

## How often parapharyngeal space is encountered in TORS oropharynx cancer resection

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**Abstract** Early stage oropharyngeal squamous cell carcinoma (OPSCC) may occasionally invade parapharyngeal space (PPS). Tumor invasion of PPS structures such as the carotid artery, internal jugular vein and cranial nerves IX–XII may add significant morbidity. We analyzed 73 patients who underwent transoral robotic surgery (TORS) for OPSCC between 2008 and 2012. Patients were selected based on preoperative evaluation including detailed physical and endoscopic examination, neck CT and/or PET-CT scan. T1, T2 and selected T3 cases were included in this study. None of the patients had obvious PPS extension on preoperative evaluation. All patients had OPSCC in palatine tonsil (60; 82.2 %) and base of tongue (13; 17.8 %). Twenty-seven patients had cT1 (37 %), 39 had cT2 (53.4 %), and 7 had cT3 (9.6 %) disease in clinical and radiologic evaluation. None of the oropharyngeal lesions had obvious radiologic PPS extension prior to operation. During TORS procedure, we encountered PPS in 18 (24.6 %) patients while resecting the deep margin. These parapharynx resections involved external carotid artery in 1, medial pterygoid muscle in 2, and parapharyngeal fat with or without styloid musculature in the remaining 15

patients. Except three cases, we were able to remove the lesions en bloc with negative surgical margins. TORS resection of oropharyngeal cancer extending to PPS appears to be a safe and feasible technique with minimal complications. Significant experience with TORS and further understanding of the endoscopic anatomy of PPS could obviate the morbidity associated with tumor resection in this dense neurovascular region.

**Keywords** Oropharyngeal carcinoma · Da Vinci robot · Transoral robotic surgery · Parapharyngeal space

### Introduction

The gradual trend toward minimally invasive organ and function preserving surgery has pioneered the development of more surgical options for the management of oropharyngeal cancers. Innovations and refinements in optic technology and introduction of the da Vinci robot have steadily improved the view, reach, and consequently the efficacy of minimally invasive transoral robotic techniques. Previous studies have established several potential advantages of TORS over traditional treatment options such as avoidance of external incision and preservation of normal surrounding structures [1, 2]. Compared to conventional radical surgeries and primary chemoradiotherapy, these advantages of TORS reduced the need for gastrostomy tube (G tube) and tracheostomy tube placement improving postoperative function and shortening hospital stay [3].

Oropharyngeal cancers may invade two clinically important potential spaces surrounding the oropharynx: posteriorly retropharyngeal space (behind the pharyngeal constrictor muscles) and laterally PPS (lateral to the pharyngeal constrictor muscles between the base of skull and

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the hyoid cornu). The PPS is classically described as having the shape of an inverted pyramid, extending from the skull base to the greater cornu of the hyoid bone. Violation of superior and middle pharyngeal constrictor muscles by oropharyngeal cancers allows access to the PPS. It has little resistance to tumor spread. Tumor invasion of PPS structures such as the carotid artery, internal jugular vein and cranial nerves (CN) IX–XII may add significant morbidity [4, 5].

TORS has demonstrated promising functional and quality of life outcomes with comparable disease control [6, 7]. Although the feasibility of the TORS in PPS surgery has been described for several benign case series [8–10], the literature lacks data on the efficacy and clinical outcomes of TORS for malignant tumors invading PPS. The goal of the current study was to evaluate the utility of TORS in resection of oropharyngeal cancers extending to PPS.

## Materials and methods

Institutional review board approval was obtained from The Ohio State University Office of Responsible Research Practices. Patients were identified from the prospective TORS clinical trial. Among 181 TORS patients, a total of 85 patients underwent TORS oropharyngectomy between 2008 and 2012. Twelve patients (cases) with carcinoma of unknown primary were excluded from the study.

TORS selection criteria were: (1) transorally resectable OPSCC based on predictive imaging and physical examination, (2) clearance for general anesthesia, and (3) written informed consent for the procedure. The exclusion criteria were: (1) poor transoral exposure, (2) active infection or unexplained fever, (3) proof of extension into deep tongue musculature, skull base, pterygoid musculature, great vessels of the neck, mandible or hyoid involvement prior to surgery, (4) pregnancy and (5) previous head and neck surgery precluding transoral exposure.

Patients were selected based on preoperative evaluation including detailed physical and endoscopic examination, neck CT and/or PET-CT scan. T1, T2 and selected T3 cases were included in this study. None of the patients had obvious PPS extension on preoperative evaluation. All patients underwent TORS radical tonsillectomy or TORS base of tongue resection with concurrent neck dissection. Our technique of TORS for oropharyngeal carcinoma resection is described previously [11].

