Functional Outcomes after Salvage Transoral Laser Microsurgery for Laryngeal Squamous Cell Carcinoma

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Abstract

Objectives. Transoral laser microsurgery (TLM) has been increasingly used in lieu of total laryngectomy to treat malignancy after definitive radiation. There are few data in the literature regarding functional outcomes. We retrospectively reviewed voice and swallowing outcomes in patients who underwent TLM for recurrent laryngeal carcinoma.

Study Design. Case series with chart review.

Setting. Tertiary care center.

Subjects and Methods. Forty-two patients were identified with recurrent squamous cell carcinoma of the larynx after definitive radiation therapy from 2001 to 2013: 28 patients with glottic recurrence and 14 with supraglottic recurrence. Swallowing outcomes were evaluated by gastrostomy tube dependence, the MD Anderson Dysphagia Inventory, and the Functional Oral Intake Scale. Voice outcomes were evaluated by the Voice Handicap Index and observer-rated perceptual analysis.

Results. No significant difference was noted between mean pre- and postoperative MD Anderson Dysphagia Inventory scores: 78.25 and 74.9, respectively (P = .118, t = 1.6955). Mean Functional Oral Intake Scale scores after TLM for supraglottic and glottic recurrences were 6.4 and 6.6, respectively. Of 42 patients, 17 (40.5%) required a gastrostomy tube either during radiation or in conjunction with the salvage procedure. Of 17 patients, 15 resumed sufficient oral diet for tube removal. Patients’ mean Voice Handicap Index score did increase from 34.3 to 51.5 (P = .047), and their mean perceptual score did decrease from 60.0 to 45.3 (P = .005). However, at 1-year follow-up, there was no significant difference in perceptual score: 61.1 to 57.1 (P = .722).

Conclusions. TLM is a successful surgical option for recurrent laryngeal cancer with acceptable functional outcomes.

Keywords
TLM, salvage, larynx cancer, voice, dysphagia

Laryngeal squamous cell carcinoma may be treated surgically with total laryngectomy, open laryngeal conservation surgery, transoral laser microsurgery (TLM), or definitive radiotherapy. The use of CO2 lasers to resect laryngeal cancers endoscopically was first described by Strong and Jako. Steiner further advanced this work by demonstrating TLM to be a viable alternative to radiotherapy. An analysis of SEER data (Surveillance, Epidemiology, and End Results) on the treatment of early supraglottic squamous cell carcinoma revealed that patients who underwent organ preservation surgery with neck dissection had better overall survival and disease-specific survival than patients undergoing definitive radiotherapy alone.

TLM is therefore considered to be a sound oncologic procedure in the treatment of early glottic and supraglottic carcinoma. Functional outcomes are comparable in terms of voice and may be better in terms of swallowing, morbidity, and complication rates as compared with those reported for open laryngeal conservation surgery and radiotherapy.

Patients with recurrent disease after definitive radiation therapy pose a unique treatment dilemma. Traditionally, these patients have undergone salvage surgery in the form of total laryngectomy or open conservation laryngeal surgery. While both procedures have proven to be oncologically

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sound, each has functional setbacks. Early data suggest that TLM as an alternative salvage surgical therapy is also oncologically sound. However, there has been little published on the functional outcomes of salvage TLM for laryngeal cancer. The goal of this study is to assess voice and swallowing outcomes after salvage TLM for recurrent laryngeal cancer.

Methods

Review and oversight of the study were provided by the Institutional Review Boards of Louisiana State University Health Sciences Center and Our Lady of the Lake Regional Medical Center. A retrospective chart review was conducted at an academic practice in a regional referral center. Forty-two patients were identified as having recurrent squamous cell carcinoma of the larynx after definitive radiation therapy from 2001 to 2013 and undergoing salvage TLM. The senior author in this single-surgeon experience had been in practice for 14 years when these data were collected, and a minimum 2-year follow-up was chosen, creating the 12-year period. Twenty-eight patients had glottic recurrences, while 14 had recurrences in the supraglottis. Sixteen patients underwent resection prior to Hurricane Katrina and, as such, had only feeding tube data and Functional Oral Intake Scale (FOIS) scores available from limited records.

