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Early experience in transoral robotic surgery (TORS) for non-oropharyngeal head and neck malignancies: a review of functional and oncologic outcomes

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Key-words. Transoral robotic surgery; TORS; oncologic outcome; functional outcome; hypopharyngeal cancer; supraglottic cancer

Abstract. *Early experience in transoral robotic surgery (TORS) for non-oropharyngeal head and neck malignancies: a review of functional and oncologic outcomes. Objective*: To review and summarize functional and oncologic outcomes after transoral robotic surgery (TORS) for non-oropharyngeal head and neck malignancies.
Data Sources: The MEDLINE database and bibliographies of relevant studies were searched through December 2014.
Methods: Search strategy was ((transoral) AND surgery) AND robotics) OR TORS. Abstracts and titles were screened for relevance and full articles of the selected records were evaluated and critically appraised after inclusion. Data concerning functional and oncologic outcomes as well as adverse effects were collected.
Results: 22 records were eventually included in the review. For TORS in the treatment of glottic, hypopharyngeal ands supraglottic cancer we retained 3 case series (26 patients), 5 case series (36 patients) and 6 case series (67 patients) respectively. 8 case reports/series (14 patients) assessing safety and feasibility of TORS for tumours in the parapharyngeal space, nasopharynx and skull base were also evaluated. In general, treatment of laryngeal and hypopharyngeal cancer by means of TORS seems to be feasible and safe with satisfying functional and short-term oncologic results. For treatment of malignant tumours in the parapharyngeal space, nasopharynx and skull base, the benefits of TORS, when compared to classic surgical techniques, are still uncertain and are particularly based on theoretical advantages.
Conclusion: TORS offers an interesting new approach for treating non-oropharyngeal head and neck malignancies. However, long term results are still not reported and TORS should be directly compared to existing therapeutic options in randomized controlled trials. Until then, its use should be subject to critical appraisal.

Introduction

The first application of robot-assisted surgery (RAS) in the head and neck region was a transoral excision of a vallecular cyst in 2005, performed by McLeod and Melder.[1] In 2006, after extensive animal and cadaveric studies, three patients with tongue base tumors underwent transoral robotic surgery (TORS) using the Da Vinci robot (Intuitive Surgical Inc, Sunnyvale, CA, USA) in the setting of a prospective clinical trial by the group of O'Malley Jr and Weinstein from the University of Pennsylvania (Philadelphia, USA).[2] After this publication, this group has been making important contributions to the field of TORS and was followed later on by other research groups, eventually leading to the Food and Drug Agency (FDA) approval of the Da Vinci surgical robot for TORS in 2009. The main advantage of the robot, a more precise and finer instrument control with greater freedom of motion in all three dimensions, has driven the application of robot-assisted surgery in the field of head and neck surgery. Especially regions that are difficult to reach (e.g. oropharynx and supraglottis) now became more accessible, eliminating – in specific indications - the need for an extensive open surgical approach, thus decreasing postoperative morbidity. Consequently, TORS has become well established in recent years, especially for the resection of oropharyngeal squamous cell carcinoma (SCC). Yielding satisfactory oncologic and functional outcomes, TORS has been increasingly investigated as a possible alternative to nonsurgical organ preservation regimens for the primary treatment of oropharyngeal carcinoma.[3-8] On the other hand, in recurrent oropharyngeal carcinoma, salvage TORS proved to yield better functional results when compared to radical open salvage surgery.[9] While most published TORS-data focus on the oropharynx, much less attention has been paid to the possible application of TORS in other head and neck sites. This paper reviews

functional and oncologic outcomes of TORS for treatment of non-oropharyngeal head and neck malignancies.

Methods

Search methods

The primary search for this review was conducted in December 2014 using the MEDLINE database. The following search strategy was used: (((transoral) AND surgery) AND robotics) OR TORS. Initially, no limitations on the search were imposed and peer-reviewed journals in all languages were included. Abstracts and titles were screened for relevance and the full articles of the selected records were reviewed. The bibliographies of relevant articles were checked to identify additional papers of potential interest.

