

Research Article

Transoral Robotic Surgery for Oropharyngeal Carcinoma: Update

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Otolaryngology Head and Neck Surgery

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Abstract

Background: Oropharyngeal squamous cell carcinoma is increasing in incidence and its epidemiology is evolving to affect more young, HPV+, non-smokers. There have been multiple paradigm shifts in the treatment of this disease. Open surgery has been largely replaced by chemo radiation; however, recently, trans-oral robotic surgery (TORS) is emerging as a new minimally invasive therapeutic modality.

Objectives: Update the evidence evaluating TORS in the treatment of oropharyngeal squamous cell carcinoma.

Methods: Descriptive review of the literature.

Results: Integrating TORS into the multidisciplinary treatment of oropharyngeal squamous cell carcinoma allows carefully selected patients to return home early with intact airway and swallowing function in the majority of cases, without sacrificing oncologic control or survival. These findings compare favorably to open surgery and chemo radiation.

Conclusions: TORS appears to be a safe, feasible, and efficacious surgical modality for the treatment of a subset of carefully selected patients with oropharyngeal squamous cell carcinoma. HPV positive non-smokers appear to particularly benefit.

Introduction

Oropharyngeal cancer

According to the American Cancer Society, there will be an estimated 42,440 new cases of cancer of the oral cavity and pharynx in 2014 leading to 8,390 deaths (Cancer facts and figures 2014). The oropharynx is the area of the pharynx extending from the soft palate to the epiglottis and is composed of the tongue base, soft palate, tonsils, and posterior pharyngeal wall [1]. Malignancies of this region are primarily squamous cell carcinoma and, as a result of rich oropharyngeal lymphatics, are characterized by early nodal spread with resultant high stage disease at diagnosis [1]. The overall 5-year survival rate of Oropharyngeal squamous cell cancer (OPSCC) has been relatively stable at 60% over the past decade [1].

While the incidence of oral, hypopharyngeal, and laryngeal squamous cell carcinoma (SCC) has been decreasing, OPSCC is actually on the rise [2]. With the increase in incidence of OPSCC, there has also been a shift in the epidemiology of the disease [2]. What was once a demographic dominated by elderly male smokers with concurrent alcohol consumption is now one characterized by younger patients with limited exposure to these carcinogens [2]. Mounting evidence suggests that these findings are associated with oncogenic HPV infection (HPV types 16 and 18) [3,4]. Weinberger et al. analyzed a sample of 79 OPSCC pathologic specimens using real time PCR and tissue microarrays, determining that 61% of cases were HPV positive and that those with p16 over-expression had improved overall and disease free survival as well as lower 5 year local recurrence rates than their HPV/p16 negative counterparts [4]. Furthermore, in 2010, Ang and colleagues retrospectively analyzed the association between tumor HPV status and survival among patients with stage III or IV OPSCC who were previously enrolled in a randomized control trial comparing accelerated to standard

fractionation radiotherapy [3]. With 4.8 years of follow up, patients with HPV positive tumors had improved 3-year overall survival and 58% reduction in the risk of death [3]. HPV-positive tumors appear to maintain normal protein sequences, and as such, when subjected to radiotherapy and chemotherapy, are more susceptible to apoptosis and immune surveillance mechanisms [2]. This has led to changing treatment patterns with a focus on de-intensification therapy [2].

Multiple paradigm shifts

The history of the treatment of OPSCC has been characterized by multiple paradigm shifts. Prior to the Veterans Affairs study in 1991, most institutions were treating head and neck squamous cell carcinoma with surgery and adjuvant radiotherapy [5]. For OPSCC, surgery often consisted of the historically so-called "commando procedure": en bloc resection of the tumor via lip split mandibulotomy, pharyngotomy, and orolingual release often accompanied by ipsilateral or bilateral neck dissection [6,7]. These procedures, while offering acceptable rates of locoregional disease control, often resulted in significant disruption of native tissues requiring insensate, adynamic flap reconstruction leading to compromised speech, swallow, and airway function [6,7].

