Swallowing Outcomes After Radiotherapy for Laryngeal Carcinoma

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Objective: To describe swallowing physiology and functional outcomes at select intervals after definitive radiotherapy for laryngeal carcinoma. We also examined associations among patient, tumor, and treatment characteristics and swallowing outcomes.

Design: Retrospective review.

Setting: The University of Texas M. D. Anderson Cancer Center, Houston.

Patients: This study cohort included 40 patients who underwent definitive radiotherapy for laryngeal carcinoma (from February 2001 to June 2004).

Main Outcome Measures: Modified barium swallow (MBS) studies were performed for 32 patients at 3 test intervals following irradiation: less than 6 months, 6 to 11 months, and 12 or more months. We recorded the presence or absence of aspiration (sensate or silent), 5 pharyngeal phase disorders, and 2 structural abnormalities. We also recorded pretreatment dysphagia complaints, feeding tube dependency, T classification, disease site, mucositis grade, and radiotherapy schedule with or without chemotherapy.

Results: Eighty-four percent of patients (27 of 32) referred for MBS studies after undergoing radiotherapy aspirated; 44% (12 of 27) did so silently. Silent aspiration was more prevalent during MBS studies conducted 1 or more years after radiotherapy. Pharyngeal phase disorders were observed more frequently than structural abnormalities ($P < .01$). Most patients required a feeding tube (78% [31 of 40]); however, 52% of the tubes (16) were eventually removed. We found no significant association between the occurrence of aspiration and disease site, T classification, treatment regimen, or pretreatment variables ($P > .05$). Pretreatment and posttreatment levels of feeding tube dependency were significantly associated ($P = .03$). Patient-reported dysphagia before treatment did not predict posttreatment swallowing outcomes ($P > .05$).

Conclusions: Dysphagia is a common outcome after laryngeal preservation with radiotherapy. Contrary to expectations, few parameters that we measured were significantly associated with swallowing outcomes in our study.


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sness swallowing function after radiotherapy with or without chemotherapy report aspiration rates of 36% to 89% in samples of patients with mixed primary lesions of the oral cavity, oropharynx, nasopharynx, hypopharynx, and/or larynx. However, there are few studies whose primary focus is swallowing outcomes in patients with laryngeal carcinoma who have been treated with definitive radiotherapy. Thus, the association between the development of dysphagia and other factors related to larynx cancer is not well documented.

The ability to predict dysphagia and prevent long-term swallowing dysfunction remains a key objective in the treatment of laryngeal carcinoma. Therefore, the purpose of this analysis was to describe swallowing physiology and functional outcomes at select intervals in patients treated with definitive radiotherapy for laryngeal carcinoma. We also examined disease characteristics and treatment variables in an effort to identify key determinants that may be predictive for dysphagia. These data will help provide the foundation for the prospective identification of patients who are at high risk for long-term dysphagia following nonsurgical laryngeal preservation with radiotherapy with or without chemotherapy.

**METHODS**

This retrospective review included a cohort of 40 patients who underwent definitive radiotherapy for advanced laryngeal carcinoma, stage III or IV, from February 2001 to June 2004 at the University of Texas M. D. Anderson Cancer Center, Houston. Patients who had previously undergone irradiation, received postoperative radiotherapy, were given radiation with palliative intent, or whose radiation was delivered in a narrow field were excluded from analysis. Patients with hypopharyngeal involvement, metastatic disease, or a second primary tumor were also excluded from analysis. Follow-up data were recorded up to the time of locoregional recurrence or salvage surgery. We reviewed patients’ medical records and recorded pretreatment dysphagia complaints, level of feeding tube dependency, T classification, disease site, peak mucositis grade, radiation schedule, and receipt of chemotherapy. Patients with self-reported dysphagia or suspected dysphagia on clinical examination were referred for modified barium swallow (MBS) studies. The timing of these studies was not standardized, and receipt of chemotherapy followed by concurrent chemoradia-
tion was not performed with the assistance of a statistical software application (SPSS for Windows; SPSS Inc, Chicago, Illinois).