Selection criteria

The primary MEDLINE search yielded 384 references. The titles and/or abstracts of all 384 records were screened and 298 records were excluded in the first instance. Exclusion criteria at this point were: 1) reviews (n=6), 2) case reports (n<10) concerning transoral treatment of oropharyngeal cancer (n=11), 3) technical, animal or cadaveric studies (n=14), 4) papers which were included by the MEDLINE search engine but which did not concern the desired subject or were published in languages other than English (n=267). After this first exclusion-round, 86 abstracts were re-assessed for eligibility depending on the subsite of the treated malignancy. If the abstract was not clear about the treated tumour site, the full text article was screened. After perusing these abstracts or full text articles and subsequent exclusion of papers concerning treatment of oropharyngeal carcinoma, cervical unknown primary, transoral robotic total laryngectomy and papers with a mixed tumorsite population, 31 relevant papers were identified. Full text analysis of these papers led to the exclusion of 11 papers: 7 papers which only included benign tumors, 1 paper which was a cost effectiveness study and did not report on outcomes, 1 paper in which the study-population was nearly the same as in another paper by the same author already included in the review, 1 paper in which transoral surgery was defined further in the text as transoral laser surgery and 1 paper about supraglottic carcinoma which included only 3 cases. Bibliography search of the selected papers rendered 2 more relevant records, bringing the total amount of full-text articles which were eventually included in this review on 22, all of which were used in the qualitative analysis regarding oncologic and functional outcomes. Results of the search strategy and selection of relevant papers are illustrated according to the PRISMA guidelines in a flow diagram (Figure 1).[10] Relevant articles were further classified into different subgroups, covering following subjects: TORS for treatment of supraglottic, glottic and hypopharyngeal cancer (14 references) and TORS for treatment of tumours in the parapharyngeal space, nasopharynx and skull base (8 references).

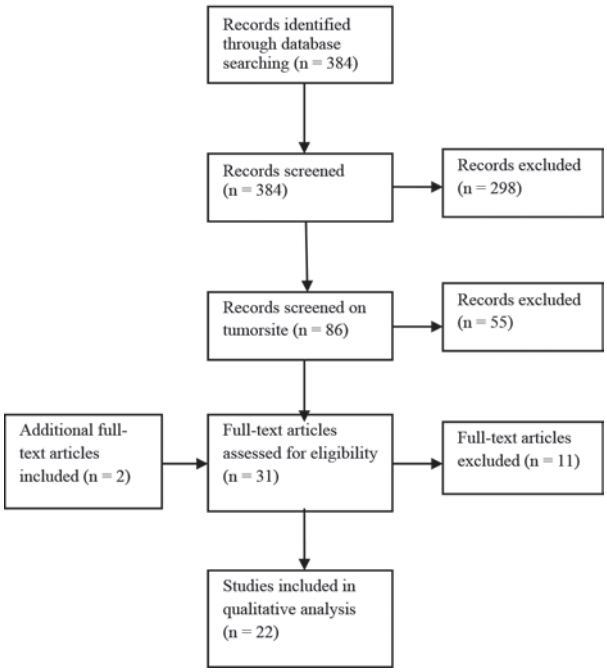

Figure 1
Flow diagram which illustrates the results of the search strategy and selection of relevant papers according to the PRISMA guidelines.

Results

Role of TORS in the management of glottic, hypopharyngeal and supraglottic cancer

Concerning the potential use of TORS in these indication, most studies concern small population (n<20) retrospective case series or single-arm prospective trials (level of evidence 4).

Carcinoma of the glottis

In 2009, Park *et al*.[11] reported for the first time on a succesful transoral robotic cordectomy in 3 cases with T1 or T2 glottic SCC using the Da Vinci surgical robot with 5 mm instruments and monopolar cautery. All surgical resection margins were free of carcinoma and no perioperative complications or mortality were observed. Feasibility was illustrated by acceptable total therapeutic times (including robotic set up time), ranging from 30 minutes to 55 minutes. Although all patients received a tracheotomy before the TORS-procedure to account for a possible postoperative airway obstruction, the definitive functional outcome was satisfying: complete swallowing function returned in all 3 patients between 4 to 7 days after surgery without the need for nasogastric tube (NGT) feeding, and decannulation could be performed between 5 to 8 days after the procedure.[11] However, because of the very small study population, the important inclusion bias (impossibility to obtain an adequate surgical view transorally was an exclusion criterion) and the unsatisfactory data about speech outcome (which is the main concern when using an imprecise instrument like a monopolar cautery), these findings need to be interpreted with caution.

Feasibility, safety and efficacy of transoral robotic cordectomy were investigated more in depth by Kayhan *et al*.,[12] who treated 10 subjects with T1 glottic carcinoma. Negative margins were obtained in all cases and mean total robotic surgery time was 21.6±6.75 minutes (range from 10 to 31 minutes). In contrast to the aforementioned study by Park *et al*.,[11] only 1 subject needed a short-term tracheotomy and an NGT. The 9 other patients started oral nutrition 6 to 24 hours after the operation. The authors concluded that transoral robotic cordectomy for early glottic carcinoma is feasible, effective and safe, and they proposed this technique as a possible alternative for transoral laser microsurgery (TLM).[12]