Operative and pathology reports of all patients were analyzed retrospectively. Violation of superior pharyngeal constrictor muscles and invasion of parapharyngeal fat with or without medial pterygoid muscle, styloid musculature, and neurovascular involvement is accepted as PPS

extension. Eighteen (24.6 %) patients were found to have PPS extension. Complication rates, local disease control and overall survival rates were analyzed in these patients and compared with patients without PPS extension.

## Statistical methods

The analyses were performed using the SPSS 16.0 software (SPSS Inc., Chicago, IL, USA). Survival probability was calculated using Kaplan–Meier analysis with comparisons by Wilcoxon test. Pearson's  $\chi^2$  test and Fisher's exact test were used in the analysis of other clinical data. *p* value less than 0.05 was considered statistically significant.

## Results

Between 2008 and 2012, 73 patients who underwent TORS oropharyngectomy were included in this study. All patients had biopsy-proven squamous cell carcinoma. Primary tumor sites were palatine tonsil in 60 patients (82.2 %) and base of tongue in 13 patients (17.8 %). The mean age at TORS was 58.6 years (age range 44.3–80.6 years). Sixteen patients were female (21.9 %) and 57 were male (78.1 %). The mean follow-up time was 34.2 months (range 7.2–62.9 months).

The majority of patients had cT1 (27; 37 %) and cT2 (39; 53.4 %) disease. Only seven patients had cT3 (9.6 %) OPSCC. All patients underwent concurrent neck dissection following TORS. Only three patients with previous excisional lymph node biopsy refused to have neck dissection. Nodal status were N0 in 7 (10 %), N1 in 8 (11.4 %), N2a in 20 (28.6 %), N2b in 28 (40 %), N2c in 2 (2.8 %), and N3 in 5 (7.2) patients (Table 1).

Adjuvant treatment, including radiotherapy (RT) or concurrent chemotherapy (CRT) was delivered within 6 weeks of TORS. Postoperative RT and/or CRT were offered if adverse features (positive margins, pT3 or pT4, N2 or N3, extracapsular nodal spread, nodal disease in levels IV or V, and perineural invasion) were present according to National Comprehensive Cancer Network guidelines. The mean RT dose was 65 Gy (60–74 Gy) divided over a 6- to 7-week treatment course. Patients with high risk of local subclinical spread were given 66–74 Gy adjuvant RT. Chemotherapy regimens were either cisplatin (75 %) or cetuximab (25 %) based. CRT was also given in patients with PPS involved surgical margin.

All patients were discharged home on a full oral diet, without requiring nasogastric tube feeding during their hospital stay. None of the patients were readmitted for dysphagia or dehydration prior to starting RT. Twelve patients required G-tube insertion at some point in their adjuvant treatment regimen after TORS (16.5 %) owing to

**Table 1** Pathologic information

Disease characteristic patients	<i>N</i>	(%)
cT stage	73	
T1	27	37
T2	39	53.4
T3	7	9.6
cN stage	70	
N0	7	10
N1	8	11.4
N2a	20	28.6
N2b	28	40
N2c	2	2.8
N3	5	7.2
Overall stage	70	
I	4	5.6
II	3	4.3
III	17	24.3
IVa	41	58.6
IVb	5	7.2

*cN* clinical node classification,  
*cT* clinical tumor classification

dysphagia and inability to maintain daily caloric needs. In 7 (58 %) of these patients, the G-tube was inserted temporarily during RT and/or CRT and was removed before 1 year post TORS. The remaining 5 G-tube (42 %) patients could not regain sufficient swallowing function to become G-tube independent. Only 1 patient required a tracheostomy tube (1 %), which was removed prior to leaving the hospital.

None of the oropharyngeal cancer had obvious PPS extension prior to operation. During TORS procedure, we encountered PPS in 18 (24.6 %) patients while resecting the deep margin of the specimen with a cuff of uninvolved tissue. All PPS extensions were observed in tonsillar cancers ( $p = 0.017$ ). These parapharynx resections involved external carotid artery in 1, medial pterygoid muscle in 2, styloid musculature in 2, and parapharyngeal fat in the remaining 13 patients. Except three cases, we were able to remove the lesions en bloc with negative surgical margins.

High risk types of human papilloma virus (HPV) and p16 positivity were 74.2 and 82 %, respectively. No statistical correlation was observed between HPV/p16 status and PPS extension ( $p = 0.725$  for HPV/ $p = 0.512$  for p16). Only six patients had perioperative complications. Two patients had oropharyngeal bleeding in postoperative 24 h which was treated conservatively. Four patients had neck hematoma requiring evacuation under general anesthesia.

