Salvage Surgery for Recurrent Cancers of the Oropharynx
Comparing TORS With Standard Open Surgical Approaches

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IMPORTANCE Surgical salvage may be the only viable treatment option for recurrent tumors of the oropharynx. To our knowledge, there have been no published reports directly comparing the oncologic and functional outcomes of patients with recurrent oropharyngeal squamous cell carcinoma (SCC) treated with transoral robotic-assisted surgery (TORS) with those treated with traditional open surgical approaches.

OBJECTIVE To compare the oncologic and functional outcomes of patients with recurrent oropharyngeal SCC treated with TORS with those treated with traditional open surgical approaches.

DESIGN Retrospective multi-institutional case-control study; study dates, March 2003 through October 2011.

SETTING Four tertiary care institutions (University of Alabama at Birmingham; M. D. Anderson Cancer Center, Houston, Texas; Mayo Clinic, Rochester, Minnesota; and Henry Ford Hospital, Detroit, Michigan).

PARTICIPANTS Sixty-four patients who underwent salvage TORS for recurrent oropharyngeal SCC were matched by TNM stage to 64 patients who underwent open salvage resection.

INTERVENTION OR EXPOSURE Salvage TORS for recurrent SCC of the oropharynx.

MAIN OUTCOME AND MEASURES Patient demographics, operative data, functional, and oncologic outcomes were recorded and compared with a similarly TNM-matched patient group that underwent salvage surgical resection by traditional open surgical approaches.

RESULTS Patients treated with TORS were found to have a significantly lower incidence of tracheostomy use (n = 14 vs n = 50; \( P < .001 \)), feeding tube use (n = 23 vs n = 48; \( P < .001 \)), shorter overall hospital stays (3.8 days vs 8.0 days; \( P < .001 \)), decreased operative time (111 minutes vs 350 minutes; \( P < .001 \)), less blood loss (49 mL vs 331 mL; \( P < .001 \)), and significantly decreased incidence of positive margins (n = 6 vs n = 19; \( P = .007 \)). The 2-year recurrence-free survival rate was significantly higher in the TORS group than in the open approach group (74% and 43%, respectively) (\( P = .01 \)).

CONCLUSIONS AND RELEVANCE This study demonstrates that TORS offers an alternative surgical approach to recurrent tumors of the oropharynx with acceptable oncologic outcomes and better functional outcomes than traditional open surgical approaches. This adds to the growing amount of clinical evidence to support the use of TORS in selected patients with recurrent oropharyngeal SCC as a feasible and oncologically sound method of treatment.


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The main treatment of primary squamous cell carcinoma (SCC) of the oropharynx has largely been nonsurgical, especially for advanced stage disease. It was recently shown that the highest treatment failure rate in this group of patients was in those who received primary chemoradiotherapy. Surgical salvage may be the only viable treatment option for attempts at disease eradication and potential cure when this occurs. Salvage surgery in the head and neck is associated with high morbidity rates, poor overall and disease-specific survival, prolonged hospital stays, and decreased quality of life.

Selecting a surgical approach that provides adequate access and visualization of the tumor is critical. The available options include open techniques via a transcervical, lingual release approach, or occasionally a mandibulotomy. These open approaches often produce defects that require microvascular reconstruction, especially in the presence of a radiated field. More recently, however, transoral approaches using a laser or robotic assistance have shown great promise in surgical resection of recurrent oropharyngeal SCC.

Despite growing outcomes data for transoral robotic surgery (TORS) for primary treatment of head and neck SCC, to our knowledge there have been no published reports directly comparing the oncologic and functional outcomes of patients with recurrent oropharyngeal SCC treated with TORS with those treated with traditional open surgical approaches. The objective of the current study was to report clinical outcomes of 2 matched patient groups, including operative time, blood loss, tracheostomy use, feeding tube duration, hospital stay, margin status, and operative complications, via a retrospective, multi-institutional study.

Methods

Patients

After approval was obtained from the institutional review board, the medical records of patients who underwent salvage surgical resection of recurrent SCC of the oropharynx at 4 tertiary care institutions (University of Alabama at Birmingham; M. D. Anderson Cancer Center, Houston, Texas; Mayo Clinic, Rochester, Minnesota; and Henry Ford Hospital, Detroit, Michigan) between 2003 and 2011 were reviewed retrospectively. Sixty-four patients were found to have undergone salvage resections via TORS during this time period, most of which were performed between 2007 and 2012. Patient demographics, including age, sex, and tumor and nodal stage, were recorded, and a similarly matched patient group that underwent open surgical resection was identified. Many of the patients who underwent open salvage surgery were selected for this technique based on the unavailability of TORS prior to 2007. No tumors in either group demonstrated bone involvement. Patients were excluded from the TORS group if their tumors were not amenable to transoral resection secondary to difficult visualization and/or palpation of margins, significant trismus, or base of tongue tumors that crossed the midline. All patients in both groups had undergone previous treatment for primary oropharyngeal SCC, including radiation, chemotherapy, surgery, or some combination of these. Selective or modified neck dissections were performed during the same operation or in a staged manner.