This statement was further propagated in a retrospective study by Lallemant *et al*.,[13] in which 13 patients with early glottic cancer were primarily treated by TORS (7 pT1a, 5 pT1b and 1 pT2). No intraoperative complications were encountered. However, one patient developed cervical emphysema and a pneumothorax postoperatively, as a result of a peroperatively unnoticed breach of the cricothyroid ligament, ultimately requiring reintervention with tracheotomy. No other patients required a tracheotomy and only 3 patients were fed postoperatively via an NGT, which could be removed after a mean of 10 days. Histopathological examination of the resected tumors confirmed free margins in 6 patients, close margins (less than 1 mm) in 2 patients and a positive margin in 1 patient. In 4 cases, the margin status could not be assessed due to thermal injury to the margins of the specimen, which is a general observation in robotic resection using the monopolar cautery. Median length of hospital stay was 5 days (range 3 to 20 days) and no adjuvant therapy was initiated. During the mean follow-up time of 15.7 months (range 7 to 32 months), 2 local recurrences involving the anterior commissure occured which were treated by salvage total laryngectomy or radiotherapy. The authors concluded that these short-term oncologic results were comparable with those reported in the literature for TLM. Remarks to be made here are that the length of hospital stay after TLM is usually much shorter,and that precision of cutting with CO_2 laser is generally assumed to be higher than what can be obtained using a cauter spatula.[13] On the other hand, tracheotomy is virtually never needed in TLM procedures. The drawback of this study is the combination of this population with 10 supraglottic cancer cases. Variables such as operative time, histopathological findings and mean follow-up time were not differentiated between both subgroups. However, exposure time and robotic system docking time for the complete population ranged from 5 to 40 minutes and 5 to 15 minutes respectively, which is in our experience definitively longer than the setup time for TLM.

Carcinoma of the hypopharynx

The feasibility and outcome of TORS for treatment of hypopharyngeal SCC was mainly investigated by the group of Park YM from Yonsei University College of Medicine (Seoul, Republic of Korea). In 2009, they published for the first time on TORS of a T2N2bM0 squamous cell carcinoma of the piriform sinus, achieving negative surgical margins. Decannulation was possible after 7 days and return to normal swallowing was achieved after 21 days.[11]

In a subsequent study the same group prospectively assessed the feasibility of TORS in a group of 10 patients with T1 or T2 piriform sinus cancer and posterior hypopharyngeal wall cancer. The neck was addressed by simultaneous dissection

if indicated and adjuvant radio(chemo)therapy added depending on the definitive pathology report. The mean robotic operative time was 62.4 min and mean robot set-up time was 17.5 min. In all cases, negative surgical margins were reported. No significant complications during the procedure were observed. Concerning functional outcomes, tracheotomy was performed systematically in all patients to prevent postoperative airway compromise, but decannulation was completed within 6.3 days postoperatively with no specific problems regarding voice reported afterwards. A normal swallowing function was obtained at 8.3 days postoperatively on average. After a mean follow-up time of 12.2 months (range 2 to 25 months), all patients were disease-free without problems concerning swallowing and phonation.[14]