**RESULTS**

Thirty-nine patients underwent definitive radiotherapy for supraglottic (n=27) and glottic (n=12) tumors; 1 additional patient had a subglottic tumor with glottic extension. Forty percent of the patients (16 of 40) were treated on conventional radiotherapy schedules and 60% (24 of 40) were treated on accelerated schedules. All patients were treated with external beam radiotherapy (range of total dosage, 66-77 Gy). Three patients received intensity-modulated radiation therapy. Seventy-five percent of patients also received chemotherapy in 1 of 3 treatment schedules: induction chemotherapy followed by radiotherapy, concurrent chemoradiation, or induction chemotherapy followed by concurrent chemoradiation. Twenty-five percent of patients (10 of 40) required total laryngectomy after radiotherapy, 9 as surgical salvage for persistent or recurrent disease and 1 as an elective treatment for a nonfunctional larynx. Patient characteristics and treatment regimens are described in Table 1.

**MBS FINDINGS**

Thirty-two patients underwent MBS studies after completing radiotherapy. Twenty-three studies were performed less than 6 months after treatment, 15 studies were performed 6 to 11 months after treatment, and 7 studies...
As part of our swallowing assessment protocol, compensatory swallowing strategies were selected and attempted based on swallowing deficits observed during the MBS study. Strategies that were successful were subsequently recommended for patients with dysphagia, including those patients who aspirated and those who did not. Although the number of patients decreased at each test interval, a little more than 70% of patients benefited from swallowing strategies at each examination point. Figure 2 summarizes the recommendations for the use of swallowing strategies at each test interval.

**FEEDING TUBE DEPENDENCY**

Sixty-eight percent of patients (27 of 40) reported swallowing problems prior to treatment. Despite this, only 15% of patients (6 of 40) required a feeding tube for nutritional support prior to the initiation of radiotherapy: 4 of 6 for partial nutrition and 2 of 6 for full nutrition. Overall, 78% of patients (31 of 40) had a feeding tube placed at some point during their course of treatment. Most of these feeding tubes were placed during the course of radiotherapy with the median placement at 3.4 weeks after the initiation of radiotherapy. Fifty-two percent of feeding tubes (16 of 31) were eventually removed, with the median tube removal at 22 weeks after placement. Most of these patients were free of disease at final follow-up (mean [SD], 70.1 [56.7] weeks) had lower rates of feeding tube dependency than those whose disease subsequently recurred and/or required salvage surgery (P = .049). Of the disease-free group, 72% (13 of 18) eventually maintained their nutrition orally. In addition, most patients who aspirated during MBS studies at the 6- to 11-month interval (6 of 11 [55%]) and at 12 or more months (+ of 6 [67%]) maintained oral nutrition despite their swallowing dysfunction. However, most patients who aspirated during MBS studies performed less than 6 months after radiotherapy remained feeding tube dependent because most had not completely recovered from acute toxic effects.
DENTRIMENTS OF ASPIRATION AND FEEDING TUBE DEPENDENCY

Overall, no statistically significant associations (see Table 3 for P values) were found between the occurrence of aspiration and the subsite of disease, T classification, treatment regimen, or mucositis grade. Pretreatment dysphagia complaints and pretreatment level of feeding tube dependency did not predict posttreatment aspiration (P > .05). These data are provided in Table 3.

Independent analysis of laryngeal disease subsite, T classification, treatment regimen, baseline dysphagia complaints, and mucositis grade did not reveal a significant association with the final level of feeding tube dependency (P > .05). However, pretreatment and posttreatment levels of feeding tube dependency were significantly associated (P = .03). Furthermore, patients who could not safely swallow thin liquids prior to the initiation of radiotherapy were significantly more likely to be feeding tube dependent, nothing per oral status, at final assessment (P = .01).

