal cancer and reported overall survival of 70% and “event-free” survival of 59% 3 years after treatment.

Despite the encouraging results of such studies in terms of locoregional control and survival, significant functional impairment after chemoradiation has also been documented. Pharyngeal fibrosis caused by chemotherapy and radiation frequently results in chronic dysphagia and aspiration. The physiology of swallowing dysfunction after chemoradiation has been evaluated using videofluoroscopic studies by several authors.¹⁶⁻¹⁹ Common abnormalities seen on videofluoroscopy include: reduced tongue strength; reduced tongue control; decreased tongue base movement toward the posterior pharyngeal wall; decreased laryngeal elevation; decreased epiglottic inversion; delayed pharyngeal swallow;

frequent residue in the vallecula and pyriform sinuses and frequent penetration of the vestibule. The compromised laryngeal closure in the presence of pharyngeal residue and decreased laryngeal sensation lead to frequent aspiration, observed in 62% to 89% of patients after chemoradiation.^{16,18,19}

Other authors have utilized the Performance Status Scale for Head and Neck Cancer Patients (PSS)²⁰ to provide a general rating of dysphagia severity after chemoradiation. The PSS assesses normalcy of diet, eating in public, and understandability of speech. Normalcy of diet on this scale ranges from 0 (non-oral feeding) to 100 (full diet with no restrictions). Graner et al¹⁹ reported a mean normalcy-of-diet score of 29 approximately 5 months after chemoradiation for head and neck cancer. Machtay et al¹⁰ evaluated long-term functional outcomes after chemoradiation for advanced-stage oropharyngeal cancer. At a median follow-up of 31 months, patients had a mean normalcy of diet score of 65. For comparison, DeNittis et al⁸ reported a mean normalcy-of-diet score of 48 at a median follow-up of 34 months after surgical management and postoperative radiation for Stage III/IV oropharyngeal cancer.

Another useful measure of swallowing outcome is assessment of G-tube dependence. G-tube dependence after chemoradiation ranges between 13% to 64% at short-term follow-up (~6 months post-treatment)^{19,21,22} and 13% to 33% at long-term (≥ 12 months) follow-up.^{10,17,21} Comparison between studies is complicated by variability in tumor subsite, chemoradiation protocol, and percentage of patients with unresectable disease.

The goal of the current study was to assess G-tube dependence after chemoradiation for advanced-stage oropharyngeal cancer. This study allows comparison with results from patients treated surgically for similar lesions at our institution. In 2003, Skoner et al¹⁴ reported short-term (4 months post-treatment) G-tube dependence after surgical

Table 4
Factors affecting G-tube dependence

Variable	G-tube dependent (% last follow-up)*	P value†
Age		
<57	7/14 (50)	
>57	7/13 (54)	0.84
T stage		
T1, T2	4/7 (57)	
T3, T4	10/20 (50)	0.74
Tumor subsite		
Tonsil	2/8 (25)	
Base of tongue	12/18 (67)	0.049
Tumor subsite (NED)		
Tonsil	1/6 (17)	
Base of tongue	5/10 (50)	0.18

NED, no evidence of disease at last follow-up.

*Length of follow-up = 23.1 ± 18.5 months.

†Chi-square test.

resection, free flap reconstruction, and postoperative radiation therapy for Stage III/IV oropharyngeal cancer. In their series of 20 patients, 50% of patients had an exclusively oral diet at 4 months, 20% had no oral intake, and 30% had some oral intake but still required tube feeds for nutritional support. These results are similar to short-term outcomes reported in the present study. Three months after chemoradiation, 33% of patients had an exclusively oral diet, 22% had no oral intake, and 45% still required tube feeds but had some oral intake.

