Outcomes Following Transoral Robotic Surgery: Supraglottic Laryngectomy

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Objectives/Hypothesis: To describe a single center outcomes following transoral robotic surgery for supraglottic laryngectomy (TORS–SL).

Study Design: Prospective data collection.

Methods: Patient records receiving TORS–SL for squamous cell carcinoma (SCCA) with at least 12 months follow-up fit inclusion for this study. Two patients with previous SCCA were excluded.

Results: 18 patients (14 male, 4 female) were included in the study, having a mean follow-up time of 28.1 months (SD = 12.1). All patients had negative margins confirmed on final pathology. Nine (50%) patients received postoperative chemoradiation therapy for advanced neck disease. No (0%) patients received tracheostomy or gastrostomy tubes. There were no (0%) local recurrences, and three (16.7%) regional recurrences. Five (27.8%) patients experienced temporary post-operative complications. Overall 2-year outcomes reached 83%, 100%, and 89% for locoregional control, disease-specific survival, and overall survival respectively.

Conclusions: Initial outcomes for TORS–SL are encouraging and are comparable to previously described treatment modalities. Larger studies are encouraged.

Key Words: Laryngeal, tumor, da Vinci, functional outcomes, cancer, head and neck.

Level of Evidence: 4.


INTRODUCTION

Following the publication of the Department of Veterans Affairs report demonstrating the therapeutic efficacy of primary chemoradiotherapy (CRT) for advanced laryngeal cancer in 1991,1 the use of CRT for all laryngeal cancers has consistently increased.2 However, when analyzing the oncologic outcomes for supraglottic squamous cell carcinoma (SCCA) over the past 20 years, the increase in “organ-preservation” therapy has been unable to improve survival rates;3 and for some supraglottic tumor stages a markedly poorer survival rate has been demonstrated.4 Notwithstanding the lack of encouraging survival patterns, primary CRT continues to be a very attractive treatment option when compared to open laryngeal conservation surgery. The attraction is likely due to the fact that required feeding tube and tracheostomy tube placement during open surgical approaches are among the most critical factors in decreasing quality of life of head and neck cancer patients.5

Beginning with Strong and Jako,6 the treatment options for supraglottic squamous cell carcinoma (SCCA) expanded to include endoscopic laser resection, along with open surgical resection and primary CRT. Endoscopic laser surgery for supraglottic tumors has improved postoperative function with limited need for tracheostomy and gastrostomy placement.7–12 Long-term oncologic outcomes of endoscopic laser resection have demonstrated equivalent recurrence rates and survival data as compared to open surgical approaches10 and nonsurgical treatment.13

However, technical challenges inherent in endoscopic laser resections may be the cause for its limited application outside of high-volume centers. Supraglottic anatomic structures and tumor bulk typically exceed the visualization of rigid laryngoscopes. Therefore, standard laser resections use piecemeal resection to identify the deep oncologic margins and to gradually improve visualization. Though never oncologically demonstrated, this deviation from classic en bloc resection has raised doubts among some practitioners. Constant adjustment of the laryngoscope is typically necessary in order to continually improve visualization. Additionally, the endoscopic laser surgeon contends with dexterity challenges. During endoscopic laser resection, one hand is needed to guide the laser beam via the micromanipulator, leaving...
only one hand to manipulate the tissue. Though the advent of the flexible fiber CO2 laser delivery has brought the laser hand-piece into the surgical field, the fragility of the fiber, along with its rigid instrumentation, has restricted its utility as an additional dissecting instrument. The ultimate technical result is an endoscopic surgical approach with less than optimal visualization and dexterity.

The application of transoral robotic surgery (TORS) to the oropharynx has addressed many challenges of the endoscopic laser approach. Wide oral retraction allows for full-field surgical view, which is displayed through bilensed endoscope, resulting in a high-definition 3D image. Along with the improved visualization, dexterity is improved by bimanual control of the robotic arms. Additionally, the surgical first assistant contributes additional suction and retraction to provide a total of four dissecting instruments during the resection. TORS outcomes for oropharyngeal SCCA have equaled to, or improved, both functional and oncologic outcomes over those of laser resection, open surgery, or CRT. Following the successful application of TORS to the oropharynx, initial feasibility trials were reported for tumors of the supraglottis. Currently, there is only one report of oncologic and functional outcomes following TORS supraglottic laryngectomy with encouraging results. Over the past 3 years, the current institution has also adopted a TORS approach to supraglottic laryngectomy for SCCA. It is the aim of this report to analyze the functional and oncologic outcomes of primary treatment of TORS for supraglottic SCCA.

