Transoral Robotic Surgery Alone for Oropharyngeal Cancer

An Analysis of Local Control

Objective: To evaluate local control following transoral robotic surgery (TORS) with the da Vinci Surgical System (Intuitive Surgical Inc) as a single treatment modality for oropharyngeal squamous cell carcinoma (OSCC).

Design: Prospective, single-center, observational study.

Setting: Academic university health system and tertiary referral center.

Patients: Thirty adults with previously untreated OSCC.

Intervention: Transoral robotic surgery with staged neck dissection as indicated.

Main Outcome Measures: Local control and margin status.

Results: Thirty patients were enrolled with previously untreated OSCC and no prior head and neck radiation therapy. Follow-up duration was at least 18 months. At the time of diagnosis, 9 tumors were T1 (30%); 16 were T2 (53%); 4 were T3 (13%); and 1 was T4a (3%). The anatomic sites of these primary tumors were tonsil in 14 (47%), tongue base in 9 (30%), glossotonsillar sulcus in 3 (10%), soft palate in 3 (10%), and oropharyngeal wall in 1 (3%). There was only 1 patient (3%) who had a positive margin after primary resection; further resection achieved a final negative margin. Perineural invasion was noted in 3 tumors (10%). No patient received postoperative adjuvant therapy. At a mean follow-up of 2.7 years (range, 1.5-5.1 years), there was 1 patient with local failure (3%).

Conclusion: As the only modality used for treatment of pathologically low-risk OSCCs, TORS provides high local control and is associated with low surgical morbidity.


TRANSPORT ROBOTIC SURGERY (TORS), a novel group of techniques first developed at the University of Pennsylvania, has been defined as a surgical approach for benign and malignant lesions of the oral cavity and laryngopharynx. It involves placing a minimum of 3 arms of the da Vinci Surgical System (Intuitive Surgical Inc) into the oral cavity with oral retractors. The TORS en-bloc surgical approach is not only a primary modality of invasive transoral resection of oropharyngeal squamous cell carcinomas (OSCCs). Local control has been exceptionally high in published series, as high as 98% in a recent report of patients with advanced therapy, but it also provides important information regarding pathologic tumor attributes that is useful to determine the need for subsequent adjuvant therapy.

To date, the main oncologic indication for TORS has been the minimally invasive transoral resection of oropharyngeal squamous cell carcinomas (OSCCs). Nonetheless, a factor confounding interpretation of the true effectiveness of TORS on local control has been that most patients in these cohorts have also had multiple histologically confirmed positive lymph nodes or extracapsular nodal disease resulting in the need for postoperative radiation or chemoradiation therapy to treat the neck as well as the primary tumor bed. In 1 large series, for example, only 2% of patients had positive margins, but the presence of nodal metastases resulted in 85% of patients receiving postoperative irradiation to the neck and primary site with or without che-

Video available online at www.archoto.com

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The use of irradiation as well as chemotherapy in a large number of cases calls into question whether the success at the primary site was related to the TORS procedure itself or the addition of postoperative radiation or chemoradiation therapy.

In an effort to discover whether TORS alone, without postoperative radiation or chemoradiation therapy, can provide effective local control for mucosal OSCC, we decided to study a cohort of patients from 2 consecutive TORS single-arm, prospective, observational trials performed at the University of Pennsylvania. Within both of these studies was a cohort of patients with previously untreated OSCC who underwent TORS alone. These patients were a subset of the world’s first research and clinical program in Transoral Robotic Surgery (TORS) utilizing the da Vinci Surgical System.

The primary objective of the current study was to assess the local control rate for a series of patients with OSCC who were treated with TORS followed by staged neck dissection as indicated without postoperative radiation therapy or chemotherapy. Secondary end points included evaluation of the safety and efficacy of this approach.