Operative data, including margin status, blood loss, and operative time, were recorded and compared between the 2

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Abbreviations: NA, not applicable; TORS, transoral robotic-assisted surgery.
matched patient groups. Functional outcomes were defined as length of feeding tube use, tracheostomy duration, hospital stay, and operative complications. Oncologic outcomes, including 2-year disease-free survival and 2-year overall survival, were also calculated and compared between the 2 patient groups.

Statistical Analysis

Associations between variables and end points were tested with the Pearson \( \chi^2 \) test, 2-tailed Fisher exact test, or \( t \) tests as appropriate. Overall and disease-free survival curves were constructed using the Kaplan-Meier method and were analyzed using the log-rank procedure. A 2-tailed \( P < .05 \) was considered statistically significant. Statistical analysis was performed using GraphPad Software (GraphPad Software Inc).

Results

Patient Population

A total of 128 patients with recurrent SCC of the oropharynx were included. Patients were divided into 2 groups: (1) 64 who underwent salvage surgical resection with TORS and (2) 64 who underwent resection with standard open surgical approaches. Demographic data and tumor staging for each group are summarized in Table 1 and Table 2. Most patients in both the TORS and open approach groups had T1- and T2-stage disease (92% and 81%, respectively). A significant proportion of these patients had advanced stage disease secondary to lymph node status: 51% in the TORS group and 59% in the open approach group had stage 3 or 4 disease. All patients had undergone previous treatment for oropharyngeal SCC consisting of chemotherapy, radiation, surgery, or some combination of these. A significantly greater proportion of patients in the open approach group had undergone previous surgery than the TORS group, 69% compared with 19% in the open approach group, respectively (\( P < .001 \)). Conversely, a significantly greater number of patients in the TORS group had previous radiation than those in the open approach group (97% compared with 70%, respectively; \( P < .001 \)). Forty-eight patients (75%) in the open approach group required free flap reconstruction, whereas no patients in the TORS group underwent reconstruction (\( P < .001 \)).

Operative Outcomes

Operative and postoperative data, including blood loss, operative time, margin status, and postoperative complications, were recorded and compared between the 2 matched patient groups. Mean blood loss was significantly lower in the TORS group (49 mL) than the open approach group (331 mL) (\( P < .001 \)). Overall mean operative time was also significantly less in the TORS group (111 minutes) than the open approach group (350 minutes) (\( P < .001 \)) (Figure 1).

A significantly greater number of patients in the open approach group had positive margins on final permanent pathologic analysis. We demonstrated positive final margins in 19 patients (29%) in the open approach group compared with 6 patients (9%) in the TORS group (\( P = .007 \)). Four patients in the TORS group were brought back to the operating room for resection of initial positive margins to ultimately achieve negative margins. This was performed on an outpatient basis. Overall, there were significantly fewer postoperative complications in the TORS group. Six patients (10%) in the TORS group had a postoperative infection compared with 14 (22%) in the open approach group (\( P = .03 \)). No patients in the TORS group developed a postoperative fistula compared with 4 patients (6%) in the open approach group (\( P = .12 \)). A similar number of patients in each group experienced postoperative airway edema requiring intervention: 13 patients (20%) treated with TORS and 12 treated (19%) with open resection (\( P < .99 \)). There was no statistical difference in the numbers of patients who experienced postoperative bleeding in the TORS group and open approach group (7 and 8, respectively) (Figure 2). It should be noted that there were several postoperative complications that were specific to those patients who underwent open surgery. These included (1) 2 patients with mandibular malunion, (2) 5 patients with bone exposure, (3) 3 patients who required hardware removal, and (4) 7 patients who required operative intervention for free flap vascular compromise.

Functional Outcomes

Functional outcomes were defined as length of hospital stay, tracheostomy use, and length of feeding tube use. The mean length of hospital stay was significantly greater for patients who
underwent open resection (8.0 days) compared with those who underwent TORS (3.8 days) ($P < .001$) (Figure 3). Significantly fewer patients in the TORS group required tracheostomy and/or feeding tube placement. Fourteen patients in the TORS group (23%) had a tracheostomy at the time of their salvage surgery, 3 of which were placed preoperatively. Fifty patients in the open approach group (79%) had a tracheostomy at the time of their surgery, only 2 of which were placed preoperatively ($P < .001$). Twenty-three patients in the TORS group (35%) had a feeding tube at the time of surgery, 10 of which were placed preoperatively, which were significantly fewer patients than in the open approach group. Forty-eight patients in the open resection group (75%) had a feeding tube at the time of their salvage surgery ($P < .001$) (Figure 4). Of those patients who required feeding tube placement, we compared duration of feeding tube dependence between the 2 groups, and it was significantly less time in the TORS group than the open surgery group. At the 1-year postoperative follow-up, only 2 patients in the TORS group (3%) still required feeding tube support compared with 20 patients in the open approach group (31%) ($P = .002$) (Figure 5).

### Oncologic Outcomes

The 2-year recurrence-free survival for the open resection group was 43% compared with 74% in the TORS group ($P = .01$) (Figure 6). The 2-year overall survival of patients in the open surgery group was 43% compared with 74% in the TORS group ($P = .02$).