The morbidity of classical surgery, and advancements in chemotherapeutics and radiotherapy led to several large studies that changed the face of Head and Neck oncology, including OPSCC therapy. Randomized control trials such as the Veteran's affairs [8] and RTOG [9] studies in the late 80s and early 90s, which compared chemoradiation therapy to surgery and adjuvant radiation, demonstrated equivalent survival but improved functional status in the non-surgical group leading most specialized centers to treat OPSCC non-operatively [10]. While the Veteran's affairs trial showed equivalent overall survival between the surgical and the chemoradiation cohorts with two thirds of patients in the latter cohort

maintaining a larynx, this trial was restricted to patients with laryngeal cancer alone [8]. In the RTOG trial, 70 patients with advanced stage OPSCC were randomized to receive pre-operative, post-operative, or definitive radiation therapy (RT) alone. The small number of patients in each of these groups did not show any significant difference in overall survival, (30%, 36%, and 33% respectively) or locoregional recurrence (43%, 52% and 38 % respectively) [9]. Nevertheless, these results have influenced most centers to treat OPSCC using non-surgical modalities.

Over 10 years ago, Parsons and colleagues undertook the largest retrospective review of operative vs. non-operative treatments restricted to OPSCC. When comparing surgery (with or without adjuvant RT) to primary external beam RT performed in a patient population primarily characterized by male smokers and drinkers, the cumulative 5-year survival was 47% for patients undergoing surgery and 43% for RT with or without neck dissection [11]. The severe complication rate was 23% in the primary surgery group and 6% in the primary RT group [11]. While this review was retrospective in nature, it highlighted that this cohort of OPSCC patients have a poor survival independent of treatment choice, albeit with a decreased rate of complication with a non-surgical treatment.

The poor overall survival of this patient population combined with the shift to treat OPSCC primarily with RT led several centers to investigate the effect of increasing doses of radiation and altered fractionation regimens. However, these interventions have been associated with serious concerns relating to both early and late toxicity, significant functional deficits and diminished quality of life [7,12]. During the course of advancing radiation technology and studying the effect of these techniques on the treatment of OPSCC, there has been a marked change in the epidemiology of OPSCC to a younger demographic with less comorbidities and an improved response to therapy. This has led to yet another paradigm shift to de-intensify therapy. This has been accompanied by a re-emergence of the potential application of surgical treatments and in particular minimally invasive surgery such as transoral robotic surgery (TORS) [2,12].

TORS

Minimally invasive transoral surgery began with the practice of transoral laser microsurgery (TLMS) [6]. TLMS uses an operating microscope, laryngoscope, microlaryngeal instruments, and a CO₂ laser to resect lesions through the open mouth [6]. In 2003 Steiner and colleagues popularized TLMS as a method of resecting OPSCC lesions without large cervical incisions, a technique which gained popularity in few specialized centers with impressive results [6]. However, this technique has not been universally incorporated and can be challenging with issues related to line of site. TLMS is mentioned here as it initially brought forth the idea of transoral resection, but is otherwise outside of the scope of this review. For more information please see the work of Li and colleagues [6].

Because of the challenges of TLMS, transoral robotic surgery (TORS) has quickly become the most commonly utilized minimally invasive transoral approach for the removal of squamous cell carcinoma of the tonsil and base of tongue [6]. TORS uses the da Vinci surgical robot to resect lesions via the open mouth [7]. TORS has been used for OPSCC since it was granted FDA approval for

transoral otolaryngology surgical procedures restricted to T1 and T2 benign and malignant lesions in 2009 [6].

The da Vinci surgical robot is made up of a surgeon console, where the surgeon is immersed in a 3D magnified image of the operative field and remotely operates the robot using hand controls and foot pedals which are transmitted via a master-slave interface that eliminates tremor and scales down movements 5:1 [7]. The robotic cart is docked at a 30-degree angle to the operating table and is equipped with either a 0 or 30 degree binocular endoscope and 2 EndoWrist instruments [7]. These EndoWrist instruments provide 7 degrees of freedom (much like the human arm and wrist) and 90 degrees of articulation [7]. The vision cart is the final component, and allows support staff and the surgical assistant providing suction and retraction to visualize the operative field [7]. A typical TORS set up can be seen in Figure 1.

