Transoral Robotic-Assisted Surgery for Head and Neck Squamous Cell Carcinoma

One- and 2-Year Survival Analysis

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Objective: To report 2-year survival outcomes for head and neck squamous cell carcinoma using transoral robotic-assisted resection.

Design: Prospective case study.

Setting: Two tertiary care centers.

Patients: Eighty-nine patients from 2 tertiary care centers (University of Alabama at Birmingham and the Mayo Clinic in Rochester, Minnesota) with head and neck squamous cell carcinoma of all stages and subsites, who underwent transoral robotic-assisted resection between March 2007 and December 2008, with a median follow-up time of 26 months.

Main Outcome Measures: Disease-free survival, cancer recurrence, and gastrostomy tube dependence

Results: Seventy-one patients had T1 (n=29) or T2 (n=42) tumors while 18 patients had T3 (n=8) or T4 (n=10) tumors. There were 24 patients with overall stage I or II disease and 65 with stage III or IV disease. At the time of the last follow-up visit (median, 26 months), there had been a total of 11 patients with recurrent cancer: 3 with local; 7, regional (2 of whom also had distant metastases); and 1, distant. Seven patients were treated for recurrent disease. Eighty-two patients had no evidence of disease, 1 patient died of the disease, 2 died of other disease, and 4 were alive with disease at the last follow-up visit. Results of Kaplan-Meier survival analysis showed that the 2-year recurrence-free survival rate for the cohort was 86.5%. None of the patients were gastrostomy tube dependent at the last follow-up visit.

Conclusion: The 2-year functional and oncologic results justify the continued treatment of select patients with head and neck squamous cell carcinoma with robotic-assisted surgical resection.


IN THE UNITED STATES, HEAD AND neck squamous cell carcinoma (HNSCC) comprises approximately 4% of all malignant neoplasms. This corresponds to an estimated 17 per 100,000 persons with newly diagnosed HNSCC per year. The current trend of treatment is preservation of organ function and minimizing treatment-related morbidity.1 In the head and neck, minimally invasive surgical strategies have used transoral laser microsurgery techniques. Since the introduction of the first surgical robot in 1985, multiple surgical specialties including cardiac surgery, urology, general surgery, and gynecology have found it a valuable tool for improving surgical outcomes. Recently, transoral robotic-assisted surgery (TORS) has been adopted for head and neck surgery as a minimally invasive technique to decrease overall patient morbidity and mortality.2 It is currently approved by the Food and Drug Administration for T1 and T2 oropharyngeal tumors.

Previous studies have demonstrated TORS to have acceptable feasibility and safety in resection of upper aerodigestive tract neoplasms, as well as acceptable functional outcomes for selected primary and salvage head and neck tumors.3,4 In a recent review of the current clinical experiences of multiple institutions, it was concluded that TORS affords potential advantages and benefits over current treatment modalities including better visualization and tumor access via a less morbid approach resulting in better overall functional outcomes.5

Despite growing safety data, to our knowledge, there have been no published reports of oncologic outcomes following TORS; however, local control rates are promising.5 There is strong evidence to suggest that good local control is based on negative surgical margins, and several studies

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have shown that to be an achievable goal with TORS.6-9 We show, for the first time to our knowledge, survival data in a population of patients with HNSCC treated with TORS. Overall recurrence-free survival is presented as well as survival statistics relating to T stage and adjuvant therapy, demonstrating the oncologic effectiveness of this technique.

METHODS

PATIENT SELECTION

Between March 2007 and December 2009, 89 patients with various stages and subsites of HNSCC underwent TORS for resection of their primary tumor. Patients received their surgery at 1 of 2 tertiary care centers, University of Alabama at Birmingham or the Mayo Clinic in Rochester, Minnesota. Institutional review board approval was obtained to perform a clinical trial using the da Vinci Robot (Intuitive Surgical Inc, Sunnyvale, California) for the resection of head and neck tumors. Inclusion criteria included lesions of the oral cavity, oropharynx, hypopharynx, or larynx that were amenable to total resection transorally. Patients were excluded preoperatively for tumors invading bone, those predicted to produce a defect requiring free-tissue transfer, those unable to provide informed consent, and those with mouth opening smaller than 1.5 cm. We did not exclude patients based on previous treatment for HNSCC, surgical or nonsurgical. All patients were evaluated preoperatively with a complete head and neck examination including fiberoptic laryngoscopy and computed tomography or positron emission tomography imaging. Patients were counseled about alternatives to TORS for tumor management.