MATERIALS AND METHODS
Institutional Review Board Approval Was Obtained for the Current Study

Clinical and surgical data was prospectively collected from all patients undergoing transoral robotic surgery for supraglottic laryngectomy (TORS–SL) at a single institution. The study spanned the time period from 1/1/2008 to 4/30/2010. The end date was chosen to include only patients with a minimum of 12 month clinical follow-up. Three patients were excluded from the present analysis for either having previous head and neck SCCA (n = 2) or no tumor found in the specimen (n = 1).

Patient Evaluation

Patients are staged clinically both by indirect laryngoscopy as well as direct laryngoscopy under general anesthesia. If not obtained prior to presentation, pathologic diagnosis is obtained during the staging endoscopy. Additionally, exposure is obtained with the operative pharyngoscope. Patients staged radiographically by PET/CT. All patients with resectable tumors and adequate intraoral exposure are offered TORS–SL.

Surgical Protocol

TORS–SL is performed with the da Vinci Surgical Robotic System (Intuitive Surgical, Sunnyvale, CA), utilizing 5-mm robotic Maryland dissector and Bovie cautery. Instead of the Bovie arm, a subset (n = 3) of tumors were resected utilizing a robotic adapter for CO2 laser fiber (Fiberlase, Lumenis, Santa Clara, CA), as previously described. Intraoral retraction was obtained in all cases using the Laryngeal Advanced Retractor System (LARS) pharyngoscope (Fentex Medical, Neuhausen, Germany). All surgeries were performed by a single surgeon (G.L.). Intraoperative margins are assessed by taking tissue from the patient following tumor extirpation.

Patients with clinically/radiographically N0 necks are treated with sentinel lymph node biopsy, as previous described. Briefly, 1-2cc of 99mTc-albumine nanocolloid is injected submucosally at the periphery of the tumor. Thirty minutes is allowed for lymphatic diffusion before primary tumor resection commences. Radioactive nodes are removed and sent for serially sectioned histopathology with immunohistochemistry staining for negative sentinel lymph nodes. Patients with positive sentinel lymph nodes return to the operating room within 2 to 3 weeks of primary resection for selective neck dissections. Preoperative N+ necks undergo concomitant TORS–SL with selective neck dissection.

Tracheostomy is not performed during TORS–SL. Patients are kept intubated overnight and are extubated postoperative day 1. Gastrostomy is not performed during TORS–SL. If supraglottic laryngectomy is limited to the epiglottis, the operating surgeon may defer routine placement of nasogastric feeding tube.

Extent of TORS–SL was classified according to the 2009 European Laryngological Society (ELS) classification system. Briefly: Type III–medial supraglottic laryngectomy, with resection of the pre-epiglottic space, without (Type IIIa) or with (Type IIIb) extension to the ventricular fold; Type IV–lateral supraglottic laryngectomy, including the ventricular fold (Type IVa) or a portion of the arytenoid (Type IVb).

Postoperative Care

Perioperative antibiotics are continued for 24 hours and perioperative corticosteroids are continued for 48 hours. Due to the rural location of the present institution, patients are kept in the hospital until safe swallow is demonstrated with both solid and liquid diets. Postoperative swallow function is assessed starting on postoperative day 1 with fiberoptic endoscopic evaluation of swallowing (FEES). Patients without aspiration on FEES are then referred for modified barium swallow study (MBSS). The demonstration of safe swallow on both modalities allows for advancement of oral diet to solids with thickened liquids followed by thin liquids.

Absolute indications for adjuvant chemoradiotherapy include positive surgical margins, N2+, and extracapsular spread of nodal metastasis.

Follow-up

Patients are seen initially in the outpatient clinic within 1 to 2 weeks of discharge for evaluation of surgical site and every 2 months for the first postoperative year. Patients are weighed at each visit to ensure adequate calorie intake. Additionally, FEES and MBSS assessments are continued until full-swallow function returns. All patients receive postoperative swallow therapy. Oncologic surveillance is assessed clinically by thorough physical examination with indirect laryngoscopy, and radiographically through annual PET/CT scans beginning 3 months postoperatively.

Data and Statistics

Clinical and demographic data was prospectively collected in a dedicated database. Swallowing function outcomes were measured as days to return of safe swallow. Count variables, such as days to swallow function, demonstrated over-dispersion...
on tests of normality. Therefore, negative binomial regression models were applied for each independent variable individually. Negative binomial regression is the test of choice when a count variable is encountered due to the inherent rightward skew of the data. Significance was defined as $p < 0.05$. Statistical analysis was performed with Stata/IC 11.1 for Mac (College Station, TX).

