# Transoral Robotic Surgery: Applications in HNC

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Minimally invasive surgery is a growing field in surgical oncology. After acquiring its first Food and Drug Administration approval in 2009 for T1–T2 malignancies of the oral cavity, oropharynx, and larynx, transoral robotic surgery (TORS) has gained popularity thanks to its wristed instruments and magnified three-dimensional view, enhancing surgical comfort in remote-access areas. Its indications are expanding in the treatment of head and neck cancer, i.e., resection of tumors of the larynx, hypopharynx, or parapharyngeal space. Head and neck cancer (HNC) incidence has increased, ranking eighth among the most common cancers worldwide in 2020 with approximately 900,000 cases yearly. Following a similar trend, head and neck surgeons in Australia and New Zealand have a TORS adoption rate of 43.6%. The main indications for TORS in all these countries are lateral oropharyngectomy, base-of-tongue mucosectomy, and surgery for obstructive sleep apnea.

transoral robotic surgery TORS head and neck cancer

## 1. Oropharyngeal Cancers

Oropharyngeal squamous cell carcinomas (SCCs) amenable to excision by TORS are mainly T1 and T2 tumors. Selected T3 (size ≈ 4–5 cm) and T4a (limited invasion or the stylo-glossus muscle) can also be treated with TORS; however, the rate of positive margins significantly increases with T-status, i.e., 13%, 17.1%, 28.2%, and 45.9% for T1, T2, T3, and T4a tumors, respectively [1][2].

Although the historical standard treatment of early-stage oropharyngeal SCC was RT, retrospective studies have validated the use of TORS in a bid to de-escalate treatment, especially for HPV-positive SCC [3]. The arguments in favor of upfront surgery are its ability to provide accurate tumor staging, and the possibility to spare adjuvant radiotherapy in selected cases (pN0–pN1 with clear margins). In practice, many patients treated with TORS + neck dissection require postoperative RT, and indications for single modality treatment with surgery are scarce [4].

Studies comparing TORS outcomes in patients with oropharyngeal p16-positive and p16-negative SCCs have demonstrated a relatively poor prognostic significance of HPV status in terms of survival [3][5]. In their study of 57 patients with HPV-negative oropharyngeal SCCs, Dabas et al. observed a locoregional control, DFS, and OS of 95.8%, 89.6%, and 93.8% after a mean follow-up of 29 months [6]. On the other hand, in a cohort of 48 HPV-positive oropharyngeal SCCs treated with TORS, the 5 year locoregional control, DSS, and OS were 98%, 100%, and 95% (**Table 1**) [7].

The results of the phase II clinical trial ORATOR were published recently, in which patients with early-stage OPSCC were randomized into two arms, i.e., TORS and neck dissection ± postoperative (C)RT versus definitive (C)RT. Outcomes of swallowing-related quality of life were better in the definitive (C)RT arm after 1 year, although the difference was not clinically meaningful and decreased over time (**Table 2**). Of note, trismus was more common in the TORS arm (26% vs. 3%), and dry mouth scores were higher in the RT arm. Lastly, pain and dental-related issues were more common in the TORS arm [8]. The conclusion of this phase II study was that TORS + neck dissection and definitive (C)RT have comparable toxicity profiles, and that patients with early-stage oropharyngeal SCC should be informed of both treatment options. The main limitation of this study is that, among 34 patients in the TORS + neck dissection arm, 71% had postoperative (C)RT, notably because of their advanced nodal stage (53% of cN2 patients). Therefore, the question of whether RT is more toxic than TORS alone in that indication remains unanswered.