Transoral robotic surgery allows for improved visualization of the oropharyngeal lesion, which is often hidden within cavernous anatomy. The improved range of motion aids the surgeon in preserving adjacent structures, obviating the need for radical open surgery and flap reconstruction [7]. The tongue base TORS defect is left to heal by contraction and granulation, which results in a sensate and dynamic resection bed [7]. In radical tonsillectomy defects, a palatal advancement flap can be easily rotated to prevent velopharyngeal insufficiency. Finally, by integrating TORS in a multi-disciplinary de-escalation therapy regimen, the pathological specimens obtained can help tailor therapy to the patient's specific disease [5].

To be a candidate for TORS, a lesion must be adequately visualized and exposed and amenable a complete excision with negative margins [7]. Those patients with extensive disease likely requiring concurrent postoperative chemoradiation are clearly not candidates. Contraindications therefore include invasion of the mandible, unresectability, extracapsular extension of involved cervical lymph

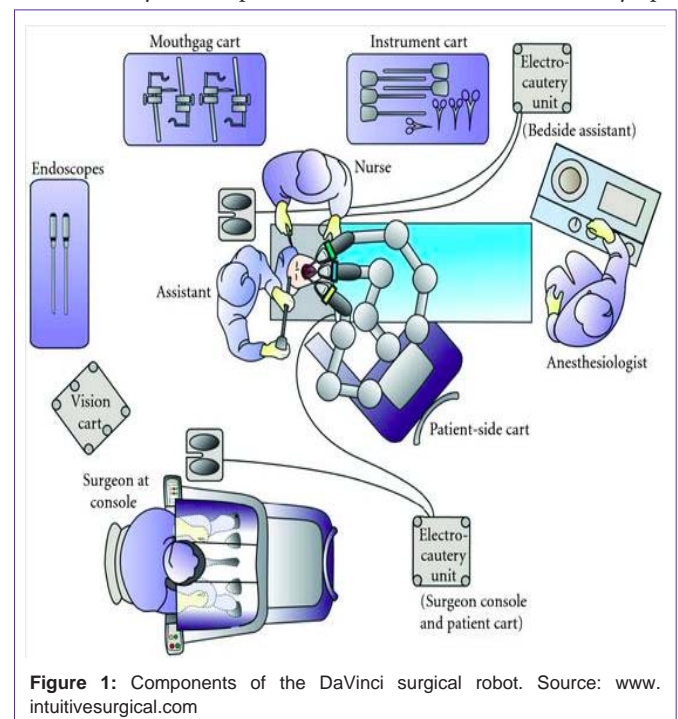


Figure 1: Components of the DaVinci surgical robot. Source: www.intuitivesurgical.com

Table 1: Oncologic Outcomes.

Study (n)	HPV (%)	T3/T4 (%)	Stage 3,4 (%)	ADJUVANT THERAPY (%)	Local Failures (%)	Regional Failures (%)	Distant Mets (%)	OS (%)	DSS (%)	Recurrence free survival (yr; %)	LC (%)	RC (%)	DC (%)	OC (%)
Moore et al. 2009 (66)	72.1	18	87.8	83.3	3	6	1.6	95.5	95.1	2yr;92.4	97	94	98.4	94
Weinstein et al. 2010 (47)	74	23	100	89	1	2	4	1yr;96 2yr;82	1yr;98 2yr;90	1 yr; 96, 2yr;79	98	96	91	85
Cohen et al. 2011 (50)	74	22	86	82	0	2	6	1yr; 96, 2yr;81	1yr;98, 2yr;93	n/a	100	98	94	n/a
Weinstein et al. 2012 (27)	n/a	22.2	88.9	93	0	0	3.7	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Weinstein et al. 2012 (30)	n/a	16	53.3	0	3	10	0	18 mo; 100	n/a	n/a	97	90	100	n/a
Park et al. 2013 (39)	n/a	12.8	66	64.1	2.6	n/a	n/a	2yr; 96	n/a	2yr; 92	n/a	n/a	n/a	n/a
Olsen et al. 2013 (18)	55.6	5.6	27.8	0	HPV+ smoke - 9.1	HPV + smoke - 0	HPV+ smoke- 0	n/a	n/a	smoke- 92.3; smoke+ 30; HPV+92.3 HPV-0	HPV+ smoke- 90.9	HPV+ smoke- 100	HPV+ smoke- 100	n/a
White et al. 2013 (64)	n/a	7.8	51	100 % recurrent disease	n/a	n/a	n/a	2yr; 74	n/a	2 yr; 74	n/a	n/a	n/a	n/a