**RESULTS**

**Demographics**

Between 1/1/2008-4/30/2011, 18 patients meeting inclusion criteria underwent TORS–SL. Postsurgical follow-up time ranged from 13 to 51 months (mean = 28.1, SD = 12.1). The study group consisted of 14 (77.8%) males. There were 16 (88.9%) cigarette smokers. Of the smokers, there was a mean pack-year history of 32.4 years (SD = 15.8). Eleven (68.8%) of the smokers had reported quitting prior to surgery. Faculty anesthesiologists graded 14 (77.8%) patients as category II on the American Society of Anesthesiologists (ASA) Physical Status classification system, with the remaining four (22.2%) graded as category III. Figure 1 reviews the presenting clinicoradiographic TNM staging, along with the supraglottic subsite involvement. Primary subsites included: epiglottis in 12 (72.2%) patients, the region of three-folds in four (22.2%) patients, and ventricular bands in one (5.6%) patient.

**Perioperative Data**

Operating room and robotic setup ranged from 12 to 55 minutes (mean = 23.5, SD = 10.4). TORS–SL surgical time, including tumor resection and acquisition of intraoperative margins, ranged from 35 to 180 minutes (mean = 93.9, SD = 43.8). Figure 1 reviews the ELS supraglottic laryngectomy classifications for the study. Negative intraoperative margins were confirmed by formal histopathologic analysis in all (100%) of the cases. Of the 12 (66.7%) patients who underwent sentinel lymph node biopsy, three patients underwent subsequent neck dissections. Of the remaining six clinically/radiographically N+ patients, four (22.2%) underwent bilateral and two (7.1%) underwent unilateral concomitant neck dissections. There were no (0%) intraoperative surgical complications. Five (27.8%) patients experienced temporary perioperative complications. Length of hospitalization ranged from 5 to 50 days (median = 11, SD = 13.4).

**Pathologic Data**

Figure 1 reviews the TNM stages modified based on histopathologic evaluation. One tumor demonstrated vascular invasion, two showed perineural invasion, and three had evidence of both lymphovascular and perineural invasion. Nine (50.0%) tumors were graded positive
for p16 by immunohistochemistry. Of the 10 (55.6%) patients with nodal metastasis, five patients had extracapsular invasion. 10/18 (55.6%) patients underwent adjuvant CRT, all of whom were pN2a or greater.

### Functional Outcomes

All TORS–SL (100%) patients were successfully extubated on postoperative day 1 without airway compromise. There were no (0%) tracheostomies performed at any point during treatment. Figure 1 reviews the time duration for the safe advancement to both solid and liquid intake. Overall, patients required between 2 to 29 days for safe swallow for solids (median = 4.5, SD = 9.41). Patients required between 2 to 45 days for safe swallow for thin liquids (median = 5.5, SD = 14.9). Significant (p < 0.001) factors associated with delayed swallow rehabilitation are presented in Table I. Female gender, advanced pathologic T-stage (III/IV), simultaneous neck dissection, and temporary postoperative vocal fold hypomobility were associated with significant delays in return of swallow function. There were no (0%) gastrostomies tubes placed at any point during treatment. No relationship was seen between ASA classification and functional outcomes.

### Oncologic Outcomes

There were no (0%) local recurrences leading to a local control rate of 100%. Three (16.7%) patients developed regional recurrences. Four (22.2%) developed distant metastases. Table II displays the individual tumor characteristics that developed regional and distant failures. No clinical or histopathologic factor was found to have a significant association with regional failures. Only overall cancer stage IV was found to be significantly associated (p = 0.042) with the development of distant metastasis. There were no disease-specific deaths, resulting in a 2-year disease-specific survival (DSS) of 100%. Two patients died during the follow-up period of cardiopulmonary failure, leading to a 2-year overall survival (OS) of 88.9%. Both deceased patients were graded as category II on the ASA classification system. Figure 2 displays the Kaplan–Meier estimates for locoregional recurrence, distant metastases, and OS by nodal status.

### DISCUSSION

The development of transoral robotic surgery for supraglottic laryngectomy (TORS–SL) can be seen as a product of the need for improved treatment modalities for laryngeal SCCA. Beginning with the VA cooperative

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### Table I. Swallowing Function Following TORS-SL.