During follow-up, locoregional recurrence was detected in six patients. Two of them had PPS extension which was resected with clear margin. There was no significant

**Table 2** Locoregional recurrence

Locoregional recurrence	<i>N</i>	<i>p</i>
Patients with PPS extension	2/18	0.405
Patients without PPS extension	4/55	

PPS parapharyngeal space

correlation identified between PPS extension and locoregional recurrence ( $p = 0.405$ ) (Table 2). Three-year overall survival and disease-specific survival rates were 86.7 and 90 %, respectively. Although there was a slight decrease observed in survival rates of patients with PPS extension, difference was not statistically significant (overall survival;  $p = 0.243$ , disease-specific survival;  $p = 0.314$ ).

Intraoperative communication from pharynx to sub-mandibular space was detected in two patients. One of the two patients had both PPS and external carotid artery invasion. Following TORS resection of primary tumor, the procedure was completed with transcervical resection of parapharyngeal extension and external carotid artery ligation at the time of concurrent neck dissection. Sub-mandibular gland reposition with digastric muscle flap reinforcement was performed to avoid postoperative fistula. The other patient had a conglomerated lymph node just lateral to posterior belly of digastric. During concurrent neck dissection, a fistula between neck and oropharynx was noticed. It is then repaired with pharyngeal musculomucosal advancement and AlloDerm (LifeCell). None of the patients developed orocutaneous fistula postoperatively.

## Discussion

Transoral robotic surgery has been demonstrated to be an effective alternative to open surgery for oropharyngeal tumors [1, 6]. TORS provides high-resolution, magnified, three-dimensional view of surgical field allowing optimal visualization of targeted anatomy. Wristed robotic instruments and tremor reduction technology ensure a precise and controlled resection within the narrow confines of the upper aerodigestive tract. These benefits of TORS assure en bloc oropharyngeal cancer resection with improved local disease control rates. Additional advantages of TORS procedures may include decreased length of hospital stay, improved cosmetic results, reduced tracheotomy requirement, and a low rate of G tube dependence, indicative of preserved swallowing function [1, 6].

Spread of oropharyngeal carcinoma may occur laterally to invade the superior constrictor muscle into the parapharyngeal and masticator spaces, with the risk of skull

base extension. PPS is anatomically shaped like an inverted pyramid with the base at the skull base and the inferior apex at the greater cornu of the hyoid bone. It is medially bound by the buccopharyngeal fascia and superior pharyngeal constrictor muscle and laterally by the posterior belly of the digastric muscle, medial pterygoid muscle, mandibular ramus, and deep lobe of parotid gland [4]. It occupies the space between the muscles of mastication and the deglutition. The PPS is further subdivided into prestyloid and poststyloid compartments. The parotid gland, fat, and lymph nodes are contained in the prestyloid compartment. Vital structures such as CN IX–XII, the internal jugular vein, and the internal carotid artery are located in the poststyloid compartment [9, 12].

Most of the PPS tumors are benign. However, obtaining access to these deep-seated tumors has been a challenge. The neurovascular anatomy is concentrated, complex and vital in this region. Violation of these anatomical structures frequently leads to serious morbidity or even mortality [13–15]. The goal of tumor extirpation is complete tumor resection with clear margins, and this largely depends on the adequacy of direct visualization. Establishing an adequate corridor for visualization has led to the development of various surgical approaches.

Transoral approach provides a direct route to PPS. However, it has received cautious criticism given the limited access and visualization [14–16]. Risk of neurovascular injury, tumor spillage, and incomplete tumor excision are the main concerns of transoral approach. For these reasons, this approach has been limited to small neoplasms that project into the oropharynx, are in close proximity to the constrictor muscles, and lack poststyloid intervention [9]. Recently, there has been an interest for the transoral approach to PPS with da Vinci robot [9, 17]. TORS provides a magnified, high-resolution view superior to the endoscope and overcomes the limitations of microscopic surgery. Three-dimensional view with angled camera and wristed instrumentation may allow delicate dissection around the tumor in PPS.

TORS has been widely used in oropharynx cancers. Its role has expanded to tumors in larynx [11], hypopharynx [18], nasopharynx [19], skull base and recently the PPS [17]. In the literature, there are 44 reported cases treated with TORS for parapharyngeal lesions. A complete tumor resection was accomplished in all patients. Histologic diagnosis was pleomorphic adenoma in 29 (65.9 %) patients. All reported lesions were benign, except 1 adenoid cystic carcinoma case. Complete tumor resection was achieved by TORS alone in 36 (81.8 %) patients. Conversion to open surgery was required only in one case. There was no severe neurovascular injury reported [17].