To address the issue of this short follow-up time, the same group published a prospective study evaluating the oncologic and functional outcomes over a period of 3 years.[15] In this study, 23 patients with hypopharyngeal wall cancer (piriform sinus in 18 patients, posterior pharyngeal wall in 4 patients and postcricoid region in 1 patient) were treated with TORS. 8 patients had T1, 8 patients T2, 3 patients T3 and 4 patients T4 disease. The average set up time was 14.5 min and the average operation time was 55.2 min, which is less compared to the times reported in the aforementioned study by Park *et al*., illustrating a learning curve.[14] No serious intraoperative complications occured and 1 postoperative bleeding stopped without the need for reintervention. Positive margins were reported in 2 patients with rT4 disease (8.7%) who previously failed definitive radiotherapy for hypopharyngeal cancer. 14 patients (60.9%) underwent adjuvant therapy (9 radiotherapy and 5 radiochemotherapy). Overall and disease-free survival at 3 years, evaluated using Kaplan-Meier curves, were 89% and 84% respectively. An NGT was required for at least 2 to 14 days and and oral diet was possible after a mean of 8.1 days. On videopharyngogram studies, no serious aspiration or delay of swallowing was observed during the pharyngeal stage of the swallowing process. Overall, 96% of patients showed satisfying swallowing abilities with functional outcome swallowing scale (FOSS) scores ranging from 0 to 2. Decannulation was possible after an average of 5.3 days. Postoperative voice status, evaluated through acoustic waveform analysis, showed an increase of fundamental frequency variation and jitter (due to decreased mobility of the ipsilateral vocal fold) and a harmonic-to-noise ratio and shimmer close to the normal range. According to the authors, the favourable oncologic results as well as the satisfying functional outcomes after TORS and adjuvant therapy reported in this prospective study supports TORS as a valid surgical, organ-preserving strategy for selected patients with hypopharyngeal cancer.[15] However, looking closely at these 2 studies, it is not clear how many cases were treated by TORS in a primary or in a salvage setting after previous radio(chemo)therapy, which is an important shortcoming. Moreover, 10 patients who had been reported on in the earlier paper by the same group[14] were again included in the later prospective study, which makes the total amount of patients small to confirm validity of this treatment modality. Furthermore, these patients were again included in a retrospective study comparing oncologic and functional outcomes of transoral robotic surgery and radical open surgery (total laryngectomy with partial or circumferential pharyngectomy) for hypopharyngeal cancer.[16] In the TORS-group (n=30) and radical surgery group (n=26), the 3-year overall survival rate was 85% and 78% respectively, and disease free-survival was 81% and 76% respectively, differences which did not reach statistical significance. These differences have to be interpreted in the light of a probable selection bias of the less extended cases to the TORS group (more T1 cases in the TORS group and more advanced cases in the radical surgery group), and also in the light of the adjuvant therapy given thereafter. No significant difference in margin negativity (n=3 in each group) was observed. However, there was a significant difference in total operation time between groups (410.7 min versus 911.2 min on average), in hospitalization time (26.1 days on average versus 43.4 days) and in time to achieve full swallowing ability (8.4 days on average versus 20.6 days). Moreover, in the TORS group, all patients received a temporary tracheotomy and were decannulated after 7.2 days on average. In the open surgery group, all but 4 patients received a total laryngectomy. On the University of Washington Quality of Life (UW-QOL) scale, conducted 6 months after treatment, significant differences were observed in the domains of pain, appearance, activity, recreation, swallowing, speech, taste and anxiety in favor of the TORS-

group. Complications were more frequent in the open surgery group (flap revision in 5 cases and pharyngocutaneous fistula in 2 patients) when compared with the TORS group (postoperative bleeding in 1 case).[16]

Lörincz *et al*.[17] also reported on feasibility and safety of TORS for early hypopharyngeal cancer in 5 patients (3 cT1 and 2 cT2, 4 primary treatment, 1 salvage treatment). Clear resection margins were achieved in all cases, temporary tracheotomy was necessary in only 1 patient and 4 patients resumed full oral diet within the first postoperative week. All patients remained disease-free during the median follow-up time of 18 months.[17]

Carcinoma of the supraglottic larynx

In 2007, Weinstein *et al*.[18] reported the first use of TORS for the resection of supraglottic SCC (SG SCC): 3 patients with SG SCC underwent a succesfull resection without operative complications and with functional laryngeal preservation.[18] Since this publication, several small case series have described TORS as a feasible treatment modality for resection of supraglottic cancer.[13,19-23] Apart from the publication by Weinstein *et al*. [18], a total of 76 patients in 6 papers were identified, with sample sizes ranging from 9 to 18 patients. All studies were single institution case series (level of evidence 4) and using TORS for early SG SCC (T1 in 20 cases and T2 in 43 cases). Average robotic operating times (when specified) ranged from 25.3 minutes to 93.9 minutes and clear resection margins were obtained in 68 patients (89.5%), illustrating feasibility of TORS in adequately resecting SG SCC. Peri-operative complications were rare, ranging from no complications to 27.8%. Concurrent neck dissection was used in 58 cases (76.3%). Adjuvant radiotherapy was delivered in 13 patients (17.1%) and chemoradiation in 23 patients (30.3%). Adjuvant therapy was thus avoided in 40 cases (52.6%). Oncologic outcomes were satisfying, with locoregional disease control and overall survival at 2 years varying from 83% to 100% and 67% to 100% respectively (Kaplan-Meier). Rates of postoperative NGT placement were not always precisely reported[19,21] , but ranged from 0%[20] to 100%.[22] Median time to safe oral intake varied from less than 24 hours after the operation[20] to 12 days.[23] Percutaneous gastrostomy tube (G-tube) placement proved necessary in 7 patients (9.2% of total population), with 3 of these patients (who received multimodality treatment) remaining G-tube dependent on last follow-up.[13,19] One study used functional outcome swallowing scale (FOSS) scores to measure subjective swallowing function, and reported scores ranging from 0 to 2 in 95% of patients, indicating favorable swallowing results.[22] Rates of tracheostomy varied from 0% to 100%. Mean decannulation time was only reported in 3 studies and varied from 3.3 days to 17 days.[13,20,22] Among all included papers, only 2 patients (3% of pooled cases), both of whom were treated with multimodality therapy, remained tracheostomy dependent on last follow-up.[19]