There were no specific protocols employed, but all patients were counseled and given the option of TLM, open partial laryngectomy, or total laryngectomy when they were appropriate candidates. Candidacy for conservation surgery was based on tumor accessibility and size as well as pulmonary function, patient commitment to rehabilitation, and family and social support. Patients who were not thought to be good candidates due to preexisting pulmonary or swallowing compromise were not offered conservation laryngeal surgery. Pulmonary function testing was not employed but rather the patient’s ability to climb 2 flights of stairs as a measure of pulmonary fitness. Imaging with positron emission tomography–computed tomography or computed tomography was performed on all patients prior to surgery to confirm staging.

Data collected included age, sex, tumor stage, resection type according to European Laryngological Society (ELS) criteria, treatment course, and recurrences. Swallowing outcomes were evaluated by the necessity for a gastrostomy tube, the MD Anderson Dysphagia Inventory (MDADI), and the FOIS, recorded 9 months to 1 year postoperatively. The MDADI is a validated and reliable self-administered questionnaire designed for evaluating the impact of dysphagia on the quality of life of head and neck cancer patients, with scores ranging from 20 to 100 (low- to high-functioning deglutition). Because it is specifically for head and neck cancer patients, the MDADI is used in our clinic. The FOIS describes the functional level of a patient’s daily oral intake of food and liquid, with consideration for modifications of either and the need for swallowing compensations. It is a validated 7-point ordinal scale, where 1 indicates nothing by mouth and 7 is a full oral diet without restrictions. The FOIS score was obtained as part of our standard history and, as such, was also readily available for retrospective data analysis.

Voice outcomes were evaluated by pre- and posttreatment Voice Handicap Index (VHI) survey and analysis of voice recordings. Voice recordings were de-identified and reviewed by 2 blinded senior speech-language pathologists with >10 years of experience. Voices were graded on a scale from 0 (aphonia) to 100 (a perfect voice). The mean score of the 2 raters was used in analysis. The first voice recording available and the first VHI score available ≥1 month postoperatively were used. Statistical analysis was performed with SPSS (Version 13.0; IBM, Chicago, Illinois). Mean values were calculated for VHI and perceptual voice grade. A paired-samples t test was used to compare mean MDADI, VHI, and perceptual score values, as the data were found to be normally distributed. Wilcoxon’s signed-rank test was utilized for comparison of the preoperative, postoperative, and 1-year perceptual voice data.

Results

Between 2001 and 2013, 42 patients with recurrent squamous cell carcinoma of the larynx after definitive radiation therapy underwent salvage TLM resections. Full-index treatment records were available for 26 patients who were treated after Hurricane Katrina. Four of 26 had chemotherapy and radiation therapy, while 22 of 26 had radiation therapy alone. There were 28 patients with glottic recurrences (postradiation, T stage rtcis/rT1 = 12, rT2 = 13, rT3 = 3) and 14 patients with recurrences in the supraglottis (rT1 = 4, rT2 = 6, rT3 = 4). No patients had positive regional or distant metastases at time of salvage. All patients with T3 disease were staged to T3 due to either preepiglottic or paraglottic space invasion. None had vocal fold fixation. All patients with T3 disease were offered neck dissection. Two patients underwent concurrent neck dissection, both with rT3 supraglottic disease. The other patients with T3 disease refused neck dissection and were followed with serial imaging. One patient required tracheostomy for postoperative laryngeal edema. Seven patients required a second transoral laser procedure, with 10 patients ultimately requiring total laryngectomy for oncologic control. Of these 10 patients, 4 had deep margins positive for carcinoma, 3 with lymphovascular invasion, 2 with perineural invasion, and 4 did not have these data available. Of these 10, smoking status was distributed with 3 nonsmokers, 6 who quit, and 1 who continued smoking. The presence of >1 of the above factors did seem to correlate with an increased likelihood of requiring salvage total laryngectomy.

Of the 28 patients who underwent salvage TLM for glottic recurrence, 20 had no evidence of disease at 2 years with larynx preserved. Eight of 28 required salvage total laryngectomy. Nine of 14 patients who underwent salvage TLM for supraglottic recurrence had no evidence of disease at 2 years with larynx preserved. Two of 14 required salvage total laryngectomy, and 3 patients died of distant metastatic disease. At 2 years, overall laryngeal preservation was 76.2%, with an overall survival rate of 81.0% and a 100% local control rate. No patients required a total laryngectomy.
for functional reasons, and no patients progressed to unresectable disease after TLM.

