

Transoral robotic surgery (TORS) continues to gain momentum in minimally invasive surgery. Not only is TORS potentially curative in many cases, but it also addresses the growing emphasis on functional outcomes and quality of life. The main anatomical areas in which TORS is used are the oropharynx and larynx; however, it is becoming increasingly common in thyroid surgery and neck dissections. With growing popularity, the number of indications for TORS in oropharyngeal and laryngeal cancer also increases. However, not all patients are good candidates for this technique, and thus patient selection is essential, with careful assessment of patient-related factors (e.g. comorbidities and endoscopic access) and disease-related variables, such as tumour location, disease staging, and the involvement of surrounding anatomical structures. The aim of the present article is to briefly review the current and emerging indications for TORS in head and neck cancer and the main factors related to patient selection.

**Key words:** minimally invasive surgery, TORS, robotic surgery, da Vinci robot, patient selection TORS, transoral robotic surgery.

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# Current indications and patient selection for transoral robotic surgery in head and neck cancer – a brief review

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## Introduction

The incidence of head and neck squamous cell carcinoma (HNSCC) is steadily rising, and it is currently the 6<sup>th</sup> most common cancer worldwide [1]. If current patterns continue, the incidence is expected to double by the year 2030 [2]. In recent years, traditional risk factors such as alcohol and tobacco abuse have decreased, and human papillomavirus (HPV)-positive disease is now considered a major driver in the surge in the incidence of oropharyngeal cancer [3]. Some authors have speculated that changes in sexual habits (e.g. oral sex, multiple sexual partners) in recent years may have increased exposure to HPV with the associated cancer risk. Oropharyngeal squamous cell cancer (OPSCC) is linked to a higher incidence, not only in specific geographic areas, but also in a specific demographic group: young Caucasian men (age 40–55 years) with little or no history of alcohol or cigarette use [1, 4].

Traditionally, the management of HNSCC consists of a multimodal treatment approach involving either surgery with possible radiotherapy or definitive chemoradiotherapy (CRT) [5]. However, due to the growing emphasis on functional outcomes and quality of life (QoL), it is now considered essential to take into account both oncological and functional outcomes when making the treatment decision. In this context, interest in minimally invasive surgical approaches such as transoral robotic surgery (TORS) continues to grow.

Transoral robotic surgery has two principal advantages over open surgery. First, it offers excellent three-dimensional visualisation through the use of double endoscopic cameras that allow for angled sightlines that facilitate 2–4-handed surgical resection. Second, TORS gives surgeons a wider range of precise, tremor-free wristed movements, thus allowing navigation through narrow openings and around anatomical structures.

Robotic surgery was first developed in 2005 by Dr. Hockstein, who used this technique to perform a supraglottic partial laryngectomy in a canine model. Two years later, 2007, Weinstein *et al.* reported the results of a study of 27 patients who underwent TORS for radical tonsillectomy. The promising results of that study made it clear that TORS warranted more research and clinical trials. In fact, just 2 years later (2009), TORS was approved by the United States Food and Drug Administration for use in head and neck surgery [6].

In Poland, the first operation using the da Vinci system in the head and neck area was performed in March 2019 by Professor Wojciech Golusiński at the Department of Head and Neck Surgery in the Greater Poland Cancer Centre, at Poznan University of Medical Sciences. Up till now from the years 2019–2022 more than 87 procedures have been performed, the majority of them in the oropharyngeal region.

In most patients with HNSCC, open surgery with concurrent radiotherapy or definitive chemoradiotherapy remains the treatment of choice. This approach has a long history and offers good oncological outcomes. However, a major drawback of this combined approach is the high risk of severe functional morbidity and radiation-induced toxicity, including mucositis, fibrosis, xerostomia, dermatitis, osteoradionecrosis, neutropaenia, and especially dysphagia, which is the most common short- and long-term complication of CRT for OPSCC [2, 7]. Expanding the use of minimally invasive approaches such as TORS has become increasingly urgent due the growing proportion of patients with HPV-positive HNSCC, because these patients are generally younger with a better long-term prognosis than HPV-negative patients. In this patient population, every effort must be made to reduce the risk of treatment-related adverse effects, which is why TORS and other minimally invasive surgical techniques such as transoral laser microsurgery (TLM) play a key role in functional organ preservation surgery [8]. Nevertheless, careful patient selection is essential to properly choose the best candidates for TORS.

Minimally invasive surgery is a rapidly evolving field, and it can be difficult to keep abreast of the changes. In this context, the aim of this article is to provide a brief review of current and emerging indications for TORS in HNSCC, with a focus on patient selection.

