Open Versus Robotic Surgery for Oropharyngeal Cancer

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KEYWORDS

- Oropharyngeal cancer • Squamous cell carcinoma of the oropharynx
- Oropharyngeal surgery • Transoral robotic surgery • TORS
- Open approach to the oropharynx

KEY POINTS

- Consider transoral robotic surgery (TORS) for human papilloma virus (HPV)-positive and HPV-negative oropharyngeal squamous cell carcinoma in a select group of patients.
- TORS offers minimally invasive technique for achieving adequate oncologic outcomes while also providing good and sometime superior functional outcomes to other treatment.
- TORS is sometimes applicable for patients with persistent or recurrent OPSCC with appropriate patient selection.

INTRODUCTION

Traditionally, patients diagnosed with oropharyngeal squamous cell carcinoma (OPSCC) are treated with open surgical approaches to resect the cancer and to perform the reconstruction. Surgery is then followed by radiation with or without chemotherapy depending on reported pathologic features.[1] Open surgery of the oropharynx is accomplished via a transcervical-transpharyngeal, transmandibular-transpharyngeal, transfacial-transpharyngeal, or even intraoral access to the tumor. These approaches often involve reconstruction by a microvascular free flap, which increases length of recovery time. These open invasive procedures also often ultimately contribute to impediments of speech and breathing, as well as longstanding dysphagia.[2]

The Veterans Administration Laryngeal trial published in 1991[3] demonstrated a role for induction chemotherapy plus definitive concurrent chemotherapy with radiation as an equal means for achieving survival in locoregionally advanced laryngeal cancer in

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comparison with surgery followed by radiation. The use of surgery to address oropharyngeal tumors declined due to extrapolation of organ-preserving protocols to the oropharynx. However, the use of concurrent chemoradiation "organ preservation" nonsurgical protocols resulted in an increase of treatment-related toxicities such as dysphagia, xerostomia, stricture, tissue fibrosis, and neuropathy.[4,5]

The work of Weinstein and O'Malley[6–8] to demonstrate feasibility and efficacy of the DaVinci Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA) for transoral "robotic" access to the upper aerodigestive tract led to approval by the US Food and Drug Administration (FDA) in 2009. The Flex Robotic System (MedRobotics, Raynham, MA) offers a platform with flexible working arms and 3-dimensional camera, which subsequently received FDA approval for transoral procedures from the lips to the larynx in 2015. Transoral robot surgery (TORS) is facilitated by exposure to the pharynx and larynx by means of a retractor specifically designed for this purpose that includes a variety of tongue blades to best expose the anatomic subsite of interest. The 3-dimensional view afforded by these robotic platforms provides direct visualization of the surgical field, aids in an often en bloc resection of the tumor, reduces the morbidity associated with transcutaneous access to the anatomic location, and improves patient recovery time.[2]

Transoral Robotic Surgery

Data pooled from a multi-institutional feasibility study suggests the most commonly addressed subsites of the upper aerodigestive tract are the oropharynx and the supraglottic larynx. This study included 177 patients who underwent TORS in which 139 (78%) were for an oropharyngeal lesion and 26 procedures (15%) were performed targeting the larynx. The remainder of procedures were performed for tumors involving the hypopharynx and oral cavity.[9]

Indications

Data from the Surveillance, Epidemiology, End Results (SEER) database demonstrate that during the time period of 1992 to 2014 the incidence of OPSCC tripled.[10] Now during the 2000s approximately 70% of OPSCCs diagnosed in the United States are associated with the human papillomavirus (HPV).[11,12] Patients diagnosed with an HPV-associated OPSCC experience a unique disease presentation, tumor biology, and survival advantage.[13] The unique presentation of HPV-associated OPSCC includes lower T stage in comparison with patients diagnosed with HPV-negative OPSCC, most commonly of the tonsil followed by the base of tongue.[14] HPV-associated OPSCC clinical presentation permits addressing the primary site surgically with ability to achieve negative resection margins.[9] Furthermore, surgical management of the primary site and neck dissection when appropriate may result in avoidance of adjuvant radiation based on the final surgical pathology, or de-intensification of adjuvant radiation. De-intensification protocols and efficacy are still undergoing evaluation in clinical trials such as the Postoperative Adjuvant Treatment for Human Papillomavirus (HPV)-positive Tumors (PATHOS).[15] The anticipated benefit of deescalation is the reduction of treatment regimens without compromise of survival outcomes while maintaining superior functional outcomes. De-intensification incorporates TORS.