Swallowing Outcomes

Of 42 patients, 17 (40.5%) required a gastrostomy tube placed preoperatively or perioperatively. Of these, 11 patients had supraglottic tumors, and 6 had glottic tumors. Of 17 patients, 15 (88%) had their gastrostomy tubes removed, and 2 patients died with their gastrostomy tubes in place. The mean length of tube dependence was 9.3 months. MDADI questionnaires were given to patients pre- and postoperatively. Twelve patients completed a preoperative MDADI, with a mean score of 78.25 (range, 48-100). Twenty-three patients completed a postoperative MDADI, with a mean score of 74.9 (range, 33-100). MDADI scores were completed between 1 and 72 months postoperatively. The mean MDADI score when including only scores obtained between 6 and 14 months postoperatively was 74.5. Overall, no significant difference was found between pre- and postoperative MDADI scores (\(P = .118\), \(t = 1.6955\)). FOIS scores were recorded for 40 of 42 patients. The median time from surgery until FOIS score was 17 months in the supraglottic group and 14 months in the glottic group. The mean FOIS score after supraglottic recurrence resection was 6.4, and the mean score after glottic resection was 6.6 (Table 1).

Voice Outcomes

VHI Data

Fifteen patients were found to have VHI data available preoperatively and at least 1 month postoperatively, 11 of whom had glottic lesions and 4 of whom had supraglottic lesions. Of the 11 glottic patients, 2 underwent ELS type 3 resections, and the other 9 underwent ELS type V and VI resections. All supraglottic patients underwent endoscopic supraglottic laryngectomy. As noted in Table 2, patients who underwent TLM for glottic recurrences had a significant increase in mean VHI, from 31.8 to 53.5 postoperatively (\(P = .026\)). For the patients who underwent TLM for supraglottic recurrences, an increase in mean VHI was noted from 41.3 to 46.0 postoperatively (\(P = .824\)). For all patients, mean VHI increased from 34.3 to 51.5 (\(P = .047\)). VHI scores were collected at least 1 month postoperatively, with a mean time to collection of 3.3 months.

Table 1. Functional Swallowing Outcomes.

<table>
<thead>
<tr>
<th>Subsite</th>
<th>Preoperative Mean</th>
<th>Postoperative Mean</th>
<th>Feeding Tube, %</th>
<th>Mean Time Tube Feed Dependent, mo</th>
<th>Postoperative FOIS Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supraglottic</td>
<td>70.5</td>
<td>74.2</td>
<td>79</td>
<td>10.1</td>
<td>6.4</td>
</tr>
<tr>
<td>Glottic</td>
<td>79.8</td>
<td>75.1</td>
<td>21</td>
<td>7.6</td>
<td>6.6</td>
</tr>
<tr>
<td>Total</td>
<td>78.25 (n = 12)</td>
<td>74.9 (n = 23)</td>
<td>40</td>
<td>9.3</td>
<td>6.5 (n = 40)</td>
</tr>
</tbody>
</table>

Abbreviations: FOIS, Functional Oral Intake Scale; MDADI, MD Anderson Dysphagia Inventory.

Table 2. Voice Handicap Index Outcomes.

<table>
<thead>
<tr>
<th>Subsite</th>
<th>Preoperative</th>
<th>Postoperative</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supraglottic (n = 4)</td>
<td>41.3</td>
<td>46.0</td>
<td>.824</td>
</tr>
<tr>
<td>Glottic (n = 11)</td>
<td>31.8</td>
<td>53.5</td>
<td>.026</td>
</tr>
<tr>
<td>Total (n = 15)</td>
<td>34.3</td>
<td>51.5</td>
<td>.470</td>
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</tbody>
</table>

Table 3. Perceptual Outcomes.