METHODS

Data were collected from a pool of 422 patients who were enrolled in 2 consecutive protocols investigating TORS. Both protocols were approved by the institutional review board of the Hospital of the University of Pennsylvania, Philadelphia. Both studies were prospective, single-arm, observational trials. The preoperative inclusion criteria for the 2 TORS studies were (1) patients aged at least 18 years at the time of treatment; (2) presence of indications for diagnostic or therapeutic surgical approaches for benign or malignant diseases of the oral cavity or laryngopharynx; and (3) written informed consent and/or consent waiver by the institutional review board.

The tumor-related indications for TORS resection included previously untreated, biopsy-proven OSCC of stage I, II, III, IVA, or IVB. The preoperative contraindications for the studies were (1) unexplained fever and/or untreated, active infection, (2) pregnancy, (3) previous head and neck surgery precluding transoral robotic procedures, and/or (4) the presence of medical conditions contraindicating general anesthesia or transoral surgical approaches. The intraoperative contraindication was inability to adequately visualize anatomy to the extent necessary to perform the diagnostic or therapeutic surgical approach transorally, as detailed previously.2

Of the original pool of 422 patients who were enrolled in the 2 consecutive prospective TORS trials, 30 had previously untreated OSCCs and underwent TORS alone between August 2005 and February 2010 at the University of Pennsylvania. These patients are the focus of the current study. Patients were observed following TORS is described elsewhere.5 Postoperative follow-up was standardized. The minimum follow-up during the first year after diagnosis was every 3 months; during the second year, every 4 months; during the third and fourth years, every 6 months; and during the fifth year, 1 annual visit. During the first year after diagnosis was every 3 months; during the second year, every 4 months; during the third and fourth years, every 6 months; and during the fifth year, 1 annual visit. At every follow-up visit, radiologic images were obtained, including either positron emission tomography (PET) or computed tomography (CT) with contrast or magnetic resonance imaging of the neck with or without chest radiographs.

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Although single-arm cohort trials may be subject to significant bias, numerous steps were taken to ensure that bias was minimized. All clinical investigators who participated in the TORS prospective trials at the University of Pennsylvania shared equipoise concerning the standard surgical and nonsurgical treatments vs TORS for the patient population under investigation. Therefore, in an effort to avoid surgical selection bias, we offered the option of participation to all patients in the Otorhinolaryngology–Head and Neck Surgery outpatient clinics who fit the eligibility criteria for the 2 University of Pennsylvania prospective TORS trials.

An additional source of bias in surgical trials is the potential for variability in surgical technique among contributing surgeons. All surgeons who contributed patients to this trial were trained in a standardized approach to each TORS procedure, and consensus was reached concerning the en-bloc surgical approach.

It is known that a potential confounder inherent to single-arm surgical cohort trials is that patients who choose to participate in a surgical study vs a nonsurgical study might be healthier overall. Patient preoperative functional status and overall health status were assessed using the Karnofsky Score and the Charlson Comorbidity Index, respectively, to ensure a measure of comparability of the results of this series with those of other nonsurgical series. Of note, 1 patient with a T1N0 SCC of the soft palate was lost to follow-up within 1 month of surgery and was excluded from the analysis.

RESULTS

PATIENT CHARACTERISTICS

From August 2005 to February 2010, a total of 30 consecutive patients at the University of Pennsylvania with stage I, II, III, or IV OSCC were treated with primary TORS alone without postoperative irradiation or chemotherapy. The minimum follow-up was 18 months, and the mean follow-up was 2.7 years. Tumor and patient characteristics of the 30 study patients are listed in Table 1. Clinical and pathologic TNM staging is presented in Table 2.

ONCOLOGIC OUTCOMES

In 30 primary TORS procedures for OSCC, final pathologic evaluation revealed 10 cases (33%) that were pathologic node positive, and 1 case with a positive margin (3%), defined as tumor presence at the inked margin. This patient had focal positivity of carcinoma in situ, and therefore reexcision at the time of neck dissection was considered a better option than postoperative chemoradiation therapy. One patient was over the weight limit for any radiation machine in our region and therefore was observed postoperatively.