Two papers reported on speech outcome after TORS for SG SCC. Olsen *et al*.[19] reported 3 patients out of 9 with normal postoperative speech, 2 with mild dysphonia and 4 with moderate dysphonia. Park *et al*.[22] conducted acoustic waveform analysis and voice handicap index 10 (VHI10) in order to quantify postoperative speech quality. They found the fundamental frequency to be increased, but jitter, harmonic-to-noise ratio and shimmer remained close to the normal range. Concerning VHI 10 results, 15 patients (93.8%) showed favorable results for voice-specific quality of life (scores between 0 and 40).[22] Details of the included studies are presented in Table 1. Park *et al*.[16] compared treatment outcomes after TORS supraglottic laryngectomy (n=17) with outcomes after open supraglottic partial laryngectomy (n=17). However, the included patients in the TORS group were also included in another study by the same group.[22] There was no significant difference in tumor stage between groups and no significant difference in 2-year overall survival and disease free survival (92% and 92% respectively in TORS group versus 94% and 88% respectively in open surgery group), nor in margin negativity. The average operating time was significant lower in TORS (265.8 vs 401.7 min) and the TORS group showed more rapid return to oral diet (average 8.1 days versus 18.5 days), quicker decannulation (9.2 days versus 13.7 days) and shorter hospitalisation (18.6 days versus 24.9 days). This group also showed a better subjective swallowing outcome on the MD Anderson dysphagia inventory conducted 6 months after the operation. On acoustic voice analysis, no significant differences in the various voice parameters were seen. Drawbacks of this study were the small population, the short follow-up time and the restrospective setting implying

Table 1

Detailed overview of relevant papers assessing the role of TORS in the management of supraglottic cancer

	Olsen *et al*.[19]	Ozer *et al*.[20]	Mendelsohn *et al*.[21]	Park *et al*.[22]	Ansarin *et al*.[23]	Lallemant *et al*.[13]
Study type	Prospective case series	Prospective case series	Prospective case series	Prospective case series	Retrospective case series	Retrospective case series
Patients, N	9	13	18	16	10	10
Mean follow-up (months)	26	6.8	28.1	20.3	25	15.7
cT-stage, N	T1 1 T2 6 T3 2	T1 1 T2 10 T3 2	T1 5 T2 10 T3 3	T1 7 T2 5 T3 4	T1 2 T2 6 T3 2	T1 4 T2 6
Mean robotic time (min)	NS	25.3	93.9	56.3	NS	NS
Margins	All clear	All clear	All clear	14 clear (88%)	6 clear (60%)	8 clear, 2 close (<1 mm)
Complications	1 late tracheostomy bleeding, 1 supraglottic stenosis	1 delayed onset airway edema and need for tracheotomy	In 5 patients temporary peri-operative complications, not further specified	nil	nil	1 bleeding at postoperative day 2
Concurrent neck dissection, N	9	12	9	14	4	10
Adjuvant therapy (N)	RT (4) RCT (2)	RT (2)	RCT (9)	RT (3) RCT (5)	RT (2) RCT (4) Re-excision + RCT (1)	RT (2) RCT (2)
Oncologic outcomes, %	LRDC 87.5 DSS 87.5 OS 66.7 (Kaplan Meier estimates 24 months)	LRDC 100 DSS 100 OS 100	LRDC 83 DSS 100 OS 89 (Kaplan Meier estimates 24 months)	DFS 91 (Kaplan Meier 12 months)	LRDC 100 OS 100	DFS 100
Swallowing outcomes	55% safe swallow 22% temporary G-tube 22% long term G-tube (findings at last FU)	84.6% immediate safe swallow 7.7% NGT (extraction day 14d) 7.7% G-tube (extraction at 40d)	0% G-tube safe swallow of solids and liquids: at day 4.5 and 5.5 resp.	-safe swallow: at day 8.3 -videofaryngogram: aspiration in 1 patient (6.3%) -FOSS: 94.9% scores between 0 and 2	70% NGT (extraction day 12) 10% G-tube (extraction at 1 month)	70% NGT (extraction day 9.3) 10% G-tube (extraction after 2 years)
Tracheostomy	78% temporary 22% long-term	7.7% temporary, decannulation at 17 days	0%	100% temporary, decannulation day 11	90%	30%, decannulation day 3
Speech outcome	33.3% normal speech 22.2% mild dysphonia 44.4% moderate dysphonia	NS	NS	-acoustic waveform analysis: increased fundamental frequency -VHI-10: 62.5% scores 0-20 / 31.3% scores 20-40	NS	NS

Abbreviations: DFS: disease free survival; DSS: disease specific survival; FOSS: functional outcome swallowing scale; G-tube: gastrostomy tube; ND: neck dissection; NG-tube: nasogastric tube; LRDC: locoregional disease control; OS: overall survival; RT: radiotherapy; RCT: radiochemotherapy; VHI10: Voice Handicap Index 10.

selection bias, that may partly explain the difference in outcome.