OS = overall survival, DSS = disease specific survival, LC = local control, DC = distant control, OC = overall control, smoke- = nonsmoker, smoke+ = smoker

nodes, resection requiring over 50% of the tongue base, resection requiring more than 50% of the posterior pharyngeal wall, carotid artery involvement, or pre-vertebral fascia fixation of the tumor [7].

There is mounting evidence that TORS can play an integral role in the treatment of OPSCC. Multiple feasibility studies have demonstrated reasonable operative times and safety [13-16], and longer term clinical trials have revealed encouraging oncologic and functional outcomes. The purpose of this review is to update the evidence evaluating TORS with the most current clinical studies in the scientific literature in order to further elucidate the role of this cutting edge surgical modality in the multidisciplinary treatment of OPSCC.

Methods

A literature search was undertaken using the Pubmed, Medline, and ISI Web of Science databases, which were queried with the following entries as both keywords and MESH subject headings alone and in combination: Robotic, Robotics, Robot, Transoral Robotic Surgery, TORS, Head, and Neck Cancer, Cancer, Oropharynx, Oropharyngeal Cancer.

The resulting articles were surveyed and only those describing the treatment of OPSCC with TORS were included for discussion. Studies with less than 10 patients and less than 6 months clinical follow up were excluded. Data relating to oncologic and functional outcomes will be reviewed.

Results

Oncologic outcomes

As further clinical trials emerge evaluating the long-term oncologic outcomes of TORS for OPSCC, the evidence continues to support the use of this modality. A summary of these primarily retrospective cohort studies can be found in Table 1. Combined, these studies include 341 patients with primarily low T stage and high overall stage secondary to advanced nodal metastasis that were treated with upfront TORS and adjuvant therapy as indicated. In these studies, local control (LC) ranged from 90.9 to 100%, regional control (RC) from 90-100%, and distant control (DC) from 91 to 100%. Overall survival ranged from 95.5 to 100% at 1 yr and between

74-96% at 2 yrs (across 4 studies). Disease specific survival ranged from 95.1 to 98% at 1 year and from 90 to 93% at 2 years (2 studies). Finally, recurrence free survival was reported to be 96% at 1 year in 1 study, between 74 to 92.4% at 2 years, and between 0-92.3% in one single modality TORS study depending on HPV and smoking status. This study will be discussed in further detail below. One should note that these figures may be somewhat skewed by 2 studies evaluating TORS without adjuvant therapy.

There are several recent studies that have yet to be reviewed in the literature and will therefore be discussed in more detail. In 2013 Park and colleagues published their prospective cohort study of 39 patients with OPSCC treated with upfront TORS with concurrent neck dissection and adjuvant therapy as indicated [17]. 12.8% of lesions were T3/T4 and 66% were overall stage III/IV [17]. They achieved clear margins in 95% of cases [17]. 64.1% of patients received some form of adjuvant therapy (radiation or combined chemoradiation therapy) [17]. They achieved an overall survival of 96% and recurrence free survival of 92% at two years' time [17].