Patients with HPV-negative OPSCC are candidates for TORS management in certain instances as well.[16] A recent publication used the National Cancer Data Base to assess survival benefit of primary TORS versus nonsurgical definitive management. The investigators performed subgroup analysis based on HPV status stratified by early stage (T1-2N0-1) and advanced stage (T3-4N0-3 andT1-4N2-3) and found a survival advantage for patients with HPV-negative OPSCC when treated

with TORS versus nonsurgical management. In their analysis when accounting for age, stage, and tumor grade, the 206 HPV-negative OPSCC patients did experience significantly better 3-year survival outcomes with TORS treatment "intensification" in comparison with patients addressed by radiation 84% (95% confidence interval [CI] 76%–91%) versus 66% (95% CI 57%–77%), $P = .01$. The investigators note the established relative radioresistance of HPV-negative OPSCC and surmise that surgical debulking of the radioresistant clones may result in the superior results for TORS basis of treatment in their study, also noting that 71% of all of the patients (both HPV-positive and HPV-negative) required adjuvant radiation therapy and 54% adjuvant chemotherapy.[17]

There is a higher local failure rate for patients with HPV-negative OPSCC than those with HPV-positive disease.[18] No matter the HPV disease status, surgical salvage is considered the best oncologic option for persistent or recurrent disease after primary radiation or chemoradiation therapy. TORS may prove efficacious for the appropriate patient in this setting. Small recurrent or persistent, or second primary OPSCC tumors are those amenable to TORS. However, larger tumors in the face of prior irradiation will benefit from concomitant microvascular reconstruction to minimize bleeding risk, particularly when re-irradiation is considered depending on pathologic findings for locoregional control of disease. It is important to note that plan for microvascular reconstruction of a defect is not mutually exclusive from TORS. TORS-assisted resection with the avoidance of mandibulotomy may prove beneficial coupled with microvascular reconstruction.[2]

Imaging assessment is key in determining patients eligible to undergo TORS anatomically. Imaging studies obtained during the evaluation and staging period for the patient's oropharyngeal cancer by contrast-enhanced computed tomography scan or MRI may demonstrate features that suggest a patient treated surgically may have positive margins or extracapsular spread of cancer involving regional lymph nodes. Both instances are indications for adjuvant chemotherapy with radiation. In selecting patients who are good candidates for TORS, the goal is to achieve R0 resection in a minimally invasive manner while also attempting to deescalate adjuvant therapies to not compromise disease control but to reduce treatment-related morbidity.[19]

When considering TORS to surgically manage tonsillar cancer, physical examination and imaging consistent with disease limitation to the tonsillar fossa are good candidates for achieving negative margins safely. Whether surgical management is open or transoral, presence of tumor surrounding the carotid artery by 270° or more is considered unresectable. Disease involvement of the prevertebral musculature or the bony vertebrae themselves are also considered unresectable. Specific to TORS, a surgical margin that requires extension beyond the periosteum of the mandible is not attainable given inability to perform marginal mandibulectomy with current robotic instrumentation. Similarly, involvement of the masticator space, pterygoids and temporalis muscles are not amenable to TORS, but often are amenable to open surgical resection with reconstruction. Involvement of the parapharyngeal space that lies posterolateral to the tonsillar fossa makes it difficult to achieve negative margins via the transoral robotic approach. Given that the posterior compartment of this space, the post-styloid space, contains the carotid sheath and cranial nerves 9 through 11, an open approach to surgical resection may preserve these vital structures while also enabling complete resection. Imaging that demonstrates medial carotid artery position abutting the tonsillar fossa also makes TORS a challenge for achieving safe surgical resection. Physical examination and imaging showing soft palatal involvement would suggest alternative treatment to achieve superior functional outcome. Surgical resection of the soft palate without reconstruction would result in the quality-of-life

changing velopharyngeal insufficiency. When physical examination and imaging demonstrate oropharyngeal tumor extension into the nasopharynx, TORS resection is likely not attainable.[19,20] The flex robotic system is, however, promising in its ability to retroflex, enabling surgeons to potentially address a nasopharyngeal component of disease.