TORS PROCEDURE

Operative treatment involved general anesthesia, transnasal or transoral endotracheal intubation, and paralysis for the duration of the transoral portion of the procedure. The operating room was arranged with the head of the bed rotated 180° from anesthesia, the surgeon’s console approximately 2.4 meters from the head of the bed, and the manipulator unit near the patient’s left hip (Figure 1). Exposure was obtained using the Feyh-Kastenbauer laryngeal retractor, the Crowe Davis retractor, or an Andrews tongue blade and cheek retractor. With adequate exposure, resection was performed. The technique of TORS for removal of tonsillar tumors and base of tongue cancer has been described in detail by Moore et al.4 Neck dissection(s), if warranted, was performed either at the same operation or in a staged operation. Adjuvant treatment with radiation and/or chemotherapy was recommended for those patients with (1) 2 or more lymph nodes involved with metastatic tumor, (2) evidence of extracapsular spread of tumor metastasis in 1 or more lymph nodes, (3) desmoplastic reaction at the primary site, (4) evidence of perineural or angiolymphatic invasion at the primary site, or (5) evidence of margins positive for tumor at the primary site.

OUTCOME MEASURES

All patients were monitored throughout their hospital stay and up to 33 months’ postoperatively. Data collected in this study included patient age, tumor site, histologic characteristics, clinical and pathologic stage, any previous head and neck cancer treatment, feeding tube dependence at the last follow-up visit, and clinical outcome including recurrence and death. Overall recurrence-free survival rate at 2 years was estimated by the methods of Kaplan and Meir. Survival comparisons at 2 years were also made based on (1) overall stage: early (I and II) vs late (III and IV), (2) tumor stage, (3) nodal stage, (4) those treated with and without radiation, and (5) those treated with and without chemoradiation. P values less than .05 were considered significant. Patients were also assessed for feeding tube dependence at their most recent follow-up visit as a measure of swallowing function.

RESULTS

We evaluated 89 patients with biopsy-proven squamous cell carcinoma of the upper aerodigestive tract who underwent TORS between March 2007 and December 2009. The mean age was 59 years (range, 36-88 years). The location of the primary tumor was in the oral cavity in 2 patients, oropharynx in 77, and larynx in 10. It should be noted that all laryngeal tumors were supraglottic in nature. The primary treatment was TORS for the majority of patients, although 7 patients (8%) underwent salvage surgery after chemoradiation. Of the patients who underwent TORS as primary treatment, 56 (63%) underwent postsurgical radiation therapy and 43 (48%) had chemotherapy either before or after surgical treatment.
Most patients (n=68 [76%]) underwent unilateral or bilateral neck dissection either at the time of TORS or in a staged manner (Table 1). Negative margins confirmed on permanent pathologic findings were obtained for all patients. The pathological staging of the cancers treated demonstrated 29 T1 tumors, 42 T2 tumors, 8 T3 tumors and, 10 T4 tumors (Table 2). There were 24 patients with early-stage disease (stage I or II) and 65 with advanced-stage disease (stage III or IV).

The median follow-up period was 26 months. At the time of the last follow-up visit, there had been a total of 11 patients with recurrent cancer: 3 local, 2 regional (1 of whom also had distant metastases), and 1 distant. Four of the patients (36%) who had tumor recurrence had undergone salvage treatment after chemoradiation failure. Most of the recurrences (n=8) were in patients with stage III or IV disease. One patient developed a new primary malignant tumor 20 months after therapy completion. The median time to recurrence was 6 months (range, 7–17 months). Seven patients underwent treatment for their recurrent disease: 1 received surgical excision of a recurrent neck mass and wedge resection of a pulmonary metastasis, 1 had excision of a local recurrence, 2 had delayed neck dissections for regional recurrences, 1 underwent salvage total glossectomy and laryngectomy, and 2 patients received reirradiation therapy. At the last follow-up visit, 82 patients had no evidence of disease, 1 patient died of the disease, 2 died of other disease, and 4 were alive with disease.

SURVIVAL

The overall 2-year recurrence free survival rate for this cohort of patients was 86.3% (Figure 2). Evaluation of patients undergoing primary TORS for their disease demonstrated an increased 2-year survival rate of 89.3%. Overall recurrence-free survival did not directly correlate with overall stage or nodal stage (P=.34 and .38, respectively). Those with earlier T-stage tumors appeared to have slightly better recurrence-free survival than those with later stages, but this was not statistically significant (P=.51). Patients who received radiation therapy, either before or after surgical resection of their tumors, did not have a significant improvement in survival (P=.45). Patients who underwent chemoradiation did not appear to have a significantly different recurrence-free survival than those who did not (P=.85).

SWALLOWING FUNCTION

Postoperative swallowing ability varied based on the location of tumor, preoperative swallowing ability, T stage, and age of the patient. Some patients tolerated an oral diet within 1 to 2 days after surgery, whereas others were discharged home with a short-term nasal feeding tube or long-term gastric feeding tube. Several patients were feeding tube dependent prior to TORS. Of note, all patients had regained full swallowing ability at the time of the last follow-up visit; no patients remained feeding tube dependent.