Under the treatment regimen of primary TORS and staged neck dissection without postoperative radiation, this cohort achieved local, regional, and distant disease control in 29 of 30 (97%), 27 of 30 (90%), and 30 of 30 (100%) cases, respectively, at a minimum follow-up of 18 months. Overall survival for this cohort at the time of last follow-up was 30 of 30 (100%), also at a minimum follow-up of 18 months.

The 1 local recurrence 3 months and 19 days after TORS occurred in a patient with a T2N0 tumor (staged rT4 at the time of recurrence because of invasion of the medial pterygoid muscle). This patient had negative margins following TORS, with pathologic analysis showing a poorly differentiated SCC with invasion to a depth of

Figure. Orientation of transoral robotic surgical specimen for pathologic analysis. A, Surgical specimen inked and pinned to cork board. B, Transection of surgical specimen to assess adequacy of deep margin.
0.3 cm and no perineural invasion, angiolympathic invasion, or dysplasia at the margin. There was no regional or distant metastasis. At last follow-up 1 year and 7 months after chemoradiation for the recurrence, this patient’s clinical examination findings and PET CT findings were negative, and full nutrition was being maintained without a feeding tube.

Three patients had a regional recurrence. One patient originally had a cT3N2b tongue base cancer that was staged at pT1N2b at histologic examination after the primary TORS. This patient underwent radical neck dissection after TORS and was found to have 16 positive nodes and extracapsular spread. The patient was advised to undergo postoperative chemoradiation, which he refused. His disease then recurred in both necks 1 year, 11 months after TORS and underwent salvage chemoradiation treatment. One patient with a cT2N0/pT2N0 glossotonsillar sulcus tumor who underwent I-IV selective neck dissection with no positive nodes found had regional recurrence in the ipsilateral high neck 4 months after TORS and was treated with chemoradiation. The third patient with neck recurrence had a cT3N1/pT2N2b tongue base carcinoma, and the nodes showed no extracapsular spread. The patient was advised to undergo adjuvant radiation therapy and refused. He then developed a contralateral neck recurrence and was treated with a neck dissection that revealed 2 positive nodes without extracapsular spread. He was again advised to undergo radiation therapy. He eventually received chemoradiation at another institution.

**PERIOPERATIVE FINDINGS**

The average intraoperative blood loss was 88 mL (range, 10-500 mL). No patient needed a blood transfusion. The average surgical time for TORS was 84 minutes (range, 31-152 minutes). No cases were converted to open resections. The average hospital stay was 3.6 days (range, 1-7 days).

**FUNCTIONAL OUTCOMES**

At last follow-up, all patients were taking full oral diet without a feeding tube. One patient underwent temporary tracheostomy owing to preoperative morbid obesity. One patient had mild nasopharyngeal insufficiency following TORS radical tonsillectomy.

**COMPLICATIONS**

Complications in the 30-day postoperative period included 1 case of temporomandibular joint capsulitis that resolved with anti-inflammatory medication; 1 case of postoperative seizure that resolved with medication; 1 case of postoperative bradycardia that resolved without intervention; 1 case of dyspepsia related to tube feedings requiring outpatient management; and 2 cases of minor bleeding episodes that resolved without sequelae. One patient had acute renal failure that resolved with medical treatment in 12 days, and 1 patient was hospitalized related to syncope and dehydration and discharged after 24 hours without further complications. There were no intraoperative or perioperative deaths and no life-threatening bleeding incidents.

**COMMENT**

The primary objective of this study was to assess the local control rates in 30 patients with OSCC treated with TORS.
The use of postoperative radiotherapy (PORT) for cancers of the head and neck has evolved from the seminal observations by Fletcher and Evers and Hamberger et al that risk of neck disease relapse increases following open transcervical surgical approaches to the primary site, especially with tumor transection, and that use of elective and comprehensive neck irradiation reduces these relapses. These observations led some radiation oncologists to favor PORT even in the absence of adverse pathologic risk features following open transcervical surgical approaches to the primary site owing to concerns of potential tumor seeding during the surgery. It is now clear that in the setting of node-negative disease with no primary site adverse features, the risk of local-regional relapse with observation will be 10% or less after open transcervical primary resection.