Role of TORS in the management of tumors in the parapharyngeal space, nasopharynx and skull base

Parapharyngeal space tumors

All studies investigating feasibility of TORS of the parapharyngeal space (PPS) include benign parapharyngeal neoplasms, most frequently pleomorphic adenoma.[24-32] The transoral robotic technique of addressing parapharyngeal lesions with the Da Vinci surgical robot was first introduced by O'Malley *et al*.,[26] who prospectively enrolled 10 patients with benign tumours of the PPS, showing no significant complications (including hemorrhage, infection, trismus or tumour spillage) and achieving a local control rate of 100% in the 7 patients with pleiomorphic adenoma after a mean follow-up time of 29.9 months.[26] Since this publication, various other studies have demonstrated TORS for parapharyngeal neoplasms as a safe and feasible technique with minimal complications when compared to traditional transcervical approaches.[25] However, only 1 case of TORS for a malignant lesion in the PPS was published: Arshad *et al*.[29] reported on 3 patients with a PPS tumour of whom one was diagnosed with adenoid cystic carcinoma on the right soft palate extending in the PPS. A wide transoral robotic excision was performed and the final pathology confirmed a completely excised adenoid cystic carcinoma with negative surgical margins. No complications were met and the patient was discharged the next day. No adjuvant treatment was administered and the patient was disease free at the end of the reported 6 months follow-up time (which is of course far too short too make any judgment).[29]

Tumours of the nasopharynx and skull base

In 2010, Wei *et al*.[33] reported the use of the Da Vinci surgical robot for transoral resection of a recurrent nasopharyngeal carcinoma in the left fossa of Rosenmüller after previous radiotherapy. After splitting the soft palate in the midline, the robot was docked and the tumour was successfully resected with clear surgical margins on frozen section. The patient resumed an oral diet on the 4th postoperative day.[33] However, data concerning the final histopathologic report of the resection margins as well as data about oncologic and functional outcomes were not reported. Due to poor visualisation of the anterior crus of the cartilaginous eustachian tube when using the midline palatal split approach, the same research unit from Hong Kong developed the lateral palatal flap approach which improved lateral exposure and instrument reach. This technique was reported in 1 patient who presented with recurrent nasopharyngeal carcinoma in the right posterolateral wall of the nasopharynx. In this case, final histopathology confirmed clear resection margins and upon follow-up of 6 months after the procedure, no trismus, hypernasal speech, nasal regurgitation or dietary problems were observed.[34] The Hong Kong group was also the first unit who published on the combined use of transnasal endoscopic and transoral robotic approaches for resection of a recurrent tumour in the roof of the nasopharynx. The inferior part of the resection was performed with the robot after splitting the soft palate and the superior part of the resection, including removal of the anterior wall and floor of the sphenoïd sinus, was performed transnasally. No complications were encountered and resection margins were clear.[35] This combined endoscopic endonasal approach – transoral robotic approach (EEA-TORS) was also successfully implemented in the clinic (after cadaveric studies) by Carrau *et al*.[36] for the primary surgical resection of an extensive infiltrating adenoid cystic carcinoma from nasopharyngeal origin extending to the sphenoid sinus, clivus, middle cranial and infratemporal fossa with important perineural involvement of the mandibular nerve (case 1) on the one hand and for the primary resection of an extensive chordoma invading the posterior and middle cranial base that extended to the craniocervical junction down tot C1 and C2 (case 2) on the other. No intra-operative complications occured and postoperative sequelae included mild velopharyngeal insufficiency and initial trismus in case 1. Both patients were administered proton beam radiotherapy.[36] However, no information regarding pathologic features of resection margins or oncologic follow-up of these high risk tumours were communicated. Most recently, Sreenath *et al*.[37] reported the use of EEA-TORS in a patient with a metastatic focus of papillary thyroid cancer in the retropharyngeal space and a patient diagnosed with a nasopharyngeal melanoma. No intraoperative complications were encountered and postoperative complications were limited to temporary trismus in patient 1. Oncologic follow-up was only

communicated for the former patient, who was disease free at a 2-year follow-up.[37] Few other case reports concerning transoral robotic retropharyngeal lymph node dissections have been published. Byeon *et al*.[38] reported on the use of TORS for dissection of the retropharyngeal lymph nodes (RPLN) in 4 patients with oropharyngeal and 1 patient with hypopharyngeal SCC. No patients experienced complications related to the transoral robotic RPLN dissection.[38] Kim *et al*.[32] reported a transpalatal robotic approach to remove a metastatic papillary thyroid cancer node in the high retropharyngeal node basin. No complications were reported and no recurrence was diagnosed within the short follow-up time (8-14 months).[32]