In 2013, White et al. conducted a retrospective multi-institutional case-control study looking at salvage TORS compared to traditional surgical excision for recurrent OPSCC [18]. This included 64 patients treated with TORS, 7.8% with T3/4 lesions and 51% with stage 3/4 disease [18]. The group that underwent TORS with staged or concurrent modified radical neck dissection achieved 74% overall and recurrence free survival at 2 years follow-up compared to only 43% in the open surgery group [18].

Two studies evaluated the oncologic feasibility of TORS as monomodal therapy for OPSCC. In 2013, Olsen and colleagues conducted a retrospective study of 18 patients treated with TORS alone from 2007-2009 at a single center and stratified the results by HPV and smoking status [19]. 55.6% of patients were HPV positive. 5.6% of patients had locally advanced primary tumors, while 27.8% of patients had stage 3/4 disease on the basis of positive regional lymph node metastasis [19]. HPV positive non-smokers achieved RC, LC, and DC rates of 90.9%, 100%, and 100% respectively. Kaplan-Meier estimated 3-year recurrence-free survival for HPV positive non-smokers was 92.3% (12 patients), but only 30% for smokers (5 patients) and 0% for HPV-negative patients (5 patients) [19]. These results are

consistent with the work of Weinstein et al. in 2012, who conducted a prospective observational study in which 30 patients were treated with TORS and staged neck dissection as indicated without adjuvant therapy [20]. 16% and 53.3% of patients had advanced primary and overall disease respectively [20]. LC, RC, and DC were 97, 90, and 100% respectively [20]. Overall survival was 100% at 18 months [20].

Functional outcomes

13 studies comprising 544 patients were included describing both objective and subjective (patient reported) measures of quality of life after TORS. Objective data is summarized in Table 2. Only 0-4.5% of patients required a PEG tube for feeding at 1 year with a mean of 2.2%. Tracheostomies were placed in 0-31% of cases at an average rate of 10.7%. Note that this is likely positively skewed by routine tracheostomy placement in several of the earlier series. In later series tracheostomy placement rates of 0% were achieved [16,21].

The most current studies will be reviewed individually. In 2013, Dziegielewski and colleagues performed a prospective cohort study of 81 patients with previously untreated OPSCC who underwent TORS, concurrent neck dissection, and adjuvant XRT (87%) or concurrent CRT (67%) when clinically indicated [22]. 72% of patients were HPV+, 10% of patients had T3/4 tumors, and 91% of patients had high stage disease [22]. Long term quality of life and functional outcomes were assessed using the objective measures of gastrostomy tube dependence and tracheotomy requirement as well as subjectively by administering the Head and Neck Cancer Inventory (HNCI) survey pre-operatively and during the follow-up period. Nine percent of patients required the use of their PEG tube at 1 year and only 1 patient (1%) required a tracheostomy, which was removed prior to leaving hospital [22]. While there was subjective early decline in several of the HNCI domains, patients maintained high QOL scores at 1 year post-TORS [22].

In the study by Olsen et al. outlined above, 55.6% of patients immediately tolerated an oral diet, while 44.4% of patients required a nasogastric feeding tube for a mean of 13.6 days [19]. No patients required a PEG tube. In another study evaluating TORS alone in the treatment of OPSCC, an oral diet was tolerable at a mean of 6

days in all patients, no serious mechanical difficulties were seen on video pharyngogram, and 97% of patients were swallowing well with FOSS scores of 0-2 [17]. In addition, nasalance scores were normal by nasometry in all patients. In this same study, park et al. found that compared to patients treated with the standard mandibular swing approach, TORS patients displayed more rapid swallowing, decannulation, and return home [17]. Furthermore, White et al. reported a 3% PEG tube rate at 1 year and 23% tracheostomy rate in their TORS group compared to 31% and 79% in the open surgery group, respectively [18].

Discussion

The growing body of literature evaluating TORS for the treatment of OPSCC is promising. These studies suggest that integrating TORS into the multidisciplinary treatment of OPSCC allows carefully selected patients to return home early with intact airway and swallowing function in the majority of cases, without sacrificing oncologic control or survival.