With other transoral surgical techniques (eg, transoral laser microsurgery [TLM]) that offer primary tumor resection without the risks of surgical seeding of the exposed neck compartments, the risk of local failure following TLM alone without irradiation for previously untreated oropharyngeal carcinomas, in patients with predominantly node-negative necks, has been reported to be 6.8%. The findings in our series suggest that TORS, even without adjuvant radiotherapy, offers local control rates similar to if not better than those seen with TLM. If so, the higher control rate may be associated with greater confidence in the surgical margin assessment seen with en-bloc resection that lends itself to potentially more accurate pathologic evaluation when the surgeon provides clear orientation of the specimen. Moreover, the high local control rates observed also provide assurance that in more advanced nodal disease following primary site treatment with TORS, greater confidence can be attributed to a negative margin. This has implications for the design and dose of adjuvant irradiation to the primary site and suggests that the post-TORS primary site could be well treated with standard postoperative doses and fields that encompass the surgical bed rather than the original, and usually larger, tumor volume. Whether the primary site in the patient with significant nodal metastases could even be excluded from PORT in the absence of any primary site pathologic risk features is a subject of ongoing research.

In 2002, Parsons et al reviewed the available literature from the prior 30 years comparing outcomes of surgery vs radiation for oropharyngeal cancer and concluded that given the higher complication rate with surgery, most oropharyngeal cancers should be treated with radiation. While Parsons et al conducted an outstanding study, the surgical approaches analyzed in their series included only open transcervical or transmandibular primary resections, which of course was appropriate for the historical period they studied from 1970 to 2000, but those procedures are very different from transoral techniques in terms of morbidity. In fact, the inherent problems with open surgical approaches were the very catalyst that led to clinical research into minimally invasive approaches such as TLM.

While TLM has been widely adopted for the management of early glottic cancer and found to be very useful for the transoral management of supraglottic SCC, by com-
comparison there is a paucity of literature reporting outcomes for TLM in OSCC. Transoral robotic surgery is a natural extension of the important and seminal research in TLM. The primary malignant indications for TORS to date have been for tumors of the oropharynx and supraglottis. Therefore, in an era in which open approaches have been largely supplanted by minimally invasive surgical approaches such as TLM and TORS, arguments denouncing the role of surgery based on the findings of Parsons et al are no longer valid.

A reasonable question is whether the results of a single-arm cohort trial from 1 institution are generalizable. Consistency in technique among the surgeons in this study was achieved by adherence to previously agreed-upon surgical and pathologic principles. Transoral robotic surgery is a novel group of specific surgical procedures that were designed to be both consistent and reproducible. In addition, an important part of developing TORS was the concurrent effort to determine which tumors and sites would be best suited for the new procedures. In our opinion, the best way to ensure that other surgeons can reproduce our excellent outcomes is through our concise and clear articulation of the techniques via standardized and validated training. Ideally, training for TORS as for any new surgical technique should include an emphasis on the indications and contraindications for applying the surgery, the actual details of the surgical technique used to achieve en-bloc resection, and the proper orientation techniques for precise pathologic analysis of the resected specimen.

The impetus for studying this subset of TORS patients was to answer the question "are successful oncologic outcomes at the primary site related to the actual TORS resection, or are they a function of combining TORS with postoperative adjuvant therapy?" While most patients in this study had advanced clinical stage, almost all of them were found to have favorable pathologic features as well as pathologic down-staging at both the primary site and the neck (Table 2), which allowed deintensification of the overall treatment approach compared with, for example, definitive chemoradiation. In conclusion, while these data support TORS alone without postoperative irradiation for oropharyngeal carcinomas with favorable pathologic features, further investigation would be valuable to allow these results to be generalized. We strongly encourage other investigators to perform high-quality, single-arm, prospective, observational trials and encourage funding of multi-institutional phase 2 trials to confirm generalizability of the TORS techniques and outcomes.

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