## Patient selection

### Patient- and tumour-related considerations

The same principles underly most minimally invasive surgical techniques (including TORS and TLM): to maximise exposure while minimizing surgical morbidity. Consequently, in the decision-making process, it is essential to consider comorbidities that could increase the risk of procedure-related complications and thus negatively impact outcomes. Numerous comorbidities are considered relative or absolute contraindications, including congestive heart failure, chronic obstructive lung disease, immunosuppression, rheumatological connective tissue diseases, and conditions such as poorly controlled diabetes and malnutrition, which increase the risk of uncontrolled bleeding. Some of these comorbidities can be resolved (or their impact can be minimised) prior to surgery, thus allowing the patient to undergo TORS.

Patient evaluation begins with a thorough medical history and physical examination, with a focus on the presence and severity of trismus as well as the mobility of the cervical spine. Cross-sectional imaging is used for staging, to determine resectability, and to rule out involvement of the internal carotid artery. Direct laryngoscopy is performed under general anaesthesia to determine the size of the tumour and whether surgery is contraindicated. Patients are also presented to the multidisciplinary tumour board to determine the optimal therapeutic approach [1]. In properly-selected patients, there is no need to perform tracheotomy, pharyngotomy, and/or formal flap reconstruction<sup>2</sup>. However, adequate operative exposure is essential. Patient selection

requires consideration of the multiple factors needed for proper endoscopic access as described by Rich *et al.* [9], known as the 8Ts: teeth, trismus, transverse dimensions (mandibular), tori, tongue, tilt, treatment (prior radiation), and tumour. Exclusion criteria, include morbid obesity, craniofacial abnormalities, micrognathia, microstomia, and any other factors that would prevent robotic access [2, 7]. Although body mass index (BMI) is often considered a limiting factor, there is no consensus about this criterion; however, some specialists consider BMI  $\geq 40$  to be a relative contraindication [10].

Luginbuhl *et al.* [11] used pre-operative CT imaging to determine the anatomic characteristics needed for sufficient robotic access in base of tongue resections [2]. In that study, the patients were classified as either having “adequate” or “restricted” exposure. The cephalometric measurements obtained with the most statistical significance in patient qualification for TORS were as follows: distance in millimetres from the posterior pharyngeal wall to the hyoid ( $\leq 30$ ) and soft palate ( $\leq 8.1$ ), and the angle between the vertical plain of the larynx and the epiglottis ( $\geq 130^\circ$ ).

Contraindications for TORS can be identified by performing a comprehensive physical examination including a detailed review of the patient’s medical history and pre-operative imaging. However, as robotic techniques and technologies advance, it seems probable that in the near future some anatomic characteristics (e.g. BMI) that are currently considered challenging (or even contraindications for TORS) may no longer be considered problematic.

### Tumour-related considerations in patient selection

While it is important to assess the patient’s suitability for TORS on an individualized basis, it is equally vital to evaluate the tumour characteristics, particularly the location and involvement of the surrounding anatomical structures. The surgeon should determine whether negative margins are feasible and, if so, the extent of the resection necessary. A wide range of exclusion criteria for TORS have been proposed [3, 6, 12–15]. Although there are some differences between these proposals, most share many of the same exclusion criteria, such as involvement of the deep tongue musculature, greater vessels, and/or prevertebral fascia [1, 7] (Table 1).

Patients who meet all eligibility criteria for TORS are likely to obtain substantial benefits from this minimally invasive procedure compared to more invasive procedures. Nevertheless, the surgeon must always keep in mind the importance of functional outcomes and the risks of surgical morbidity. Because TORS is increasingly accepted as an alternative to other surgical approaches, the number of current and emerging indications for this technique in head and neck surgery continues to grow. At present, the main tumour sites for TORS are the oropharynx, larynx, thyroid, and lymph nodes of the neck (Table 2). Below we describe the role of TORS in those localisations.

## Oropharyngeal cancer

The tumour type with the strongest evidence base and longest history for TORS is oropharyngeal cancer, particularly early-stage OPSCC. Several studies have shown favourable oncological outcomes with TORS. For instance, Baskin *et al.* reviewed 410 patients who underwent TORS, most of whom (83.5%) were stage T1–T2, N0–N1. In that study, the 3-year overall survival and disease-specific survival rates were 87.1% and 94.5%, respectively [2], results that are equivalent to or better than definitive radiotherapy.