Landmarks studies such as the RTOG and Parsons et al. shifted practice at many cancer centers toward organ preservation with CRT and away from the highly morbid traditional surgical procedures. While the presented retrospective studies are limited by their inherent retrospective nature, involvement of different centres, and different patient samples, nonetheless, compared to recent OPSCC CRT trials, several observations can be made. In a carefully selected cohort of OPSCC patients, upfront TORS excision followed by adjuvant therapy as clinically indicated appears to decrease PEG dependency and patient morbidity with comparable disease control and survival [23,24]. In the most recent CRT series mean PEG duration was 7.9 months with 2.9% PEG retention at 1 year and overall survival and local control of 90 and 92% respectively [23,24].

By adding TORS tumor resection, which can achieve oropharyngeal organ preservation in the majority of cases, the target volume for irradiation is significantly decreased accounting for decreased morbidity [25]. It was particularly interesting to note that in carefully selected HPV positive non-smokers, TORS obviated the need for adjuvant therapy all together, yielding comparable survival and disease control [19].

Table 2: Functional Outcomes.

Study (n)	HPV (%)	T3/T4 (%)	Stage 3,4 (%)	Adjuvant therapy (%)	PEG tube at 1 yr (%)	Tracheostomy (%)
Genden et al 2007 (27)	n/a	22.2	88.9	89	4	7.4
Weinstein et al. 2007 (27)	n/a	22.2	88.9	93	3.7	7.4
Moore et al. 2009 (66)	72.1	18	87.8	83.3	4.5	25.8
Moore et al. 2009 (45)	n/a	26.6	86.7	73.4	0	31
Weinstein et al. 2010 (47)	74	23	100	89	2.4	10.6
Richmon et al. 2011 (20)	50	10	45	n/a	0	0
Sinclair et al. 2011 (42)	n/a	0	76	76	0	0
Leonhardt et al. 2012 (38)	n/a	13.2	73.6	76.3	2.7	2.6
Weinstein et al 2012 (30)	n/a	16	53.3	0	0	3.3
Park et al 2013 (39)	n/a	12.8	66	64.1	0	n/a
Dziegielewski 2013 (81)	72	10	91	87 XRT, 67 CRT	9	1
Olsen et al. 2013 (18)	55.6	5.6	27.8	0	0	16.7
White et al. 2013 (64)	n/a	7.8	51	100 % recurrent disease	3	23

XRT = Radiotherapy, CRT = Chemoradation

One must interpret these results with cautious optimism; however, as these studies are characterized by significant selection bias owing to the stringent inclusion criteria for a TORS procedure. Furthermore, the improved survival observed over time may be in part due to advances in therapy, but also a shift in disease demographics from smokers and drinkers to younger HPV positive non-smoking patients with inherently improved prognosis.

The primary weaknesses of TORS as a therapeutic modality include the significant cost of purchasing and maintaining the robot as well as the time investment required to train support staff, residents, and surgeons in this novel technique. According to a recent survey of 300 TORS surgeons, the most frequent complications included post-operative hemorrhage, tooth damage, dehydration, and aspiration pneumonia [26]. Post-operative hemorrhage is the most common complication and is significantly greater after TORS than open surgery, likely secondary to the complex network of blood vessels that must be controlled from an unfamiliar orientation [27].

The steep learning curve of TORS was highlighted in one study by a significant drop in overall complication rate from 17.3% in surgeons performing fewer than 25 TORS cases to 6.1% in those performing more than 50 cases [26]. Surgeons implementing TORS into their practice are urged to begin with benign and low T-stage lesions before progressing to more challenging malignant cases [28]. Simulation also has a role to play in training TORS-competent surgeons. A recent study demonstrated that using the DaVinci Skills simulator, a group of medical students could achieve competency in 12 TORS-related tasks in 100% of cases with durability of newly acquired skills over time [29].

