Transoral treatment strategies for head and neck tumors

Abstract

The introduction of transoral endoscopic surgery has initiated a fundamental change in the treatment of head and neck cancer. The endoscopic approach minimizes the intraoperative trauma. Due to the lower burden for the patient and the savings potential these methods have gained wide acceptance. These transoral accesses routes allow experienced surgeons to reduce the morbidity of surgical resection with no deterioration of oncologic results. This suggests a further extension of the indication spectrum and a high growth potential for these techniques and equipment in the coming years. For selected patients with selected tumors the minimally invasive transoral surgery offers improved oncological and functional results. In the present paper, different surgical access routes are presented and their indications discussed.

Keywords: transoral surgery, endoscopy, laser, minimally invasive surgical indications, limits

1 Introduction

In the “conventional” open transcervical surgical resection of lesions or tumors of the upper aerodigestive tract visible mutilation often occur with unfavorable aesthetic and functional results, in particular, failures to swallowing, breathing and voice disorders. Non-surgical treatment options such as radiotherapy (RT) with or without chemotherapy respective immunotherapy (RCT) are therefore considered as treatment alternatives with less morbidity. The statement by Posner: “For advanced resectable tumors of the larynx, hypopharynx and oropharynx, surgery has taken a back seat to organ-preserving strategies that retain speech and swallowing. Chemoradiotherapy therapy is now standard of care for such cases”, points to this direction, although the RCT is fraught with a high rate of acute and long-term toxicity [1].

Due to reduced morbidity, while maintaining function and lack of toxicity transoral minimally invasive surgery is of growing importance in selected cases as an alternative to primary and onerous RCT. Correspondingly, minimally invasive transoral endoscopic surgery has become more important over the last three decades and replaces many conventional surgical procedures. Miniaturization and adaptation of instruments, endoscopes and microscopes as well as the development of the laser have taken place in recent years and optimized surgical techniques. Transoral minimally invasive, microsurgical resections are now part of a general trend, which is also observed in other surgical disciplines and leads to more individualized tumor therapy. Patient and tumor selection as well as the experience of the surgeon are of crucial importance to improve oncological and functional results.

The transoral access routes take advantage of the natural body openings to the larynx, hypo- and oropharynx, thyroid, parapharyngeal space, clivus and retropharyngeal space. Depending on the anatomical location endoscopes enlarge the point of view and microscopes improve the differentiation of the tissue. Special instruments ensure or improve access to the various regions in the neck. Laser, Coblation, HF as well as robots are used to facilitate the resection and hemostasis. By maintaining the regular anatomical structures of the neck functional integrity of the upper aerodigestive tract is improved and postoperative morbidity and hospitalization are reduced. On the other hand a reduced overview of the surgical field, a resection, which is often left to spontaneous prolonged wound healing, extended operation time and the difficult access as well as threatening complications such as severe bleeding in the surgical area are perceived as a disadvantage of the method. Knowledge of transcervical surgery to control these complications is still indispensable.

The aim of the present paper is to present today’s technical possibilities of transoral endoscopic therapy and to discuss the literature regarding the application and its results.

2 Transoral endoscopic surgery (TES)

2.1 Historical development

At the beginning of the 19th century Bozzini described a “Lichtleiter” that could be used to look into body cavities through a body orifice by means of which he developed the first endoscope. His report on this new tool created a big sensation. Bozzini described additionally in his publications the possibility to perform operations inside the body by using this special light guide. In spite of all the criticism he was object of, Bozzini was able to start an international dis-
cussion and an assembly of a great number of physicians to study and evaluate his idea, although the development stage of his endoscope was still somehow inadequate [2], [3]. Following the first direct laryngoscopy was performed by Horace Green, who removed a vocal fold polyp under sunlight [4]. The endoscopic removal of a vocal fold carcinoma was performed in the 19th century by Elsberg and Fränkel in 1886 and by Schnitzler in 1888 by indirect laryngoscopy [5]. In 1895 Alfred Kirstein performed the first transoral resection of a vocal fold carcinoma by means of the laryngoscope he himself had developed and that allowed a direct insight on the larynx [6], [7], [8].

Killian then developed the direct laryngoscopy to be used on a bent head offering bimanual treatment of laryngeal structures in 1912. Further on Hasslinger developed a special designed distending laryngoscope and Seiffert the chest support for improved exposure of the larynx in 1922 [9], [10]. In 1915 Lynch described the direct removal of a small vocal fold carcinoma by a modified version of Killian’s laryngoscope. He supported the unquestionable demand to master the transcervical and transoral resection techniques in order to be able to choose the best possible treatment option for each patient [11].