The inclusion of TORS in multimodality therapy for stage T3–T4, N2–N3 OPSCC has been shown to improve survival rates [2]. In these cases, TORS is the first-line treatment followed by concurrent CRT. The key advantage of this approach is that resection of the primary tumour without opening the neck greatly reduces the risk of tumour seeding. In addition, by reducing the size of the primary tumour, the radiation dose to the surrounding constrictor muscles is reduced, which in turn decreases the risk of late swallowing complications [16]. Initially, the main indication for TORS was early-stage OPSCC; however, in recent years, the number of indications has grown to include late-stage disease, partially due to the growing focus on organ preservation and QoL.

In patients with tonsillar carcinoma, imaging plays a key role in selecting eligible candidates for TORS and/or in ruling out nonoperative patients. For example, patients with tumours limited to the tonsillar fossa that have not spread to surrounding structures would make excellent candidates for TORS. The post-styloid parapharyngeal area is surgically equivalent to the “carotid space”, which includes the internal carotid artery, internal jugular vein, and cranial nerves 9–11 [5]. Cancer invasion in this region is an important finding in evaluating TORS eligibility, mainly due to the difficulty of achieving clear margins with a transoral approach, which means pre-styloid parapharyngeal space involvement is a relative contraindication [17]. Transoral robotic surgery may also be ineffective if the tumour has spread into the nasopharynx due to difficulties in surgical access to the nasopharyngeal component for excision. Another relative contraindication is medialization of the carotids, a known anatomic variation [5]. A patient with a medialized internal carotid artery would be at higher risk of vascular damage during pharyngeal excision. Finally, determining the extent of soft palate involvement is critical because a large soft palate resection may result in a significant functional deficit with associated velopharyngeal insufficiency, negating the potential functional benefits of an upfront surgical approach and necessitating more complex microvascular reconstructive methods to reduce the risk of downstream functional deficit.

In tongue-base carcinomas, the findings of imaging scans are crucial. Invasion of the hyoglossus muscle or extension into the neck are absolute contraindications for TORS in this tumour type, mainly because an open

**Table 1.** Reasons to exclude transoral robotic surgery as a treatment option

| Author                         | Exclusion criteria  |
|--------------------------------|---|
| Weinstein <i>et al.</i> , 2007 | <ul style="list-style-type: none"> <li>• Unresectability of involved neck nodes</li> <li>• Mandibular invasion</li> <li>• Tongue base involvement requiring resection of more than 50% of the tongue base</li> <li>• Pharyngeal wall involvement necessitating resection of more than 50% of the posterior pharyngeal wall</li> <li>• Radiologic confirmation of carotid artery involvement</li> <li>• Fixation of tumour to the prevertebral fascia</li> </ul> |
| Cohen <i>et al.</i> , 2011     | <ul style="list-style-type: none"> <li>• Inferior vena cava lesion</li> <li>• AJCC stage T4b lesion</li> <li>• Oropharyngeal lesion extending to the midline of the posterior pharyngeal wall</li> <li>• Deep tongue musculature involvement greater than 50%</li> <li>• Prevertebral muscle involvement</li> <li>• Unresectable nodal metastasis</li> </ul>  |
| Moore <i>et al.</i> , 2012     | <ul style="list-style-type: none"> <li>• Poor exposure</li> <li>• Submucosal tumour</li> <li>• Mandible or hyoid involvement</li> <li>• Extension into the deep tongue musculature, mandible, hyoid, skull base, prevertebral fascia, or pterygoid musculature</li> <li>• Extensive involvement of the great vessels</li> <li>• Lateral extension into the soft tissues of the neck</li> </ul>  |
| Park <i>et al.</i> , 2012      | <ul style="list-style-type: none"> <li>• Small retrognathic mandible or poor mouth opening</li> <li>• Involvement of thyroid cartilage or prevertebral fascia</li> <li>• Unresectable nodal disease (e.g., carotid artery invasion)</li> </ul>  |
| White <i>et al.</i> , 2013     | <ul style="list-style-type: none"> <li>• Lesion with bone involvement that may require free-flap reconstruction</li> <li>• Significant trismus (mouth opening &lt; 1.5 cm)</li> </ul>   |

**Table 2.** Tumour sites for transoral robotic surgery

| Anatomic site                                | Indication   |
|--|--|
| Oropharynx                                   | Benign tumours<br>Selected T1–T2, T3, T4a carcinomas |
| Larynx/hypopharynx                           | Benign tumours<br>Selected T1, T2 and T3 carcinomas  |
| Parapharyngeal space/<br>infratemporal fossa | Benign tumours                                       |
| Nasopharynx                                  | Early recurrent T1–T2 carcinomas                     |

technique is better suited to locating and preserving the continuity of the hypoglossal nerve. Given the proximity of this nerve to the lingual artery, extensive invasion of the genioglossus is a relative contraindication [18]. Furthermore, this type of invasion would require a near total or total glossectomy, which could result in post-operative dysphagia or aspiration, thus making TORS contraindicated in these cases [19]. Another contraindication is any cancer that invades and undercuts the tongue because this cannot be resected with TORS due to the risk of tongue devascularization. The best

imaging approach to detect this type of invasion is sagittal magnetic resonance imaging.