COMMENT

To our knowledge, this is the first study to evaluate 2-year oncologic outcome data and functional data after robot-assisted resection of upper aerodigestive tract tumors. Previous studies have confirmed that transoral surgical management of oropharyngeal cancer, especially early stage, is a safe treatment option with good functional re-

### Table 1. Primary Characteristics of 89 Patients With Head and Neck Squamous Cell Carcinoma

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients, No. (%)</th>
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<tbody>
<tr>
<td>Tumor site</td>
<td></td>
</tr>
<tr>
<td>Oral cavity</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>77 (87)</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>0</td>
</tr>
<tr>
<td>Larynx</td>
<td>10 (11)</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>88 (99)</td>
</tr>
<tr>
<td>Adenoid cystic carcinoma</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Radiation therapy</td>
<td></td>
</tr>
<tr>
<td>Before surgery</td>
<td>7 (8)</td>
</tr>
<tr>
<td>After surgery</td>
<td>56 (63)</td>
</tr>
<tr>
<td>None</td>
<td>26 (29)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>43 (48)</td>
</tr>
<tr>
<td>No</td>
<td>46 (52)</td>
</tr>
<tr>
<td>Neck dissection</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>68 (76)</td>
</tr>
<tr>
<td>No</td>
<td>21 (24)</td>
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</table>

### Table 2. TNM Classification for 89 Patients With Head and Neck Squamous Cell Carcinoma

<table>
<thead>
<tr>
<th>N</th>
<th>T Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classification</td>
<td>T1</td>
</tr>
<tr>
<td>N0</td>
<td>10</td>
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<tr>
<td>N1</td>
<td>4</td>
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<td>N2a</td>
<td>4</td>
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<td>N2b</td>
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<tr>
<td>N2c</td>
<td>3</td>
</tr>
<tr>
<td>N3</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
</tr>
</tbody>
</table>
In the present study, we demonstrate 2-year survival data for primary treatment of oropharyngeal disease of 89.3%, which is comparable to standard treatment modalities.

**ONCOLOGIC OUTCOMES**

Our oncologic outcomes are similar to those quoted in the literature for other methods of transoral surgical management of oropharyngeal cancer. Studies have reported a 2-year overall survival rate in previously untreated tonsil cancer of 92.2% and 90.0% for base of tongue cancers. A similar study quoted a 3-year survival of 85% for patients treated with primary surgery for early stage oropharyngeal cancer. Surgery was the primary treatment for all of the patients included in these studies. Our data are confounded by 7 patients in whom surgery was salvage treatment, which negatively affected our survival outcomes. Two-year recurrence-free survival was 86.3% for the entire cohort; however, a 2-year survival rate of 89.3% was achieved in patients undergoing primary treatment. Of the 11 recurrences, 4 were in patients who had previous recurrence, and most were in patients with stage III or IV disease (n=8). We found that more than half of our salvage patients had recurrences. Patients undergoing surgery for recurrent oral cavity and oropharyngeal disease have recurrence rates between 30% and 60%. Historically, patients with regional recurrences who undergo salvage neck dissections seem to do poorly.

The initial surgical management of patients with HNSCC, regardless of the technique used, allows for the most accurate staging possible. Staging based on surgical pathologic findings from the primary site and lymph nodes provides good prognostic information that is not well defined by clinical and/or radiographic staging alone. In our study, 26 patients (29%) with T1-2/N0-1 disease did not need adjuvant therapy following TORS, thereby shortening their treatment course, decreasing overall cost, mitigating recovery time, and saving other treatment modalities for recurrent disease or new primary tumors. Patients treated with multimodality therapy avoided full-dose radiation and/or the toxic effects of combined chemotherapy. Accurate surgical staging allows true combined modality therapy to be reserved for those patients with the worst prognostic factors, namely, lymph node extracapsular spread. Although human papillomavirus status testing is not currently available at our institution, TORS would also allow for de-escalation of treatment in human papillomavirus-positive patients.

**SWALLOWING OUTCOME**

There is a definite proven functional advantage in patients who are treated with surgery alone or with a reduced dose of radiation following surgical resection without the need for chemotherapy. The addition of concurrent chemotherapy to radiation therapy for locally advanced HNSCC is directly correlated with increased long-term dysphagia. Shiley et al report a gastrostomy tube placement rate of 82% in patients undergoing chemoradiation for advanced-stage oropharyngeal squamous cell carcinoma; almost half of whom (47%) were still feeding tube dependent at 1 year after treatment. Early data favor TORS over chemoradiation in terms of swallowing outcomes. Most preliminary studies thus far have quoted significantly lower rates of gastrostomy tube dependence at 1 year after treatment with TORS. These rates range from 0%, as in studies by Moore et al and Weinstein et al, to 9.5% observed in the 2009 study by Iseli et al.