Upfront TORS is also an option for selected stage III/IV oropharyngeal SCC to intensify therapy, especially in HPV-negative oropharyngeal SCC [9]. When followed by (C)RT, TORS has proved to improve survival outcomes [10]. This is in keeping with observations outside the context of TORS, where upfront surgery followed by adjuvant (C)RT results in better survival than definitive (C)RT [11][12]. In a recent retrospective study of 136 patients with HPV-positive SCCs, Zebolsky et al. showed that upfront TORS + neck dissection was an appropriate first line treatment for cN0–cN2a cases without clinical signs of ENE, in order to reduce postoperative RT dose/extent and/or avoid adjuvant chemotherapy. Pathologic ENE was present in 35.6% of cN2b patients, with a threefold higher likelihood compared to cN1–cN2a patients [10][13].

## 2. Carcinomas of Unknown Primary

After a negative workup and negative palatine tonsillectomy, performing a base-of-tongue mucosectomy (lingual tonsillectomy) with either TORS or transoral laser microsurgery could detect the primary tumor in about half of cases [14][15][16][17][18]. However, the recommendations of the main academic societies differ significantly and evolve rapidly as knowledge in the field progresses. Given the consequences on treatment initiation delay, the morbidity of this procedure, and the variable availability of TORS, the American Society of Clinical Oncology (ASCO) guidelines state that indication for base-of-tongue mucosectomy and its laterality remain at the discretion of the surgeon [19]. The National Comprehensive Cancer Network (NCCN) guidelines support base-of-tongue mucosectomy after a negative palatine tonsillectomy. Of note, they advise against bilateral palatine and lingual tonsillectomy due to the risk of circumferential oropharyngeal stenosis [20]. On the contrary, the AHNS advocates for simultaneous bilateral palatine tonsillectomy with ipsilateral base-of-tongue mucosectomy, due to allegedly high rates of finding a primary in the contralateral palatine tonsil (15–25%) and in the ipsilateral lingual tonsil (6%) [18]. However, a recent systematic review challenged this as it highlighted a lower rate of contralateral tonsillar primary, i.e., 10% and 1% of bilateral and contralateral tonsillar primary, respectively [21]. These numbers likely vary as the prevalence of HPV-associated SCC varies between countries. This variation may, therefore, justify the global difference of practices and recommendations regarding palatine and/or lingual tonsillectomy.

With respect to the HPV status, the likelihood of finding the primary tumor in a base-of-tongue mucosectomy in HPV-negative carcinomas of unknown primary seems much lower than in their HPV-positive counterparts (13% versus approximately 50%), and most studies to date included mainly HPV-positive patients [14][22][23]. Therefore, in HPV-negative carcinomas of occult primary, the risk/benefit balance of base-of-tongue mucosectomy seems currently unfavorable.

## 3. Laryngeal Cancers

Most indications for TORS excision of laryngeal SCC are early-stage (T1–T2 N0–N1) supraglottic SCCs. However, TORS also allows performing cordectomies for early glottic cancers, as well as total laryngectomies for more advanced tumors. Similarly to transoral laser microsurgery, the rationale for using TORS in early laryngeal tumors is to carry out a single modality treatment and to avoid the morbidity of external approaches. Indeed, TORS can provide favorable functional outcomes thanks to the preservation of key structures for swallowing, e.g., infrahyoid muscles, pharyngeal constrictor muscles, hyoid bone, thyroid cartilage, and superior laryngeal nerve. This results in fewer prophylactic tracheostomies, a faster recovery time and return to oral feeding, lower risk of aspiration pneumonia, and a shorter hospital stay [24].

Supraglottic laryngectomy: After the first use of TORS for supra-glottic laryngectomy in a canine model in 2005, this technique has spread widely and has now become a routine therapeutic option for supraglottic cancer [25]. However, supraglottic cancers are rarely diagnosed at an early stage, and surgical exposure is the main limiting factor for their excision by TORS. A recent systematic review by Lechien et al. studied the outcomes of TORS supraglottic laryngectomy in 422 patients. The majority of cases were cT2 (48.6%), followed by cT1 (35.8%) and cT3 (5.1%). Tumors involved the epiglottis, aryepiglottic fold, or false vocal cords in 55.4%, 31.2%, and 5.1% of cases, respectively [26]. Three studies reported conversion to open surgery despite adequate preoperative evaluation of the exposure: 2.1% for Dabas et al., 4.4% for Lallemant et al., and 20% for Ansarin et al. [27][28][29].