In contrast to the report by Skoner et al,¹⁴ long-term swallowing outcomes were also evaluated in this study. We noted that 53% of patients had an exclusively oral diet 1 year after chemoradiation, whereas 47% still required tube feeds including 1 patient (5%) who was unable to take anything orally. Even in patients with long-term follow-up (>1 year) and no evidence of recurrence, nearly one-third (31%) still required tube feeds for nutritional support. This G-tube dependence rate of 31% at 1 year after treatment is within the range reported in the surgical literature. After surgical resection, free flap, and postoperative radiation for advanced-stage oropharyngeal cancer, rates of G-tube dependence 6 to 12 months vary between 6%¹² and 39%.¹³

As seen in Table 4, only tumor subsite seemed to correlate with swallowing outcome. At most recent follow-up, 67% of patients treated for base-of-tongue lesions still required tube feeds versus only 25% of patients treated for tonsil lesions ($P = 0.049$, χ^2 analysis). When patients with recurrences were excluded, only 1 patient (17%) treated for a tonsil lesion required tube feeds vs 50% of the patients treated for base-of-tongue tumors. This difference was no longer significant on χ^2 analysis ($P = 0.18$) due to the small sample size. Patient age and T-stage did not seem to correlate with rates of G-tube dependence. The protocol of chemoradiation administered did not seem to impact swallowing outcome (data not shown), but the small sample size precluded meaningful statistical analysis.

In summary, rates of G-tube dependence after chemoradiation for advanced-stage oropharyngeal cancer seem similar to results after surgical management. At this institution, the short-term (3 to 4 months) rate of G-tube dependence was 67% after chemoradiation and 50% after surgical management. At long-term (≥ 1 year) follow-up after chemoradiation, patients without recurrence typically have at least some oral intake, but one-third still require supplemental tube feeds. These results suggest that organ-preservation protocols do not reduce the prevalence of chronic dysphagia and G-tube dependence after management of oropharyngeal carcinoma. In addition to dysphagia, short-term sequelae of chemoradiation including mucositis and neutropenia were observed, and 2 patients died during treatment from chemotherapy-related toxicity.

Weaknesses of the current study include the small sample size and the retrospective study design. The small sample size primarily reflects the objective of including only patients treated for oropharynx cancer. The majority of

Table 5
Comparison of swallowing function

Lesion	Skoner et al. ¹⁴ (%)	Shiley et al. (%)
Base of tongue	55	67
T stage 4	40	56
Stage IV	85	93

studies evaluating efficacy of chemoradiation and functional outcomes include all tumor subsites in the head and neck. Each site within the upper aerodigestive tract, however, contributes to speech and swallowing through different mechanisms. For this reason, one would expect the presence of a tumor and the effects of chemoradiation to impact swallowing function differently at various subsites. The value of focusing analysis on a specific subsite is highlighted by the difference in swallowing outcome observed between tonsil and base-of-tongue lesions in the current study. This series is one of few studies that evaluate functional outcomes after chemoradiation administered specifically for oropharyngeal carcinoma.

Our retrospective study design precluded the use of videofluoroscopic swallow evaluations to provide insight into the physiology of dysphagia after chemoradiation. A subset of patients did have videofluoroscopic studies available for review, and these demonstrated the typical findings described above.¹⁶⁻¹⁹ It was also not possible to incorporate the Performance Status Scale into the current retrospective study. As a result, conclusions cannot be drawn about the patients' normalcy of diet and ability to eat in public. The rate of G-tube dependence, however, is another meaningful outcome and allows comparison with other surgical and nonsurgical series.

Another criticism of this study relates to the obvious selection bias underlying the patient population. As seen in Table 5, the patient population in the current study was similar to the surgically-treated group evaluated previously at this institution. However, no attempt was made to determine the basis for selecting chemoradiation as treatment for the patients in the current study. Similarly, the rationale for surgical treatment was not detailed in the report by Skoner et al.¹⁴ It is possible that factors influencing treatment choice such as tumor size and location could also affect swallowing outcome after management. Until there are prospective, randomized studies comparing functional outcomes after surgery vs chemoradiation, the ability to draw conclusions by comparing the various reports is limited. To our knowledge, this is the only report that allows functional outcomes after chemoradiation and surgical treatment to be compared for patients treated at the same institution for similar tumors. Based on our results and a review of the literature, the rate of G-tube dependence is similar after surgical and nonsurgical treatment of advanced-stage oropharyngeal cancer.

CONCLUSIONS

Approximately two-thirds of patients are G-tube dependent 3 months after chemoradiation for advanced-stage oropharyngeal cancer. One year after treatment, all patients without recurrence have at least some oral intake, but one-third still require tube feeds for nutritional support. These rates of G-tube dependence after chemoradiation are similar to outcomes after surgical treatment based on the experience of this institution and a review of the literature. Patients treated for base-of-tongue lesions are more likely to require tube feeds after treatment than patients with tonsil tumors.

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