In spite of the above challenges, multiple academic centers have adopted TORS successfully to the benefit of their patients by using lead surgeons with TORS fellowship training, a nurse education program involving didactic sessions on the rationale behind and operating room setup of TORS, and simulated cases involving the entire multidisciplinary team [16,30].

In conclusion, TORS appears to be a safe, feasible, and efficacious surgical modality for the treatment of a subset of carefully selected patients with OPSCC. HPV positive non-smokers appear to particularly benefit. Future work should include randomized control trials comparing TORS to CRT for the treatment OPSCC in patients stratified by HPV status.

References

- Lubek JE, Clayman L. An update on squamous carcinoma of the oral cavity, oropharynx, and maxillary sinus. *Oral Maxillofac Surg Clin North Am.* 2012; 24: 307-316, x.
- Genden EM. The role for surgical management of HPV-related oropharyngeal carcinoma. *Head Neck Pathol.* 2012; 6 Suppl 1: S98-103.
- Ang KK, Harris J, Wheeler R, Weber R, Rosenthal DI, Nguyen-Tân PF, et al. Human papillomavirus and survival of patients with oropharyngeal cancer. *N Engl J Med.* 2010; 363: 24-35.
- Weinberger PM, Yu Z, Haffty BG, Kowalski D, Harigopal M, Brandsma J, et al. Molecular classification identifies a subset of human papillomavirus-associated oropharyngeal cancers with favorable prognosis. *J clin oncol.* 2006; 24: 736-747.
- de Almeida JR, Genden EM. Robotic surgery for oropharynx cancer: promise, challenges, and future directions. *Curr Oncol Rep.* 2012; 14: 148-157.
- Li RJ, Richmon JD. Transoral endoscopic surgery: new surgical techniques for oropharyngeal cancer. *Otolaryngol Clin North Am.* 2012; 45: 823-844.
- Park ES, Shum JW, Bui TG, Bell RB, Dierks EJ. Robotic surgery: a new approach to tumors of the tongue base, oropharynx, and hypopharynx. *Oral Maxillofac Surg Clin North Am.* 2013; 25: 49-59, vi.
- [No authors listed]. Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. The Department of Veterans Affairs Laryngeal Cancer Study Group. *N Engl j med.* 1991; 324: 1685-1690.
- Kramer S, Gelber RD, Snow JB, Marcial VA, Lowry LD, Davis LW, et al. Combined radiation therapy and surgery in the management of advanced head and neck cancer: final report of study 73-03 of the Radiation Therapy Oncology Group. *Head Neck Surg.* 1987; 10: 19-30.
- Moore EJ, Hinni ML. Critical review: transoral laser microsurgery and robotic-assisted surgery for oropharynx cancer including human papillomavirus-related cancer. *Int j radiat oncol biol phys.* 2013; 85: 1163-1167.
- Parsons JT, Mendenhall WM, Stringer SP, Amdur RJ, Hinerman RW, Villaret DB, et al. Squamous cell carcinoma of the oropharynx: surgery, radiation therapy, or both. *Cancer.* 2002; 94: 2967-2980.
- Adelstein DJ, Ridge JA, Brizel DM, Holsinger FC, Haughey BH, O'Sullivan B, et al. Transoral resection of pharyngeal cancer: summary of a National Cancer Institute Head and Neck Cancer Steering Committee Clinical Trials Planning Meeting, November 6-7, 2011, Arlington, Virginia. *Head & neck.* 2012; 34: 1681-1703.
- Dean NR, Rosenthal EL, Carroll WR, Kostrzewa JP, Jones VL, Desmond RA, et al. Robotic-assisted surgery for primary or recurrent oropharyngeal carcinoma. *Arch Otolaryngol Head Neck Surg.* 2010; 136: 380-384.
- Benazzo M, Canzi P, Occhini A. Transoral robotic surgery with laser for head and neck cancers: a feasibility study. *ORL J Otorhinolaryngol Relat Spec.* 2012; 74: 124-128.
- Cognetti DM, Luginbuhl AJ, Nguyen AL, Curry JM. Early adoption of transoral robotic surgical program: preliminary outcomes. *Otolaryngol Head Neck Surg.* 2012; 147: 482-488.
- Richmon JD, Agrawal N, Pattani KM. Implementation of a TORS program in an academic medical center. *Laryngoscope.* 2011; 121: 2344-2348.
- Park YM, Kim WS, Byeon HK, Lee SY, Kim SH. Oncological and functional outcomes of transoral robotic surgery for oropharyngeal cancer. *Br J Oral Maxillofac Surg.* 2013; 51: 408-412.
- White H, Ford S, Bush B, Holsinger FC, Moore E, Ghanem T, et al. Salvage surgery for recurrent cancers of the oropharynx: comparing TORS with standard open surgical approaches. *JAMA Otolaryngol Head Neck Surg.* 2013; 139: 773-778.
- Olsen SM, Moore EJ, Laborde RR, Garcia JJ, Janus JR, Price DL, et al. Transoral surgery alone for human-papillomavirus-associated oropharyngeal squamous cell carcinoma. *Ear Nose Throat J.* 2013; 92: 76-83.
- Weinstein GS, Quon H, Newman HJ, Chalian JA, Malloy K, Lin A. Transoral robotic surgery alone for oropharyngeal cancer: an analysis of local control. *Arch Otolaryngol Head Neck Surg.* 2012; 138: 628-634.
- Sinclair CF, McColloch NL, Carroll WR, Rosenthal EL, Desmond RA, Magnuson JS, et al. Patient-perceived and objective functional outcomes following transoral robotic surgery for early oropharyngeal carcinoma. *Arch Otolaryngol Head Neck Surg.* 2011; 137: 1112-1116.
- Dziegielewski PT, Teknos TN, Durmus K, Old M, Agrawal A, Kakarala K, et al. Transoral robotic surgery for oropharyngeal cancer: long-term quality of life and functional outcomes. *JAMA Otolaryngol Head Neck Surg.* 2013; 139: 1099-1108.
- Lawson JD, Otto K, Chen A, Shin DM, Davis L, Johnstone PA. Concurrent platinum-based chemotherapy and simultaneous modulated accelerated radiation therapy for locally advanced squamous cell carcinoma of the tongue base. *Head Neck.* 2008; 30: 327-335.
- de Arruda FF, Puri DR, Zhung J, Narayana A, Wolden S, Hunt M, et al. Intensity-modulated radiation therapy for the treatment of oropharyngeal