<table>
<thead>
<tr>
<th></th>
<th>Solid Diet</th>
<th>Liquid Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Female gender</strong></td>
<td>4 (22.2%)</td>
<td>17.5 27.5</td>
</tr>
<tr>
<td><strong>Male gender</strong></td>
<td>14 (77.8%)</td>
<td>5.0 26.0</td>
</tr>
<tr>
<td><strong>Late T-stage</strong></td>
<td>5 (27.8%)</td>
<td>32.0 3.0</td>
</tr>
<tr>
<td><strong>Early T-stage</strong></td>
<td>13 (72.2%)</td>
<td>5.0 2.0</td>
</tr>
<tr>
<td><strong>Simultaneous neck</strong></td>
<td>6 (33.3%)</td>
<td>29.5 28.0</td>
</tr>
<tr>
<td><strong>Sentinel lymph node biopsy</strong></td>
<td>12 (66.7%)</td>
<td>5.0 15.5</td>
</tr>
<tr>
<td><strong>Vocal fold hypomobility</strong></td>
<td>5 (27.8%)</td>
<td>34.0 5.0</td>
</tr>
</tbody>
</table>

The significant (p < .001) clinical factors associated with prolonged swallow rehabilitation are presented with the median duration to regain safe swallow for solid and liquid intake. Univariable negative binomial regression model coefficients are included with the 95% confidence intervals. (IQR = Interquartile Range; Coef = Coefficient; CI = Confidence interval).

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### Table II. Tumor Recurrence Following TORS-SL.

<table>
<thead>
<tr>
<th>No.</th>
<th>Primary Tumor</th>
<th>Neck Treatment</th>
<th>Adjuvant Therapy</th>
<th>Adverse Pathology Findings</th>
<th>Time (mo) to recurrence</th>
<th>Site of Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>T1N2aM0</td>
<td>Bilateral MRND</td>
<td>Yes</td>
<td>Extracapsular Spread</td>
<td>8</td>
<td>Neck</td>
</tr>
<tr>
<td>2</td>
<td>T2N2bM0</td>
<td>SNLB</td>
<td>No</td>
<td>Perineural Invasion</td>
<td>6</td>
<td>Neck</td>
</tr>
<tr>
<td>3</td>
<td>T1N2aM0</td>
<td>Ipsilateral MRND</td>
<td>Yes</td>
<td>none</td>
<td>7</td>
<td>Neck</td>
</tr>
<tr>
<td>4</td>
<td>T1N2bM0</td>
<td>SNLB followed by Ipsilateral MRND</td>
<td>Yes</td>
<td>Cartilage Invasion, Vascular Invasion</td>
<td>10</td>
<td>Distant metastases</td>
</tr>
<tr>
<td>5</td>
<td>T3N2cM0</td>
<td>SNLB followed by Bilateral MRND</td>
<td>Yes</td>
<td>Extracapsular Spread, Vascular Invasion, Perineural Invasion</td>
<td>12</td>
<td>Distant metastases</td>
</tr>
<tr>
<td>6</td>
<td>T1N2bM0</td>
<td>Unilateral MRND</td>
<td>Yes</td>
<td>none</td>
<td>12</td>
<td>Distant metastases</td>
</tr>
<tr>
<td>7</td>
<td>T1N2bM0</td>
<td>Bilateral MRND</td>
<td>Yes</td>
<td>Extracapsular Spread</td>
<td>13</td>
<td>Distant metastases</td>
</tr>
</tbody>
</table>

(mo = months; MRND = Modified Radical Neck Dissection; SNLB = Sentinel Lymph Node Biopsy)
study, the concept of “organ preservation” treatment has resulted in the popularization of chemoradiotherapy (CRT) for laryngeal SCCA. Patients previously faced with open supraglottic surgical treatments had to contend with prolonged tracheostomy dependence, enteral feeding, and hospital stays. With the popularization of primary curative CRT, patients could otherwise find equivalent oncologic control noninvasively. As such, the incidence of laryngeal tumors treated with CRT has risen steadily. However, use of primary CRT is beset by several negative considerations. First, there are substantial immediate and long-term complications and risks for patients undergoing primary radiotherapy, which are compounded when chemotherapy is included. Severe mucositis, pain, and dysphagia can be debilitating during treatment, as well as continue long after cessation of treatment. Additionally, because of the significant chance of regional metastasis from supraglottic tumors, patients with clinically negative lymph nodes can typically receive full curative radiation doses to both sides of the neck. In other words, early staged (II) supraglottic SCCA can receive identical CRT treatment as advanced staged (IV) tumors. Additionally, with a significant majority of early staged supraglottic SCCA surviving beyond 5 years, the risk of development of second aerodigestive primary tumors should factor into primary treatment decisions. If radiation is used early in treatment for resectable tumors, this modality will not be available when second tumors arise in a substantial percentage of these patients, as has been demonstrated in the endoscopic laser supraglottic laryngectomy experience.