Oncological outcomes of TORS supraglottic laryngectomies appear satisfactory, although no randomized controlled study has compared it to open partial laryngectomies or (C)RT to date. All comparisons are retrospective and suffer from a selection bias. In Lechiens's systematic review, the rate of positive margins was 5.4% and ranged from 0% to 40% [29]. In all series from this research, the 2 year local and regional control rates exceeded 94.3% and 87.5% respectively. The 2 year OS ranged between 66.7% and 88.0%, with a distant metastasis rate of about 9%. In the largest series published to date, OS and disease-free survival (DFS) were 86.9% and 95.1% at 2 years, and 78.7% and 94.3% at 5 years, respectively (**Table 1**). Of note, half of them required adjuvant radiotherapy [30].

Postoperative outcomes of TORS supraglottic laryngectomies are favorable. Contrarily to open partial laryngectomy, the rate of tracheotomy is low in TORS supraglottic laryngectomy. In a French series of 84 patients, 24% of patients had a tracheostomy, for a median period of 8 days. Only one patient could not be decannulated during follow-up [31]. Prophylactic tracheostomies were performed to improve the surgical exposure or to secure the airway in case of postoperative edema or bleeding, which peak at 48 h post TORS [32].

Total laryngectomy: Future developments of TORS include total laryngectomy. Its theoretical advantages are the preservation of pre-laryngeal soft tissue and muscle, which could decrease the risk of fistula and avoid the need for flap coverage. Its main drawbacks are the difficult exposure and the extended operative time, estimated around 300 min in the largest series published [33]. Its indications are restricted to situations where a neck dissection is not indicated, i.e., selected cases of salvage laryngectomy for small endolaryngeal tumors, a nonfunctional larynx, or histologies with limited potential for lymphatic spread, e.g., chondrosarcoma and adenoid cystic carcinoma [25]. For all these reasons, only five case series of TORS total laryngectomy have been published until today [33][34][35][36][37].

The latest and largest case series included 10 patients. Excision margins were negative in all cases. Two fistulas (20%) and one minor postoperative hemorrhage occurred. Time to oral feeding resumption ranged from 6 to 24 days [33]. The small size of published cohorts prevents drawing a clear comparison with the standard of care.

## 4. Hypopharyngeal Cancers

Few studies in the literature have reported outcomes of TORS hypopharyngectomy; however, these are promising [38]. The largest study published to date is that of Mazerolle et al., in which 57 patients underwent TORS for T1–T2 pyriform sinus SCC. After 2 years of follow-up, the OS and DFS rates were 84% and 74%, respectively. After 4 years, they were 66% and 50% [39]. Another team reported favorable outcomes of TORS hypopharyngectomy ± adjuvant treatment in 22 patients. Patients started oral feeding on average 7 days postoperatively and were discharged after a median period of 13 days. The 5 year DSS, DFS, and OS were 91.7%, 57.1%, and 53.7%, respectively [40]. TORS with simultaneous neck dissection was performed in 38 patients, in a study by Park et al., where the DFS at 5 years was 100% for early-stage disease and 68.6% for late-stage disease (**Table 1**) [41].

Therefore, TORS shares the survival benefits of surgery over concomitant (C)RT, but with better functional outcomes than open surgery [38]. In the absence of a consensus regarding the treatment of hypopharyngeal SCC, TORS is a viable single modality therapeutic option for selected T1–T2 N0–N1 hypopharyngeal tumors. However, such indications are rare, and difficulties of exposure are frequent; therefore, this approach requires a high experience in TORS. Future developments of flexible single-port robotic systems may extend indications of TORS hypopharyngectomy [42].