**Table 3. Associations Among Study Variables and Aspiration**

<table>
<thead>
<tr>
<th>Variable</th>
<th>&lt;6 mo Post-XRT (n=23)</th>
<th>6-11 mo Post-XRT (n=15)</th>
<th>≥12 mo Post-XRT (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No Asp</td>
<td>Cough</td>
<td>Silent</td>
</tr>
<tr>
<td>Dysphagia complaints pre-XRT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3:16 (19)</td>
<td>10:16 (63)</td>
<td>3:16 (19)</td>
</tr>
<tr>
<td>No</td>
<td>2:7 (29)</td>
<td>3:7 (43)</td>
<td>2:7 (29)</td>
</tr>
<tr>
<td>Feeding tube dependency pre-XRT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeding tube + PO</td>
<td>0:2 (0)</td>
<td>2:2 (100)</td>
<td>0:2 (0)</td>
</tr>
<tr>
<td>NPO</td>
<td>0:1 (0)</td>
<td>1:1 (100)</td>
<td>0:1 (0)</td>
</tr>
<tr>
<td>T classification</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1:7 (14)</td>
<td>6:7 (86)</td>
<td>0:7 (0)</td>
</tr>
<tr>
<td>3</td>
<td>4:15 (27)</td>
<td>7:15 (47)</td>
<td>4:15 (27)</td>
</tr>
<tr>
<td>4</td>
<td>0:1 (0)</td>
<td>0:1 (0)</td>
<td>1:1 (100)</td>
</tr>
<tr>
<td>Site of disease</td>
<td></td>
<td></td>
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<tr>
<td>Subglottic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glottic</td>
<td>1:7 (14)</td>
<td>4:7 (57)</td>
<td>2:7 (29)</td>
</tr>
<tr>
<td>Supraglottic</td>
<td>4:16 (25)</td>
<td>9:16 (56)</td>
<td>3:16 (19)</td>
</tr>
<tr>
<td>Radiation schedule</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conv</td>
<td>1:8 (13)</td>
<td>5:8 (63)</td>
<td>2:8 (25)</td>
</tr>
<tr>
<td>Chemo</td>
<td>4:15 (27)</td>
<td>8:15 (53)</td>
<td>3:15 (20)</td>
</tr>
<tr>
<td>No chemo</td>
<td>3:8 (38)</td>
<td>4:8 (50)</td>
<td>1:8 (13)</td>
</tr>
<tr>
<td>Induct</td>
<td>0:3 (0)</td>
<td>2:3 (67)</td>
<td>1:3 (33)</td>
</tr>
<tr>
<td>Conc</td>
<td>2:10 (20)</td>
<td>6:10 (60)</td>
<td>2:10 (20)</td>
</tr>
<tr>
<td>Induct + conc</td>
<td>0:2 (0)</td>
<td>1:2 (50)</td>
<td>1:2 (50)</td>
</tr>
<tr>
<td>Mucositis grade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>0:2 (0)</td>
<td>2:2 (100)</td>
<td>0:2 (0)</td>
</tr>
<tr>
<td>3</td>
<td>5:21 (24)</td>
<td>11:21 (52)</td>
<td>5:21 (24)</td>
</tr>
</tbody>
</table>

Abbreviations: accel, accelerated; asp, aspiration; chemo, chemotherapy; conc, concurrent; conv, conventional; induc, induction; XRT, radiation therapy; NPO, nothing per oral; PO, per oral.

aData are given as ratio (percentage).

bPearson χ².

Our study offers new perspectives on swallowing outcomes after laryngeal preservation. Most studies that report swallowing outcomes based on objective examinations present laryngeal preservation data as a subset analysis from a population of patients with mixed primary sites. Our primary focus was the analysis of objective, instrumental, swallowing evaluations at select intervals after radiotherapy for laryngeal preservation.

Our study results indicate that dysphagia, particularly aspiration, is common after definitive radiotherapy with or without chemotherapy for laryngeal carcinoma. We found that 84% of patients (27 of 32) who were referred for MBS studies after radiotherapy aspirated, and 44% (12 of 27) did so silently. Other studies6,8 have reported aspiration rates of 36% to 44% in similar populations. However, it is difficult to compare the findings from our study with these investigations because of the retrospective nature of the analyses and different patterns of referral for MBS studies between institutions. It is possible that our study showed a higher prevalence of aspiration because many of our patients received their swallow studies based on their report of dysphagia after treatment.