Discussion

Role of TORS in the management of glottic, hypopharyngeal and supraglottic cancer

One of the most important advantages of TORS when implemented for these tumors is its possibility to overcome the limits of the line-of-sight issue and subsequent tangential-only cutting plane as encountered in transoral laser microsurgery (TLM), giving access to tumors unapproachable by TLM.[11,13,17] This feature is especially interesting for tumors which are difficult to visualise by means of a laryngoscope such as glottic tumors invading the anterior commissure, or tumors of the hypopharyngeal region. In selected setting this would allow for multi-planar en bloc resection in contrast with TLM piece-meal resection. When treating supraglottic carcinoma, the ability to remove the pre-epiglottic fat and paraglottic space en bloc with the lesion is a possible advantage of TORS supraglottic laryngectomy when compared to TLM.[22,39]

Another advantage of TORS as a primary surgical approach is the possibility of restricting adjuvant therapy to patients classified into a high risk group based on pathologic information, avoiding radio(chemo)therapy in low risk groups. On the other hand, when adjuvant treatment proves neccessary, the low morbidity and complication rate of TORS do not cause a delay in initiating adjuvant treatment and the average dose of radiation can be decreased when compared to definitive radiation therapy, reducing radiation related morbidity and complication rates.[15,19,21]

There are also some drawbacks of TORS when addressing these specific tumors. Because the Da Vinci system has not been designed for laryngeal or hypopharyngeal surgery, the access to the larynx can frequently be an issue and subsequently does not entirely overcome the limitations of TLM. Furthermore, TORS is definitely associated with a longer setup time when compared to TLM. When the working arms are advanced further into the aerodigestive tract, the angles between the arms become increasingly acute, eventually leading to contact interference, a problem which is less prominent in TORS for oropharyngeal lesions.[19] Resection of tumors involving the anterior commissure of the glottis larynx also remains difficult, as is witnessed by 2 local recurrences at the anterior commissure reported by Lallemant *et al*.[13] These findings stress the need for proper pre-operative patient selection and development of more conventient mouth retractors and smaller robotic systems which could be a solution for this exposure-problem in the near future.

Comparing TORS with TLM, it does not seem that the theoretical advantages of TORS in addressing laryngeal or hypopharyngeal lesions has been proved. Ansarin *et al*.[40] retrospectively examined their first 10 consecutive TLM supraglottic laryngectomy patients and compared them with the first 10 TORS patients. This small retrospective study suggests that both of these minimally invasive techniques provide similar overall results. TORS seems as safe and effective as TLM, but for laryngeal exposure, length of feeding tube placement, postoperative pain and margin evaluability, TLM was superior. The authors believe that the prolonged postoperative dysphagia and pain in the TORS-group, could be attributed to the monopolar cautery which is used in the TORS-procedure and which creates probably more thermal damage to the tissues when compared with carbondioxide laser used in TLM.[40] Combining TORS with a carbondioxide laser could be a solution for this issue.

When compared with open surgical approaches, treating early stage laryngeal or hypopharyngeal malignant lesions by TORS seems associated with similar oncologic results but more satisfying functional outcome. Compared with radical open surgery, robotic resection of hypopharyngeal carcinoma seems to yield comparable overall survival and disease free survival rates, and results

in statistically better results for decannulation, swallowing, hospitalization and quality of life scores.[16] As mentioned earlier, these results are to be interpreted with caution due to the selection bias in this study. The same group compared treatment outcomes after TORS supraglottic laryngectomy with outcomes after open supraglottic partial laryngectomy. No significant differences in 2-year overall survival and disease free survival and in margin negativity were observed but functional results were significantly more satisfying in the TORS-group.[41]

Concerning costs, a cost comparison study of open approach, transoral laser microsurgery and TORS for partial and total laryngectomiesshowed TORS being more expensive than open surgery and TLM.[42]

In general, studies assessing the role of TORS in the treatment of glottic, supraglottic and hypopharyngeal cancer are highly selected, small population, single arm studies with short postoperative follow-up times. In most studies, it is unclear how many patients were treated by means of transoral robotic resection in a salvage setting. When reporting on functional outcome, most studies present limited information. There is obviously an urgent need for multi-institutional randomized controlled trials comparing the long term oncologic and functional outcomes of primary TORS with primary conservative organ preservation treatment and comparing salvage TORS with salvage radical open surgery. Randomized controlled trials comparing oncologic and functional results of TORS with TLM are also needed. In these future trials, the cost aspect needs to be included in order to evaluate the cost-effectiveness of TORS for these indications. When reporting on functional outcome, more attention should be paid to qualitative speech analysis (especially in cases of glottic carcinoma), swallowing function (by means of videopharyngography, fiberoptic endoscopic evaluation and scoring systems) and standardized quality of life questionnaires.