**Table 1.** Oncologic outcomes of transoral robotic surgery.

| N (Patients) | Follow-Up | DSS | DFS | OS | Loco-Regional Control | |
|---|---|---|---|---|---|---|
| Oropharyngeal SCC | | | | | | |
| De Almeida (2015) [3] | 410 | 2–3 years | 94.5–92.5% | - | 91–87.1% | 91.8–88.8% |
| Dabas * (2017) [10] | 57 | 29 months | - | 89.6% | 93.8% | 95.8% |

| N (Patients) | Follow-Up | DSS | DFS | OS | Loco-Regional Control | |
|---|---|---|---|---|---|---|
| Nichols ** (2021) [4] | 48 | 2.5 years | 100% | - | 95% | 98% |
| Supraglottic SCC | | | | | | |
| Lechien (2020) *** [27] | 422 | 5 years | - | 94.3% | 78.7–80.2% | 87.7–89.2% |
| Doazan (2018) [31] | 122 | 42.8 months | - | 94.3% | 78.7% | 90.2% |
| Hypopharyngeal SCC | | | | | | |
| Mazerolle (2018) [39] | 57 | 4 years | - | 50% | 66% | - |
| Park (2017) [43] | 38 | 5 years | Stage I/II: 100% | Stage I/II: 100% | - | - |
| | | | Stage III/IV: 74% | Stage III/IV: 68.6% | | |
| Hassid (2020) [42] | 22 | 5 years | - | 57.10% | 53.10% | - |

**Table 2.** ORATOR clinical trial: Long term swallowing outcomes.

| MDADI at 1 Year | MDADI at 2 Years | MDADI at 3 Years | |
|---|---|---|---|
| Radiotherapy | 86.9 ± 11.4 | 86 ± 13.5 | 88.9 ± 11.3 |
| TORS + ND | 80.1 ± 13 | 84.8 ± 12.5 | 83.3 ± 13.9 |
| *p*-value | 0.049 | 0.74 | 0.12 |

MDADI: MD Anderson Dysphagia Inventory.

## 5. Retropharyngeal Neck Dissection

Retropharyngeal lymph nodes are a common metastatic site for some head and neck cancers, and their involvement often leads to the disease being considered unresectable [43]. However, TORS has been used to treat retropharyngeal node metastasis instead of RT or as an adjunct, in order to reduce RT toxicity and to provide a reliable staging that could guide treatment [44][45]. It is especially useful in cancers for which the standard treatment is surgery, e.g., retropharyngeal metastasis of papillary thyroid carcinoma [25][44][45][46]. While the literature about TORS for retropharyngeal node dissection is too scarce to define its potential role and indications, it is clear that TORS can provide adequate access to the retropharyngeal space [46]. The ideal indication may be an isolated retropharyngeal node <3 cm in size [25].

## 6. Parapharyngeal Space Surgery

The parapharyngeal space is a deep space of the face with a complex anatomy. It contains major vasculature which poses a surgical risk. According to tumor characteristics and local extension, the approach can be transoral and/or transparotid–transcervical [47]. TORS can be used for selected well-defined tumors of the parapharyngeal space with oropharyngeal bulge. Surgical exposure depends on mouth opening and tumor extension. Contraindications for TORS are medialization of the internal carotid artery by the mass effect, tumor extension past the stylomandibular ligament, or location less than 1 cm from the skull base.

A significant drawback of TORS is the absence of haptic feedback, which makes it difficult to feel tumor extensions. This is why surgeons often resort to finger palpation in the midst of a TORS. Major vessel injury during a transoral procedure is likely to result in a conversion into open surgery for ligation. Other complications include dehiscence of the pharyngeal incision, nerve injury, or rupture of the tumor [47][48][49]. Of note, capsular breach of salivary gland tumors, possibly due to lack of palpation, has been reported to be higher via TORS than via open approaches [50].

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