Our findings also reveal a high proportion of patients with dysphagia compared with other investigations3,12 that have employed patient-reported or quality-of-life assessments to measure swallowing outcomes. We, therefore, agree with other investigators who have rec-
ognized instrumental testing as a more valid tool for evaluating swallowing dysfunction compared with methods that rely on patient self-reporting.

An important finding of our study was that silent aspiration was more prevalent during MBS studies performed 12 or more months after the completion of radiotherapy. This suggests that patients are less sensitive to chronic aspiration over time and may accommodate to it. Although this finding is interesting, we are reluctant to draw conclusions about changes in swallowing function between early and late MBS studies because fewer patients were seen for MBS studies 12 or more months after radiation, and patients were more likely to be referred for late MBS studies if they continued to demonstrate marked swallowing problems. Patients who did not complain of dysphagia were not routinely referred for testing after completing radiotherapy. However, increased rates of silent aspiration over time have been reported in the head and neck cancer literature and require further examination of this outcome prospectively. Furthermore, our findings regarding silent aspiration underscore the importance of instrumental swallowing examinations, such as the MBS examination, to evaluate dysphagia after treatment for laryngeal cancer.

In our study, the rate of stricture was 9%, which is consistent with rates reported in the literature (1%-23%) in head and neck cancer survivors. The examination of choice for patients with oropharyngeal dysphagia is the MBS study. Patients who receive laryngeal irradiation are at high risk for both oropharyngeal dysphagia and stricture. Therefore, the MBS study is generally the first examination to be administered. However, there are other examinations, specifically, the barium esophagram, that provide more sensitive assessments of esophageal stricture. During the MBS study, the speech pathologist and radiologist evaluate the patient in collaboration. At our institution, when narrowing or stricture is identified, the MBS procedure is modified, and the patient is given dense stock barium to better coat the cervical esophagus for definitive examination in anterior-posterior and lateral views. Patients with stricture or narrowing are subsequently referred for endoscopic assessment and treatment.

In our study, aspiration and pharyngeal phase disorders had similar rates of occurrence. This is not surprising because hyolaryngeal excursion, base of tongue retraction, and epiglottic inversion are important for airway protection. Moreover, movement disorders of the pharyngeal phase occurred at a higher rate than structural abnormalities (supraglottic edema and stricture). This finding supports recently published data that suggest that exercises that target pharyngeal range of motion, if started early and adhered to consistently, may offer the best potential for prevention and remediation of long-term swallowing deterioration. Further evaluation of the effectiveness of swallowing exercise regimens in this population is needed.

Seventy-eight percent of our patients (31 of 40) had a feeding tube placed during the course of treatment; 52% of these tubes (16) were eventually removed. Seventy-two percent of patients who were disease-free (13 of 18) ultimately returned to oral nutrition. At our institution, we encourage patients to continue to swallow as much as long as possible throughout the course of treatment in an effort to preserve oropharyngeal swallowing physiology and prevent long-term feeding tube dependence. Protocols for targeted swallowing therapy are designed based on the findings of instrumental examinations to potentially avoid fibrosis and prevent long-term functional deterioration.

We found that most patients who aspirated and who were identified 6 or more months after radiation treatment did not require a feeding tube and were able to maintain their nutrition orally. This finding illustrates the inconsistency between feeding tube requirements and dysphagia. That is, the ability to maintain an oral diet does not always equate with normal swallowing physiology, nor does abnormal swallowing physiology always prevent oral intake. We, therefore, agree with other investigators who advocate against the use of feeding tube status or diet level as the sole indicator of dysphagia, particularly in patients with cancer of the oropharynx, larynx, and hypopharynx. Furthermore, the mechanisms that allow patients to continue eating safely despite their aspiration have not yet been fully delineated. It is our contention that decisions regarding the ability to eat by mouth require careful analysis that should combine both objective examination and patient characteristics because there are no data currently available that define tolerance for aspiration. The effects of chronic aspiration in a population already at high risk for medical complications may be substantial and should not be ignored.