Role of TORS in the management of tumours in the parapharyngeal space, nasopharynx and skull base

TORS for treatment of malignant lesions in the PPS, nasopharynx or skull base is not well investigated at the moment. The technique seems feasible in highly selected patients, and the rate of peroperative and postoperative complications seems low, but evidence is limited to a few case reports and none or only short-term oncologic follow-up is presented. For malignant tumors in the PPS, evidence is extremely limited, with only 1 case report.[29] In a review by Chan *et al*.,[24] 44 patients who underwent TORS resection of PPS neoplasms were identified. Twenty-nine (65.9%) of these neoplasms were pleomorphic adenomas, of which 7 (24%) had unintended capsule violation or tumor fragmentation during TORS. However, this rather high reported rate of capsule violation in transoral robotic resection of pleomorphic adenomas suggests possible problems concerning radicality of resection of malignant PPS tumors. This high rate of capsule violation is probably due to the combination of the sharp instrumentation of the robot, the lack of haptic feedback, the impossibility for bimanual palpation, the limited space to manipulate the tumor and the sharp instrument angulation when deep dissection in the lateral aspect of the PPS is performed. Another disadvantage of the TORS approach of the PPS, is the need for dividing the pharyngeal mucosa and superior constrictor musculature, which is associated with considerable postoperative pain, questioning the true minimally invasive character of this approach when compared with the low-morbidity transcervical approach.[24] This remark is less an issue for TORS nasopharyngectomy: when resection of a nasopharyngeal tumor does not prove possible by endoscopic endonasal approach, TORS could be a valuable alternative for the invasive maxillary swing approach. TORS nasopharyngectomy seems to have a place for resection of small (recurrent) tumours located over the lateral nasopharyngeal walls, difficult to access by EEA resection, while larger tumours extending laterally should be addressed by the maxillary swing approach.[33] This limited use of TORS to small nasopharyngeal lesions is mainly due to the nearness of the internal carotid artery (ICA). Because the lack of tactile feedback poses a risk of injuring the ICA during dissection in the lateral PPS, some authors limit the use of TORS nasopharyngectomy to small lesions that are at least 1 cm medial to the ICA in order to prevent exposure of this vessel.[34] Apart from lack of haptic feedback, another limitation of TORS in skull base surgery is the lack of instruments for manipulation of bone, which has stimulated the development of the

combined EEA-TORS approach. Having also the limited superior and anterior reach of the robotic instruments and the limited inferior and lateral reach of endoscopic instruments in mind, these techniques complement each other, especially for resection of more extensive lesions in the nasopharynx, sphenoid floor, clivus, posterior skull base and infratemporal fossa.[35-37] As a conclusion, given the limited evidence, we may state that for these indications, the benefits of TORS when compared to classic surgical techniques are still uncertain and are particularly based on assumed and theoretical advantages which will need to be confirmed in the future by sound clinical evidence.

Conclusion

In contrast with the important amount of evidence supporting the benefits of TORS in treating oropharyngeal tumors, much less evidence is available regarding the potential use of TORS in addressing malignant lesions elsewhere in the upper aerodigestive tract. In general, evidence is limited to small population retrospective or prospective case series with insufficient data about long-term oncologic or functional outcome. The early experience in the treatment of laryngeal and hypopharyngeal cancer by means of TORS suggests an acceptable feasibility and safety and a functional advantage when compared to open surgical approaches with comparable oncologic results. However, no direct comparison between oncologic and functional outcomes of TORS and conservative organ preservation treatment regimens is available in the literature. As long-term results of conservative organ preservation treatment for laryngeal and hypopharyngeal malignancies are well investigated, it seems acceptable practice to use TORS for these tumours in a salvage setting rather than in a primary setting until more long-term data become available. For treatment of malignant tumours in the parapharyngeal space, nasopharynx and skull base, evidence is even more limited. In these cases, the benefits of TORS when compared to classic surgical techniques (EES or open surgery) are still uncertain and are particularly based on theoretical advantages. Nevertheless, it is surely an interesting approach for salvage resection of recurrent tumours that would be otherwise very difficult to resect (e.g. recurrent nasopharyngeal carcinoma with spread in the PPS and lateral pharyngeal wall). As a conclusion, we may state that TORS offers an interesting new approach for treating non oropharyngeal head and neck malignancies. However, long term results are needed and TORS should be directly compared to existing therapeutic options in randomized controlled trials. Until then, its use should be subject to critical appraisal.

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