### Laryngeal cancer

As robotic surgery has continued to progress, TORS is now routinely used in the treatment of laryngeal cancer, mainly for supraglottic lesions. Despite the relatively good accessibility of laryngeal tumours, it can be difficult to manoeuvre the surgical instruments due to anatomic restrictions. Consequently, when determining whether a patient is eligible for transoral robotic supraglottic laryngectomy (TORS-SGL), it is crucial to ensure the feasibility of achieving complete oncological resection with preservation of the neurophysiological functions (protective, respiratory, and phonatory functions). For this reason, the main indications for TORS in these cases are selected stage T1, T2, and T3 tumours. However, these tumours must be carefully assessed based on their specific local extension. The extent of the resection will largely depend on the presence or absence of local invasion of the lateral pharynx and vallecula [20]. Absolute contraindications for TORS-SGL include the following: inadequate transoral exposure; compromised arytenoid or vocal cord mobility; invasion of the paraglottic space, thyroid, or cricoid cartilage; invasion of the posterior commissure; and involvement of > 2 cm of the base of the tongue mucosa or involvement of the tongue base muscles [20]. To date, TORS total laryngectomy (TORS-TL) has only been performed in only a few exceptional cases at a limited number of specialised centres. In most cases, bilateral neck dissection is also required, which is why the open surgical approach is usually necessary. However, experienced surgeons who perform TORS-TL suggest that there are 3 clinical scenarios in which neck dissection can be obviated. First, salvage surgery after radiotherapy or CRT to treat a locally recurrent primary tumour in which salvage partial laryngectomy is contraindicated. A second indication would be rare cases involving a benign or malignant tumour of the larynx presenting only limited local spread that does not require extensive perilaryngeal dissection. This would include, for example, patients presenting with low-grade chondrosarcoma, chondroma, or adenoid cystic carcinoma. A third indication for TORS-TL would be the treatment of patients with long-term tracheotomy, refractory laryngeal dysfunction, and those on enteral feeding. This clinical scenario can occur in patients with neurodegenerative disorders or high-grade sequelae from laryngeal trauma who have undergone multiple surgical interventions with no benefit, and in patients with severe chronic post-radiotherapy toxicity. In all cases, patient selection must be done with extreme caution given that the associated pharyngeal dysfunction would not improve without mucosa repair with a flap.

### Thyroid cancer

Open thyroidectomy is the standard of care for thyroid cancer, but it leaves significant and highly visible scarring

on the neck. Several TORS techniques have been developed to reduce scarring, using a different route of access in a less visible location (e.g. axilla, breast, or post-auricular area); nevertheless, all these techniques leave a small but visible scar [21]. For this reason, the transoral endoscopic thyroidectomy vestibular approach (TOETVA), which leaves no visible scars, is becoming increasingly popular. In addition, this approach also makes total thyroidectomy easier due to its midline access to both lobes [22]. Nonetheless, candidates must meet strict eligibility criteria for TOETVA, including preoperative ultrasound of the thyroid gland and cytological testing. Eligibility criteria are as follows: thyroid diameter  $\leq 10$  cm and volume  $\leq 45$  ml; size of primary nodule  $\leq 50$  mm; and presence of a benign tumour (e.g. follicular neoplasm, thyroid cyst, or goitre) or papillary microcarcinoma without metastasis [23]. Exclusion criteria for this technique include recurrent laryngeal nerve palsy; biochemical signs of hyperthyroidism; oral abscess; previous head or neck radiation therapy; poorly or undifferentiated cancer; substernal and retropharyngeal goitres; and/or N1b differentiated thyroid cancer [22, 23]. A study performed in 2015 involving 200 patients who underwent TOETVA reported the following adverse effects: temporary hoarseness ( $n = 8$ , 2.6%), temporary hypoparathyroidism ( $n = 35$ ; 17.5%), seroma formation ( $n = 10$ ; 5%), subcutaneous emphysema ( $n = 7$ ; 3.5%), and postoperative haematoma ( $n = 1$ ) [21]. No long-term complications were seen. Importantly, this technique can cause nerve damage that is rare or non-existent with conventional thyroid surgery. The robotic transaxillary technique has been associated with transient brachial plexus damage, although this risk can be mitigated with correct arm posture [22, 24]. Furthermore, in the postauricular facelift method, the marginal branch of the facial nerve and the great auricular nerve can be damaged, probably due to nerve compression by a robotic device in the small working space. Injuries to the mental nerves can also occur when using the transoral approach [22, 25, 26]. Thyroid surgery is evolving, and it is clear that TOETVA is possible in selected cases, offering excellent medical and cosmetic results.