Involvement of the extrinsic tongue musculature, extension of base of tongue disease significantly into the pre-epiglottic space, involvement of bilateral lingual arteries, and tumor extending across midline where both neurovascular bundles would require sacrifice for resection are all better suited for open surgical resection with reconstruction of the defect. These instances would result in tongue devascularization and loss of tongue bulk and structure contributing to poor long-term functional outcomes and may contribute to inadequate resection by a transoral approach.[19]

When anatomic imaging suggests TORS is feasible both with respect to adequate, safe resection and anticipated functional outcome, exposure of the primary site is considered. Adequate exposure is assessed by patient ability to achieve maxillary-mandibular interincisor excursion, flexibility of the neck, the width of the mandibular arch, presence of bony tori of the mandible, and degree of macroglossia if present.[2]

Description of procedures

Briefly, for resection of tonsillar OPSCC via TORS, the Feyh-Kastenbauer (FK) retractor (Gyrus ACMI, Southborough, MA) is used for exposure and suspension. The procedure begins with incision of the pterygomandibular raphe. This incision exposes the superior constrictor, which serves as the lateral resection margin, while elevating the buccopharyngeal fascia. The resection was completed by incising the soft palate medially carried down to the constrictor freeing the muscle from the prevertebral fascia. Inferiorly, the styloglossus and stylopharyngeus muscles are transected and dissection proceeds from superior to the inferior incision (**Fig. 1**).[21]

Access to the base of tongue requires retraction for adequate exposure. Early use of the DaVinci system by O'Malley and colleagues[22] found use of the FK retractor provided advantages over the Crow Davis and Dingman retractors. Namely, the lateral retraction blades as well as the variety of tongue blades provided exposure for complete tumor resection. Utilization of both the 0° and 30° camera enabled adequate visualization of the surgical field to complete resection. These investigators describe exposing the vallecula using the open laryngeal blade to first make these vallecular incisions. The appropriate tongue blade with cut-out is exchanged for the laryngeal blade to enable the superior and lateral cuts next. These incisions are carried deep to the inferior depth desired for margin control enabling en bloc resection. The lingual artery is surgically clipped when it is encountered.[22]

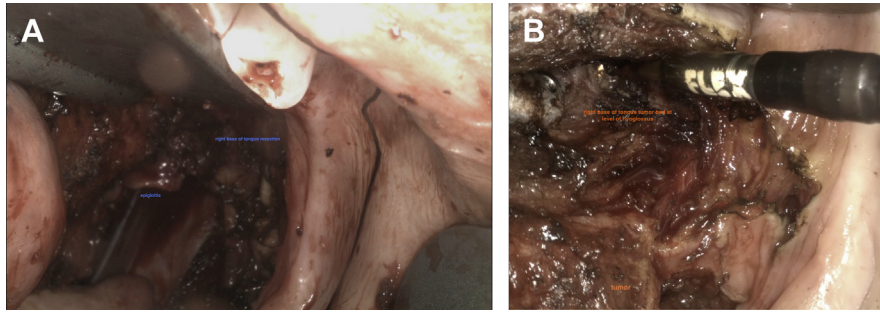

Fig. 1. Transoral robotic radical tonsillectomy and partial pharyngectomy.

Advantages of TORS versus open surgical technique or radiation-based therapies are related to the decreased damage to the pharyngeal musculature or to the major neurovascular structures and surrounding normal tissues. There are multiple reports of decreased hospital stay, decreased dysphagia, and decreased need for tracheostomy and feeding tube dependence. The impact of radiation-based therapies on HPV-positive patients is significant given this demographic is typically younger with greater life expectancy to experience the ongoing consequences of radiation fibrosis, dysphagia, xerostomia, and loss of taste sensation.[23,24]

Disadvantages associated with TORS include the initial cost and maintenance. The cost may preclude institutions from purchase. This in turn leads to subsequent inability of a given patient population to have access to this minimally invasive technique. In addition, disparity among hospital institutions contributes to potentially serious complications for those specialized surgeons using this technology, discharging patients without tracheostomy after a shorter time period where a postoperative hemorrhage at home may lead to death. Yet another potential disadvantage is limitations of robotic instrumentation, whereby access to the more distal upper aerodigestive tract may pose a significant challenge.[25] Flexible robotic systems may improve on this problem.