### Discussion

The results of this retrospective investigation indicate that TORS is a reasonable alternative surgical option for selected patients with recurrent oropharyngeal SCC. It was shown to be associated with shorter operative times, less blood loss,
lower incidence of postoperative complications, shorter hospital stays, less functional disability, and acceptable 2-year survival rates when compared with standard open surgical approaches. For the patient who develops recurrent disease, quality-of-life issues, such as postoperative complications and speech and swallowing function, become the patient’s primary concerns. In our study, patients who underwent TORS were shown to have significantly improved outcomes in speech and swallowing function compared with those undergoing open surgery. In this study, most patients who underwent open surgery required a tracheostomy, either temporarily or permanently. The same was true for placement of enterogastric feeding tubes. It is true that a greater proportion of patients in the open approach group had a feeding tube placed preoperatively, which definitely played a factor in postoperative swallowing rehabilitation. It has been shown in the literature that very few patients (8%) undergoing salvage surgery for oropharyngeal tumors return to a normal diet, and 56% retain their enterogastric feeding tubes. We found that only 2 patients in the TORS group (3%) still had a feeding tube at the 1-year follow-up.

Previous studies report that nearly 50% of patients who undergo open salvage surgery for recurrent head and neck cancers develop postoperative complications or wound healing problems. The same was true in our study. It is important to note that there are several complications that the patients treated with open surgery experience that those treated with TORS are not at risk for, based simply on the minimally invasive nature of the TORS operation. These include mandibular malunion, free flap vessel compromise, bone exposure, and the need for hardware removal. To date, there are limited studies of robotic-assisted salvage surgery for comparison, but the complication rate seen in this study was significantly lower than that for open surgery, as expected.

It was previously thought that very few patients (<20%) were good candidates for salvage surgery. These patients are typically not in their ideal state of health, having been through previous HNSCC treatment(s). Therefore, it is important in their preoperative consultation to consider operative details, such as expected blood loss, length of surgery, and length of hospital stay. These factors could potentially influence the decision of a patient on whether to undergo surgery. The TORS cases in our study had on average 6.7 times less blood loss and took on average one-third of the operative time of an open approach case, and the average hospital stay was decreased by 50%.

Like transoral laser microsurgery (TLM), the decision to perform TORS in a patient with oropharyngeal cancer is based on several factors, but not on whether the cancer is primary or recurrent. In general, the decision to perform TORS is based on T stage, anatomic location, exposure limitations, patient outcomes (considering the surgical defect created by the surgery), and surgeon experience. If patients are known to have bone involvement, they are obviously more suitable for an open approach. We did not include in our study any patients who required bone resection. We acknowledge that not every salvage case is a candidate for TORS. When a patient presents with recurrent cancer, the decision for TORS (or TLM) vs an open operation is based on the same criteria as for patients presenting with primary disease.

There was most likely selection bias between the open approach and TORS groups based simply on the TORS criteria, in that those with more ill-defined tumors were selected for the open approach group. This could have had a significant impact on the outcomes, particularly in the ability to achieve negative resection margins. This would undoubtedly partially account for the difference in recurrence-free survival between the 2 groups and improved functional outcomes seen in the TORS group.

Recurrent HNSCC is associated with poor overall survival rates. Surgical salvage, however, may be the only option at potential cure for the patient. It is important to compare survival rates of any new proposed treatment option with current known survival rates. Salvage transoral laser surgery for malignant lesions of the oropharynx has been shown to have
an overall 2-year survival rate of 51%, and traditional open surgical resection has shown rates of 64.5%. Our study demonstrated similar 2-year overall survival of patients in the open surgery group at 43% and an improved 2-year survival in the TORS group at 74%. This significant difference in survival between the 2 groups was reflected in the significantly higher positive margin status of the open resection group. We were able to achieve a lower incidence of final positive margins in the TORS group because many of the patients could be brought back to the operating room for resection of their initial positive margins to achieve final negative margins. A resection of margins was performed in 4 patients treated with TORS to achieve negative margins. This was performed on an outpatient basis and was nearly impossible to accomplish in the open resection group.

In conclusion, this study demonstrates that TORS offers an alternative surgical approach to recurrent tumors of the oropharynx with acceptable oncologic and better functional outcomes than traditional open surgical approaches. This adds to the growing amount of clinical evidence to support the use of TORS in selected patients with recurrent oropharyngeal SCC as a feasible and oncologically sound method of treatment.

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Study concept and design: White, Ford, Holsinger, Ghamen, Carroll, Rosenthal, Magnuson.

Acquisition of data: White, Ford, Bush, Holsinger, Moore, Ghamen, Carroll.


Drafting of the manuscript: White, Ford, Bush.

Critical revision of the manuscript for important intellectual content: White, Holsinger, Moore, Ghamen, Carroll, Rosenthal, Magnuson.

Statistical analysis: White, Ford.

Administrative, technical, and material support: Magnuson.

Study supervision: Holsinger, Moore, Carroll, Rosenthal, Magnuson.

Data collection: Ghamen.

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REFERENCES