Supraglottic SCCA patients need no longer choose between “organ-sacrificing” surgery and “organ-preserving” CRT. Rather patients who are surgical candidates can choose between “function-preserving” surgery and “function-risking” CRT. While nonsurgical CRT has been described as leaving anatomic structures intact, base of tongue motion, posterior pharyngeal wall contraction, laryngeal elevation, and laryngeal vestibule closure are all impaired significantly following curative CRT for advanced stage cancer. Additionally, the anatomic targets of supraglottic SCCA are of vital importance to long-term function as increased total dose to the laryngeal structures, along with constrictor musculature, has significantly impaired swallow function. In point, the current study with over 55% of the patients with advanced stage (III/IV) tumors all (100%) had normal swallowing function at the time of follow-up, with 45 days being the longest interval before resumption of unrestricted intake. However, direct functional comparisons are challenging due to associated functional derangements caused by CRT effects such as xerostomia. For instance, CRT has resulted in 20% rate of long-term swallowing dysfunction, with 10% rate of nonoral feeding for supraglottic SCCA, while endoscopic supraglottic SCCA postoperative rates of long-term swallowing dysfunction have ranged between 2% to 13%. Though long-term feeding tube dependence has been previously reported at 22% following TORS–SL, the encouraging outcomes of the present study would fit within the endoscopic laser resection experience.

Data analysis has revealed high-risk factors for prolonged postoperative swallow dysfunction. TORS–SL patients with advanced T-stage and concurrent neck dissection can be counseled regarding the possibility of slower swallow rehabilitation. Also, patients with postoperative vocal fold hypomobility are also likely to have...
prolonged swallowing rehabilitation. Understanding the true effect of these associated factors will require larger studies to allow for multivariate analysis. However, based on univariate analysis, low-risk patients—including those with early staged tumors undergoing staged neck dissections—can lead to a median postoperative interval of 3 days for solids intake and 5 days for liquids.

The functional benefit of TORS–SL was also seen through the avoidance of tracheostomy placement. While the only previous report of TORS–SL had a 78% rate of temporary tracheostomy placement, this was admittedly ascribed to an overly conservative practice due to the limited experience with postoperative TORS–SL airway edema. The present series, along with previous endoscopic laser supraglottic laryngectomy experience, demonstrate that the complete avoidance of temporary tracheostomy can be responsibly achieved.

The heterogeneous nature of supraglottic cancer treatment studies makes oncologic outcome survival comparisons imprecise. For instance, the patient cohort presented in the present study was comprised of 55.6% patients with pN2 or greater. Previous supraglottic endoscopic laser studies reported stage N2 or greater, ranging between only 13.2% to 38.5%, whereas some studies were limited to N0 patients. Patient composition from CRT studies are even more heterogeneous as the percent of patients undergoing postoperative treatment varies widely. Following resection, such population differences create substantial comparative discrepancies.

Comparisons between surgical approaches is also challenging as the percent of patients undergoing postoperative adjuvant therapy varies widely. Following endoscopic laser supraglottic laryngectomy, adjuvant therapy has been administered as rarely as 13.0% (in the report only treating clinically N0 patients) and as high as 55.9%, which is similar to the present study’s level of 55.6% patients receiving adjuvant therapy. However despite the comparative drawbacks, the overall oncologic outcomes from TORS–SL is very encouraging when compared to alternative treatment modalities, including endoscopic laser resection, open surgical resection, and primary CRT.

The inherent selection bias included in surgical prospective data collections is an acknowledged shortcoming of this study. Though it is the authors’ practice to offer TORS–SL to all supraglottic SCCA patients, data was not kept regarding number of patients either declining or not cleared for surgical intervention. Future studies should include comparative outcomes for these nonsurgical patient groups as case controls.

CONCLUSION

In conclusion, the initial oncologic and functional outcomes following TORS supraglottic laryngectomy are very encouraging. In addition to favorable initial oncologic outcomes, TORS functional outcomes equal or exceed those previously reported with alternative supraglottic cancer treatments of primary radiotherapy and endoscopic laser resection. Additional study is required to corroborate these initial encouraging results. Institutions with experience in robotic surgery should consider offering TORS supraglottic laryngectomy to patients with laryngeal squamous cell carcinoma.

BIBLIOGRAPHY