In our series, all patients had primary OPSCC. None of the patients with oropharyngeal cancers had obvious PPS

extension prior to operation. During TORS procedure, we noticed lateral cancer invasion through the superior pharyngeal constrictor muscle into the PPS in 18 (24.6 %) patients while resecting the deep margin of the specimen with a cuff of uninvolved tissue. These parapharynx extensions include external carotid artery in 1, medial pterygoid muscle in 2, styloid musculature in 2, and parapharyngeal fat in the remaining 13 patients. Using the da Vinci robot, we were able to excise tumor en bloc with negative surgical margins in all patients except three. The patient with external carotid artery invasion required transcervical resection of parapharyngeal tumor at the time of concurrent neck dissection.

Locoregional recurrence was detected in 6 (8.2 %) patients after TORS oropharyngectomy. Two of them had PPS extension which was resected with clear margin. There was no significant correlation identified between PPS extension and locoregional recurrence ( $p = 0.405$ ). Three-year overall survival and disease-specific survival rates were 86.7 and 90 %, respectively. Although there was a slight decrease observed in survival rates of patients with PPS extension, difference was not statistically significant (overall survival;  $p = 0.243$ , disease-specific survival;  $p = 0.314$ ).

In addition to fine functional and cosmetic results, our preliminary data indicate that this less invasive surgery does not apparently compromise oncological outcomes. In particular, the high rates of locoregional disease control rate including 7 cT3 cases, at least, establishes the sufficient extirpation of tumor is feasible by the TORS. However, we should note that current application of this method excludes tumors, which involve the mandible, superior medial pterygoid muscle, and the lateral pterygoid muscle. Tumors with mandibular bone involvement necessitate segmental or marginal mandibulectomy. Tumors involving the superior part of medial pterygoid muscle and/or the lateral pterygoid muscle, if resectable, a mandibular swing approach should be employed to obtain sufficient surgical space and to cope with possible bleeding from the pterygoid venous plexus that seems to be difficult to control under the surgical view of TORS [14–16, 20].

We have experienced early postoperative oropharyngeal bleeding only in two patients who were treated conservatively. This is unlike high complications rates of transcervical approaches to the PPS including, dysphagia, trismus, paresis of the marginal mandibular and the hypoglossal nerve [16, 21, 22]. These complications, the morbidity of the surgical approach, and the subsequent scar of a transcervical approach become the motivation to reconsider alternative transoral approaches in the first place. Our analysis of TORS for OPSCC extending PPS found complications including two pharyngeal dehiscences that were treated intraoperatively. There were no neurovascular

injuries, trismus, or pain noted. In addition, the shorter total operating time to open approaches, minimal blood loss, short length of stay and almost immediate return to oral diet support the feasibility of TORS in the treatment of selected PPS neoplasms.

Transoral surgical techniques have clear advantages if the PPS is encountered during tumor resection. First, the main incentive is optimal bleeding control. PPS is an area rich in vascular structures including the internal carotid artery, internal maxillary artery and their branches [9, 12]. Using the robotic magnified view, we were able to easily identify and manage the vessels. This allowed the surgeon to conduct a safe and precise excision of the mass. Another clear advantage is the absence of a visible scar. Conventional techniques include cervical and facial incisions that cause disfigurement, and the scar may be visible even after years [6, 11, 23].

Disadvantages of the TORS approach to tumors invading PPS include the limited space to manipulate the tumor and inability to perform wide resection of invasive neoplasms in PPS due to lack of haptic cue, bone cutting arm, and navigational imaging systems. Tactile feedback is an important component of surgery that may provide surgeon to differentiate tissues, perceive the amount of force applied, and determine the contour and compliance of tissue. Implementation of navigation systems and haptic sensors help to identify crucial neurovascular structures avoiding significant morbidity and mortality.

Limitations of this study include the relative small sample size and absence of conventional surgery control group. Although this study supports the feasibility of TORS for resection of PPS neoplasms, there is insufficient long-term data to demonstrate an equivalent or decreased recurrence rate over an open approach. Therefore, further analysis will be needed to assess the functional outcomes, quality of life and cost benefit in using TORS for resection of PPS neoplasms.

## Conclusion

In this case series, TORS resection of oropharyngeal cancer extending to PPS appears to be a safe and feasible technique with minimal complications when compared to traditional transcervical techniques. Magnified 3D visualization allows the surgeon en bloc resection of the tumor, close to vital structures. Significant experience with TORS and further understanding of the endoscopic anatomy of PPS could obviate the morbidity associated with tumor resection in this dense neurovascular region.

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**Conflict of interest** None.

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