Another objective of our study was to identify potential determinants of dysphagia after laryngeal preservation. Pauloski et al found that dysphagia complaints at the time of evaluation, not necessarily at baseline, were significantly correlated with aspiration in patients with head and neck cancer treated with radiotherapy with or without chemotherapy. However, we examined the association between aspiration after treatment and the complaint of dysphagia at baseline. We found no association between dysphagia complaints at baseline and aspiration at any posttreatment test interval. This is an interesting outcome from our retrospective medical chart review, but prospective studies with instrumental testing are needed to draw definitive conclusions.

Investigators have also identified associations between dysphagia and other variables, such as the addition of chemotherapy or T classification, in patients with cancers of the oral cavity and oropharynx. However, no significant associations between aspiration and site of laryngeal disease, T classification, or treatment regimen were found in our cohort of patients with laryngeal carcinoma (P > .05). The addition of chemotherapy to radiation has been shown to increase acute toxicity and dysphagia because of the intensifying effects. However, we cannot draw conclusions from our data regarding the swallowing outcomes in patients who were treated with radiation alone vs those who were treated with combined radiotherapy and chemotherapy because of the small sample sizes and the limitations of retrospective analysis. We recognize the importance of this comparison and have included it in a prospective analysis we are currently performing.

Two important associations were found in our study. Our data showed significant associations between the pre-
treatment and posttreatment levels of feeding tube dependency (P = .03) and the ability to safely swallow thin liquids at baseline and to eat orally at final assessment (P = .01). Most patients who required feeding tube placement before treatment remained feeding tube dependent at final assessment after radiotherapy. In addition, patients who could not swallow liquids prior to radiotherapy were more likely to remain feeding tube dependent at last follow-up.

Our results offer important information about swallowing outcomes after laryngeal preservation with radiotherapy. We recognize the limitations and biases of a retrospective review that does not include assessment at consistent time intervals and the ability to assess changes in swallowing function longitudinally. Our findings showed a high rate of aspiration in patients referred for MBS studies after laryngeal irradiation (84% [27 of 32]). We acknowledge that this finding may represent a selection bias as a function of retrospective analysis. A prospective evaluation of a representative sample that includes objective swallowing evaluation at baseline with uniform time frames for posttesting is needed to confirm our findings.

In conclusion, our data clearly establish that dysphagia is an important complication in some patients treated with radiotherapy with or without chemotherapy for laryngeal carcinoma. Interestingly, the findings of this retrospective study showed few notable associations between T classification, treatment regimens, and patient characteristics and the occurrence of posttreatment dysphagia. We are now prospectively evaluating swallowing outcomes in this population, not only to confirm these findings but also, more important, as a first step in improving our ability to predict dysphagia following nonsurgical laryngeal preservation with radiotherapy or chemoradiation. This information will help clinicians identify patients who are at risk for poor swallowing outcomes following radiotherapy with or without chemotherapy, thereby improving treatment selection aimed at cancer control with functional preservation.

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Author Contributions: Mss Hutcheson, Barringer, and May and Drs Rosenthal, Roberts, and Lewin had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Hutcheson, Barringer, Rosenthal, May, and Lewin. Acquisition of data: Hutcheson, Barringer, Rosenthal, and May. Analysis and interpretation of data: Hutcheson, Barringer, Rosenthal, May, Roberts, and Lewin. Drafting of the manuscript: Hutcheson, Roberts, and Lewin. Critical revision of the manuscript for important intellectual content: Hutcheson, Barringer, Rosenthal, May, and Lewin. Statistical analysis: Roberts. Administrative, technical, and material support: Rosenthal and May. Study supervision: Rosenthal and Lewin.

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REFERENCES