Open Surgery of the Oropharynx

As described in other sections of this article, the trend for surgical approach to the oropharynx has moved from an open approach to less invasive procedures, including transoral laser microsurgery and TORS.[26,27]

Indications

Indications for an open surgical approach include advanced tumors not amenable to the less invasive procedures given tumor characteristics, body habitus, or need for trimodality therapy. In addition, open surgery is commonly indicated for salvage surgery in previously treated malignancy for which surgery is the only remaining option. In these circumstances, wide surgical margins are advocated, which are readily accomplished through an open approach. This often results in pharyngeal communication with the neck requiring complex tissue inset into the defect.[26]

Description of procedures

The transmandibular-transpharyngeal approach to the oropharynx involves the use of a mandibulotomy or segmental mandibulectomy to gain access accomplished by a traditional lip split incision. An alternative approach is the visor flap whereby a large incision is made in the anterior neck and the skin is elevated superiorly over the mandible (**Fig. 2**).[27] The mandible is then divided with care taken to avoid injury to the mental nerve when oncologically feasible. The tongue musculature is transected permitting direct access to the oropharynx while protecting the neurovascular bundle if desired. If the tumor demands, a segment of involved mandibular bone is accessible for resection or a marginal mandibulectomy performed as needed for margins. Primary closure, adjacent tissue transfer, or microvascular free tissue transfer provide adequate reconstruction methods.[27,28]

Alternative approaches to accesses the oropharynx avoiding the morbidity associated with mandibulotomy include lateral pharyngotomy, transhyoid pharyngotomy, and suprahyoid pharyngotomy. The lateral pharyngotomy approach is facilitated by performing a selective neck dissection, thereby exposing the posterior belly of the digastric, hyoid bone and musculature, and branches of the external branch of the carotid. For tumors of the lateral and posterior pharyngeal wall, the hypoglossal nerve is protected superiorly by releasing the musculature from the superior aspect

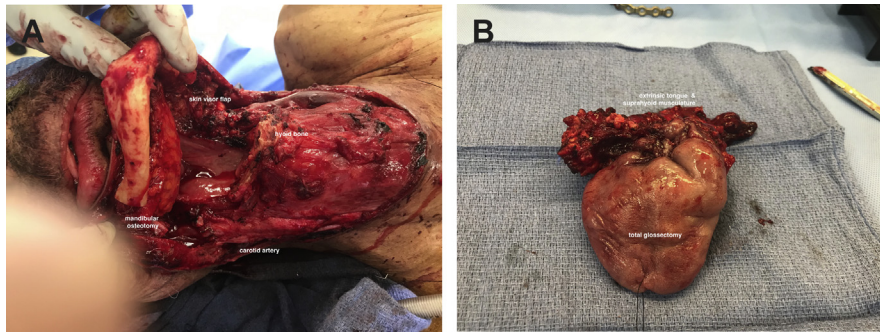

Fig. 2. Open total glossectomy, right partial glossectomy, and bilateral neck dissections via transcervical-transmandibular approach. A visor skin was used rather than lip splitting incision.

of the hyoid bone and reflecting cranially. The inferior muscular attachments to the hyoid are released for access to the ipsilateral vallecula. The lingual artery is ligated at this point and potentially saved for microvascular reconstruction. Resection of the lateral hyoid bone may aid direct visualization. Exposure is facilitated further by transection of the lateral portion of the thyroid cartilage in a vertical plane to access the posterior pharyngeal wall, or anteriorly with transection of the styloglossus and sacrifice of the facial nerve, or by excision of the tip of the angle of mandible. If an isolated posterior pharyngeal wall lesion is encountered, preservation of the hyoid bone is possible while the middle pharyngeal constrictor is incised along the length of the thyroid lamina.[29]

Suprahyoid pharyngotomy is an approach to base of tongue tumors from anterior. This is accomplished through a transcervical incision anteriorly carried down to the hyoid complex. Once isolated, the suprahyoid musculature is released in the midline with care taken to stay directly on the bone, thus avoiding the hypoglossal nerve and lingual vascular pedicle. The hyoepiglottic ligament is followed posteriorly leading to the mucosa of the vallecula, which is then incised. This approach allows for excision with primary closure assuming the tumor does not extend to the anterior tongue or deep tongue musculature. The muscles are then resuspended to the hyoid before closure.[29,30] A variation of this approach is useful to access lateral tongue lesions by transection of the hyoid and excision of the lateral tongue base, lingual vessel, and hypoglossal nerve as dictated by the tumor.[31]