All patients in our study had their feeding tube removed by their 2-year follow-up visit, demonstrating an excellent long-term functional outcome. It can be implied that such good swallowing outcomes may be partially secondary to the lower doses of radiation therapy needed at the primary site after initial resection of the tumor. All patients in this study had negative margins via TORS and therefore did not receive more than 60 Gy to the primary site, if they required radiation treatment at all. Twenty-six patients (29%) in our study did not require adjuvant radiation. Teguh et al have previously shown a significant direct relationship between increased mean dose of radiation to the superior constrictor muscle and worsened swallowing findings obtained by fiberoptic endoscopic evaluation of the swallowing process.

**CRITICAL EVALUATION OF THE ROLE OF TORS**

The surgical robot has several advantages over traditional endoscopic approaches, including 3-dimensional visualization, tremor filtration, and greater freedom of instrument movement providing improved ability to manipulate tissue during resection. Open approaches are often associated with multiple morbidities including cosmetic deformity, malocclusion, and dysphagia.

Numerous studies have observed shorter operative time, decreased hospital stay, and faster return to normal function in patients undergoing TORS. Average hospital stay ranges from 2 to 7 days. Numerous studies have quoted significantly lower rates of gastrostomy tube dependence at 1 year after treatment with TORS. These rates range from 0%, as in studies by Moore et al and Weinstein et al, to 9.5% observed in the 2009 study by Iseli et al.

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Not all patients are good candidates for TORS. We have found several limiting factors, mostly based on inability to achieve adequate surgical exposure of the tumor. Factors contributing to this include significant trismus, narrow arched mandible, full dentition, and retrognathia. This should be assessed for preoperatively in clinic or in most cases in the form of a separate preoperative endoscopy procedure, usually performed for biopsy and tissue diagnosis, prior to scheduling TORS. Ability to obtain adequate exposure improves with experience.

The surgeon is required to undergo specialized training in order to perform TORS, and there is a definite need for highly skilled and dedicated pathologists as part of the multidisciplinary team. It is also important that patients are counseled preoperatively on the possible need for an open neck dissection and that TORS does not always eliminate the need for additional radiation therapy and chemotherapy.

Time required for operating room setup can be a disadvantage early on. However, this has been shown to drastically decrease based on increasing experience. Cost of maintenance and the initial purchase of the robot have...
also limited its widespread use. Profitability increases with increased caseload, decreased hospitalization, and possibly individualized care. Most institutions have numerous surgical specialties that use the robot.

This study has several weaknesses that warrant mention. There is a relatively small patient number and therefore few recurrences during the follow-up period. This makes it difficult to achieve overall statistical significance when evaluating several of the outcome measures. Future studies should stratify patients into groups based on positivity for high-risk human papillomavirus and P16 and/or p53 overexpression to evaluate the influence these factors have on oncologic outcomes. Recently it has been shown that these tumor profile findings are associated with improved survival in HNSCC. Also, it would be helpful to compare functional and oncologic results in patient groups, matched by stage and tumor factors, for those undergoing TORS vs chemoradiation as their primary treatment. This would most likely require further multi-institutional participation to gain adequate numbers.

CONCLUSIONS

We have found that TORS offers a technically feasible and oncologically sound alternative treatment method for selected patients with HNSCC. It is still a relatively new technique, however, and long-term oncologic outcomes are not available. The early functional and oncologic results justify the continued treatment of select patients with HNSCC with robotic-assisted surgical resection.

Submitted for Publication: March 29, 2010; final revision received August 3, 2010; accepted September 5, 2010.

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Author Contributions: Drs White, Magnuson, Moore, Rosenthal, and Desmond had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: White, Moore, Rosenthal, Carroll, and Magnuson. Acquisition of data: White, Magnuson, Moore, Carroll, Rosenthal, and Olsen. Analysis and interpretation of data: White, Moore, Magnuson, and Desmond. Drafting of the manuscript: White, Moore, Magnuson, and Rosenthal. Critical revision of the manuscript for important intellectual content: White, Moore, Rosenthal, Carroll, Olsen, and Magnuson. Statistical analysis: Desmond. Obtained funding: Rosenthal. Administrative, technical, and material support: Moore, Carroll, and Magnuson. Study supervision: Moore, Rosenthal, Carroll, Olsen, and Magnuson.

Financial Disclosure: None reported.

Previous Presentation: This study was presented orally at the annual meeting of the American Head and Neck Society; April 29, 2010; Las Vegas, Nevada.

REFERENCES