### Neck dissection

Retropharyngeal metastasis in patients with head and neck cancer is mainly treated with radiotherapy due to its complex anatomic location (making these less ideal TORS candidates), which makes it difficult to treat with conventional surgical methods [27]. The boundaries of the retropharyngeal space include the skull base superiorly, carotid sheath laterally, prevertebral fascia posteriorly, and pharynx anteriorly [27]. Inferiorly, this space is continuous with the posterior mediastinum [27]. Classically, nodal metastasis in this area comes from advanced T-stage head and neck cancers and thyroid cancer [28, 29]. Thus, the presence of metastatic spread in this area is recognized as an important prognostic factor that may affect overall survival [29]. With the introduction of TORS, retropharyngeal lymphadenectomy is now possible, and dissection of the metastatic lymph nodes could play a key role in increasing survival rates [29].

Involvement of the vascular space and/or carotid involvement and deep lymph nodes are 2 unequivocal contraindications for TORS (as well as conventional surgery). Extranodal extension has been associated with a lower likelihood of recurrence-free survival [30]. Patients without suspected nodal involvement on radiographs and a solitary node < 3 cm would be suitable candidates for TORS. In these patients, if no additional pathologic features are present, surgery alone could be used to treat the neck disease. Adjuvant therapy is almost always required in patients with multiple metastatic nodes. Patients with extranodal extension or a large number of affected nodes require adjuvant chemotherapy. Published data on TORS in neck dissection are limited, and more studies are needed to better assess the safety and effectiveness of transoral robotic retropharyngeal node dissection.

### Future directions – clinical trials

Patients who have HPV-positive illness have a substantially better prognosis with conventional therapies and may be suitable candidates for treatment de-intensification because HPV-positive disease is more responsive to chemotherapy and radiation than HPV-negative cancer. There are also several ongoing clinical trials that are investigating various treatment de-intensification strategies, such as the use of minimally invasive surgery followed by lower doses of adjuvant therapy (chemotherapy and/or radiotherapy), to see if adjuvant treatment can de-escalate based on the pathologic findings of surgery. These trials aim to help reduce toxicity levels while maintaining high rates of cure.

The ECOG 3311 is a phase II trial (NCT01898494) involving 519 patients with stage III/IV HPV-positive OPSCC treated by transoral surgery and neck dissection. This deintensification trial's objective is to ascertain whether the same results can be obtained with a lower dosage of postoperative radiation. Current results show that primary TOS and reduced PORT retained outstanding oncologic outcomes at 35-month follow-up, with favourable QOL and functional outcomes, in intermediate-risk HPV + OPC [31].

The ORATOR study (The Oropharynx: Radiotherapy vs. Trans-Oral Robotic Surgery) (NCT01590355), which compares QoL and survival results in OPSCC treated with either primary radiation or TORS, is a single-institution trial. The ORATOR findings do not clearly identify the best treatment. Instead, these findings offer crucial contextual information to aid doctors and patients in picking the best treatment approach in a tailored way based on patient and disease characteristics, available technology, and institutional experience [32].

The PATHOS (Post-operative Adjuvant Treatment for HPV Positive Tumours) study (NCT02215265) includes patients with HPV-positive malignancy (T1–3, N0–2b), who are undergoing transoral surgery and neck dissection. The purpose of the study is to locate patients in whom transoral surgery-related adjuvant treatment can be reduced. According to their pathologic results, patients are divided into 3 groups and given either

50 or 60 Gy of adjuvant radiation with or without chemotherapy [33].

### Conclusions

Transoral robotic surgery plays an important and growing role, together with other minimally invasive surgical techniques, in the treatment of head and neck cancer, typically as a part of the multimodal approach for these cancers. One of the main advantages of TORS over open surgery is that it provides better functional and QoL outcomes. Nonetheless, patient selection is crucial. As this review shows, there are many current and emerging indications for TORS. As more long-term data on safety and oncological outcomes become available, and as more advanced robotic instruments are developed, the indications for TORS.

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