The main advantages of open surgery include wide surgical field and exposure, especially in approaches in which mandibulotomy is performed. An additional advantage of the open surgical approaches is de-intensification of therapy where the tumor is completely excised and no additional treatment is required. This is realized when compared with quality-of-life measures seen in patients treated with primary radiation or chemoradiation where long -erm toxicities are often experienced.[2,26]

Disadvantages of open surgery are well documented and can have a significant impact on quality of life. Alteration of the tongue musculature impacts speech as well as swallowing, which is further impacted by pharyngeal surgery.[26,27] If mandibulotomy is performed, complications include malocclusion, hardware extrusion, osteomyelitis, and osteoradionecrosis in previously radiated bone.[28] Additional disadvantages are prolonged hospitalization, gastrostomy dependence, tracheostomy dependence, need for vascular free flap reconstruction, and cosmetic deformity of the lip if a lip split approach is used.[26,28]

Transoral Robotic Surgery Versus Open Surgery

An early report comparing TORS with open surgical approaches prospectively enrolled TORS patients and retrospectively matched this group to patients with OPSCC treated by open surgery. Patient demographics, tumor staging, and pathologic data including HPV status were similar between the groups. The investigators found patients treated with open surgery fared worse than those treated by TORS, which was not explained by pathologic outcomes of margin status or extracapsular spread. Survival analysis revealed 1-year, 2-year, and 3-year survival rates for TORS patients was 94%, 91%, and 89%, whereas for patients treated with open surgery, the rates were 85%, 75%, and 73% ($P = .035$). As stated previously, in tumor "debulking" by TORS enough radioresistant cancer cell clones may render adjuvant (chemo)radiation more efficacious in locoregional control of disease.[16] In addition, the period between TORS to adjuvant therapy in comparison with open surgery time to adjuvant therapy may have benefit of shorter period contributing to suboptimal disease control in patients undergoing open surgery.[17]

One major rationale for performing TORS is improved function in comparison with other treatment modalities. A prospective trial comparing oncologic and functional outcomes after TORS versus conventional surgery for T1-3 tonsillar cancer found significant differences in patient return to oral diet, hospital stay, and time to decannulation in favor of TORS. Return to oral diet occurred in 6.5 ± 4.2 days for TORS group versus 16.7 ± 5.3 for mandibulotomy approach ($P < .001$). Similarly, hospital stay for the TORS group was 14.6 ± 4 days in comparison to mandibulotomy approach of 24.6 ± 5.9 days ($P = .001$). In addition, time to decannulation in TORS patients occurred at 5 ± 1 days compared with the mandibulotomy approach at 13.2 ± 6. days ($P<.001$). The investigators also noted that as the study progressed, patients in the TORS group no longer underwent prophylactic tracheostomy at all.[32]

Complications associated with TORS notably occurred more often initially following FDA approval of the DaVinci system in 2009; Memorial Sloan Kettering reported 33% complication rate in 2010, progressively declining to 10% rate in 2015. The investigators reported that resection involving more than 2 subsites as increased odds for complication. Surgical resection involving more than 2 subsites infers a large tumor volume with likely resultant dysphagia contributing to aspiration pneumonia and greater raw surface area that may contribute to postoperative bleeding.[33]

Cost to purchase a robot may provide a significant challenge for many institutions. In 2009, Weinstein and colleagues[34] reported purchase cost for a DaVinci system of $1.5 million, yearly maintenance of $100,000 and $200 cost for each case performed to provide the disposable instrumentation.

In summary, TORS is advantageous when selected for appropriate patients. These patients include HPV-positive patients with OPSCC who may avoid adjuvant therapies in certain instances or who may enjoy adjuvant treatment de-intensification pending clinical trial evidence. Furthermore, some HPV-negative patients may prove good candidates based on tumor anatomy with some reports of improved survival in this patient population compared to open surgery or nonsurgical management.[16,17] Finally, TORS may also serve certain patients undergoing surgical salvage.

DISCLOSURE

The authors have nothing to disclose.

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