<table>
<thead>
<tr>
<th>Subsite</th>
<th>Preoperative</th>
<th>Postoperative</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supraglottic (n = 4)</td>
<td>70.6</td>
<td>52.6</td>
<td>.219</td>
</tr>
<tr>
<td>Glottic (n = 16)</td>
<td>57.0</td>
<td>43.5</td>
<td>.017</td>
</tr>
<tr>
<td>Total (n = 20)</td>
<td>60.0</td>
<td>45.3</td>
<td>.005</td>
</tr>
</tbody>
</table>

Perceptual Data

Twenty patients had adequate voice recordings prior to and at least 1 month after surgery. Of 20 patients, 16 underwent resection for glottic recurrence, and 4 underwent resection of supraglottic recurrence. Of the 16, 2 underwent ELS type 3 resections; 2, ELS type 6 resections; and the remaining 12, ELS type 5 resections. All supraglottic patients underwent varying endoscopic supraglottic laryngectomy. As noted in Table 3, for patients who underwent TLM for glottic recurrence, a decrease in mean perceptual score was noted from 57.0 to 45.3 postoperatively (\(P = .017\)). For the patients who underwent TLM for supraglottic recurrences, a decrease in mean perceptual score was noted from 70.6 to 52.6 postoperatively (\(P = .219\)). For all patients, mean perceptual score decreased from 60.0 to 45.3 (\(P = .005\)). All postoperative recordings were performed at least 1 month after surgery, with a mean time to postoperative recording of 1.8 months.

Discussion

TLM has become an important surgical procedure in the treatment of laryngeal cancer, with ample data demonstrating equivalent oncologic results with TLM in the treatment...
of early-stage laryngeal cancers as compared with radiation therapy. There is also a growing body of evidence suggesting that TLM may be used, with acceptable oncologic results, as salvage therapy after radiation failure.\textsuperscript{9-15} In a meta-analysis of the available data on salvage TLM at 2 years, Ramakrishnan and colleagues noted a mean laryngeal preservation rate of 72.3\%, local control rate of 70.9\%, and overall survival of 74.8\%.\textsuperscript{14} Dysphonia, dysphagia, and aspiration are well-known side effects of radiotherapy for laryngeal cancer.\textsuperscript{16,17,22-24} One concern with salvage TLM is that, given radiation changes limiting laryngeal function, patients will not have sufficiently functional larynx postoperatively. In particular, we were concerned about voice production after glottic resections and about safety of swallowing after supraglottic resections, given our personal experience as well as the literature. In comparing functional results at 1 month between 5 patients who underwent salvage TLM for supraglottic carcinoma and 5 patients who underwent primary TLM, Hutcheson and colleagues noted that 5 of 5 patients in the salvage group demonstrated persistent aspiration at 1-month follow-up and 1 patient was feeding tube dependent, while no patients in the primary group required a feeding tube and only 1 of 5 demonstrated penetration or aspiration. Again at 1 month, salvage patients had worsened but functional voice.\textsuperscript{22} However, in assessing patients’ functional outcomes 1 year after salvage TLM for laryngeal and pharyngeal carcinoma, Grant and colleagues noted that only 4\% of patients were feeding tube dependent and patients’ average Functional Oral Swallowing Scale score was zero, indicating “normal swallowing function and asymptomatic.” However, 28\% of their patients required nasogastric tubes postoperatively, and another 24\% had planned gastrostomy tubes placed perioperatively. As only approximately one half of their patients had laryngeal cancer, it is not surprising that their patients had a mean communication score of 1, consistent with mild dysphonia only.\textsuperscript{13} Del Bon and colleagues compared functional outcomes at 2 years postoperatively between 10 patients with recurrent glottic cancers who underwent TLM and a group of matched controls who underwent TLM for primary treatment of laryngeal carcinoma. They found no significant difference in postoperative MDADI score, GRBAS score (grade, roughness, breathiness, asthenia, strain), VHI, jitter, shimmer, or maximum phonation time between the primary and salvage treatment groups. However, they did note increased rates of penetration and aspiration on videonasal endoscopic evaluation of swallowing in the salvage group.\textsuperscript{17} Our data show that patients undergoing salvage TLM, particularly of the supraglottis, are at increased risk of postoperative dysphagia and aspiration, with possible feeding tube dependence. As expected, patients who underwent supraglottic resections had a much higher rate of feeding tube dependence than patients who underwent glottic resections (Table 1). However, as noted in the literature, the majority of patients return to a highly functional oral diet. Likewise, our data show that in the first few months after surgery, patients’ voices do worsen. Interestingly, while there was a larger increase in voice handicap in the glottic group than the supraglottic group, there was a comparable change in perceptual score between the groups (Tables 2 and 3). However, in agreement with Del Bon and colleagues, our limited long-term data set indicates continuing improvement over time to a usable voice.