- carcinoma: the Memorial Sloan-Kettering Cancer Center experience. *Int j Radiat oncol biol phys.* 2006; 64: 363-373.
25. Weinstein GS, O'Malley BW Jr, Cohen MA, Quon H. Transoral robotic surgery for advanced oropharyngeal carcinoma. *Arch Otolaryngol Head Neck Surg.* 2010; 136: 1079-1085.
26. Chia SH, Gross ND, Richmon JD. Surgeon experience and complications with Transoral Robotic Surgery (TORS). *Otolaryngol Head Neck Surg.* 2013; 149: 885-892.
27. Pollei TR, Hinni ML, Moore EJ, Hayden RE, Olsen KD, Casler JD, et al. Analysis of postoperative bleeding and risk factors in transoral surgery of the oropharynx. *JAMA Otolaryngol Head Neck Surg.* 2013; 139: 1212-1218.
28. Vergez S, Lallemand B, Ceruse P, Moriniere S, Aubry K, De Mones E, et al. Initial multi-institutional experience with transoral robotic surgery. *Otolaryngol Head Neck Surg.* 2012; 147: 475-481.
29. Zhang N, Sumer BD. Transoral robotic surgery: simulation-based standardized training. *JAMA Otolaryngol Head Neck Surg.* 2013; 139: 1111-1117.
30. Nichols AC, Fung K, Chapeskie C, Dowthwaite SA, Basmaji J, Dhaliwal S, et al. Development of a transoral robotic surgery program in Canada. *Journal of otolaryngology - head & neck surg.* 2013; 42: 8.