Patients were more likely in our data set to require advanced resections than patients who underwent TLM for primary disease. This is due to (1) the increased margins required in the radiated field, with the increased difficulty in visualizing tissue planes requiring more extensive resections, and (2) recurrent tumors after definitive radiation being “bad actors.” When we compared our salvage data with our previously presented data on advanced primary TLM resections, we noted comparable results, with a mean postoperative perceptual score of 39.0 in primary tumors versus 45.3 in the salvage group. Therefore, patients should be counseled appropriately to expect prolonged rehabilitation of voice and swallowing. However, they can also be counseled that they will very likely have a highly functional voice and will tolerate an oral diet with only early gastrostomy tube dependence.

It should be noted that all patients were carefully selected to undergo conservation surgery in lieu of total laryngectomy. In our practice, patients undergo preoperative evaluation and counseling with a speech therapist in addition to a surgeon, at which time they are assessed for rehabilitation potential and started with swallowing therapy. An exercise regimen is tailored to the patient’s needs at that time. Patients who are not thought to be good candidates because of either poor compliance with therapy or social issues limiting rehabilitation are counseled to undergo total laryngectomy. It is possible that starting rehabilitation sooner might further optimize outcomes. This is an area requiring further research.

Our study represents the largest data set analyzing functional outcomes after TLM for recurrent laryngeal carcinoma and the first to compare pre- and postoperative voice and dysphagia scores. However, it has several limitations. Many patients in our database did not complete the VHI or MDADI, as they underwent the procedure before we began to collect these data or they chose not to complete the form in the clinic. Our data set is also limited by a lack of objective testing, such as acoustic and aerodynamic measures or video endoscopic evaluation of swallowing, as was performed by Del Bon and colleagues.\textsuperscript{17} As such, there were likely patients in our data set who were aspirating to some degree. However, as they were not feeding dependent and did not have clinical history of pneumonias in chart review except as noted above, they were unlikely to be suffering with clinically significant aspiration. Finally, due to our practice pattern and the retrospective nature of the study, we did not have a control group to assess how similar patients might fare from a functional standpoint with open partial laryngectomy.

**Conclusion**

Our study sought to define voice and swallowing outcomes in patients undergoing TLM for recurrent squamous cell...
carcinoma of the larynx after definitive radiation or chemoradiation. We found (1) voice significantly worsened at early follow-up, with improvement at 1 year, and (2) swallowing outcomes at 9 months to 1 year to be acceptable. TLM represents a viable surgical salvage alternative in carefully selected patients.

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Author Contributions
Daniel S. Fink, conception, design, acquisition, analysis, and interpretation. primarily responsible for writing each draft of the work. along with all other listed authors, was responsible for final approval of the version to be published and agrees to be accountable for all aspects of the work; Haley Sibley, helped conceptualize project, created de-identified videos, gathered data, helped with analysis and writing of manuscript. along with all other listed authors, was responsible for final approval of the version to be published and agrees to be accountable for all aspects of the work; Melda Kunduk, helped conceptualize project, graded de-identified videos, helped with data analysis and interpretation. specifically, reviewed scores after analysis to determine what she felt were appropriate interpretations of the numbers in terms of functionality. reviewed manuscript and assisted in appropriately drawing and wording conclusions. along with all other listed authors, was responsible for final approval of the version to be published and agrees to be accountable for all aspects of the work; Collin Sutton, helped conceptualize project, created de-identified videos, helped with data analysis and interpretation. specifically, reviewed scores after analysis to determine what she felt were appropriate interpretations of the numbers in terms of functionality within the manuscript thus helping to revise the manuscript critically. along with all other listed authors, was responsible for final approval of the version to be published and agrees to be accountable for all aspects of the work; Anagha Kakade-Pawar, helped with statistical point of view from conceptual perspective. data analysis and interpretation. helped revise initial manuscript to make most appropriate interpretation of statistical analysis. along with all other listed authors, was responsible for final approval of the version to be published and agrees to be accountable for all aspects of the work; Andrew J. McWhorter, conception, design, acquisition, analysis, and interpretation. senior author who guided study through entire process. specifically aided in clarifying data about selection and interpretation of data in discussion thus critically editing the manuscript. along with all other listed authors, was responsible for final approval of the version to be published and agrees to be accountable for all aspects of the work.

Disclosures
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