Kleinsasser developed microlaryngoscopy (MLS) under general anesthesia using a surgical microscope with a 400 mm lens and specialized microsurgical instruments. Till today his technique is the worldwide standard method for diagnosis and therapy of laryngeal lesions [12].

After initial criticism and skepticism concerning the oncological safety of a radical removal of malignant tumors transoral microlaryngoscopic resection of small larynx carcinomas prevailed and was further supported by the introduction of the laser as a cutting instrument in the 70s [13].

The application of the laser led to the rapid development of the TES in the entire upper aerodigestive tract. Grossenbacher, Rudert and Steiner expanded the indications for transoral laser surgery in head and neck region and developed this technique much further. They showed that transoral laser assisted surgery had benefits in terms of hemostasis and accuracy of tissue resection and that this approach was suitable to remove larger tumors in the larynx and hypopharynx with preservation of laryngeal neck dissection.

TES is now a widely used method for the treatment of small and medium-sized tumors of the larynx, hypopharynx, and oropharynx [18], [19], [20], [21], [22], [23].

A prerequisite for TES is a sufficient endoscopic exposure and limited depth of infiltration of the tumor. The experienced surgeon can see tumor margins during microscopic controlled resection and evaluates surgical margins by frozen section analysis. Glanz et al. and Steiner et al. showed that comparable results can be achieved by TES and conventional transcervical surgery [22], [23].

Due to the development of distending laryngoscopes and the resulting improved exposure of hypo- and oropharyngeal lesions, the indication for TES of tumors in these regions has been expanded (Figure 1). Good oncologic results prompted some authors to resect even larger tumors.

Figure 1: Different distendable laryngoscopes and surgical instruments for TES

Because of good tolerability and low rate of complications, TES was applied in older, multi-morbid patients who would not tolerate transcervical surgery or had a RT as the only therapeutic option.

2.2 Preoperative preparation – panendoscopy – evaluation of patients – selection of tumors

TES of laryngeal, hypopharyngeal, and oropharyngeal tumors requires careful preoperative evaluation and preparation of the patient. All available diagnostic options should be applied to obtain an accurate picture of the superficial and deep extension of the lesion. Furthermore, the lymph node status is evaluated before the most appropriate therapy, particularly the TES in combination with single-stage or two-stage neck dissection, can be planned. Nakayama detected an endoscopic underestimation in laryngeal cancer between 40–55% [24]. This may lead to an incorrect planning of the therapeutic approach as

Figure 1: Different distendable laryngoscopes and surgical instruments for TES
well as a poorer locoregional control. Computed tomography is the procedure of choice in the radiologic evaluation of tumors in the head and neck region. Only in cases of possible involvement of the paraglottic space and arrosion of the thyroid cartilage additional MR imaging is required in laryngeal and hypopharyngeal tumors [25]. Panendoscopy, the gold standard, should always be performed under general anesthesia and pre-therapeutic. The use of rigid and flexible endoscopes allows a precise tumor assessment in most cases (Figure 2). To optimize the diagnostic process endoscopic imaging techniques, e.g., fluorescence endoscopy, narrow band imaging, optical coherence tomography, etc., can be applied [26]. As an alternative to CT and MRI, high frequency endoluminal ultrasound can also be used during panendoscopy, offering at least an equivalent picture quality to one of the conventional methods [27].

The integration of endoscopic findings and radiological imaging in treatment planning is necessary to assess the tumor correctly.

The goal of panendoscopy is to perform an accurate assessment of the primary and exploration for the presence of possible secondary tumors. Panosetti et al. describe an incidence of second cancers of 9.4% [28]. Furthermore, the exposure of the tumor and the possibility to get a sufficient view on the surgical field during TES is clarified, since this is of vital importance to the selection of patients for transoral resection. One advantage of panendoscopy is that diagnosis and treatment can be performed in a single stage procedure under general anesthesia. During the same session, if not done during a previous ambulatory consultation, biopsies can be taken for precise pretherapeutic histological work-up or an immediate transoral endoscopic resection after previous frozen section analysis can be performed.

In multi-morbid patients at high risk of anesthesia, the indications for panendoscopy respectively transoral resection of the tumor have to be critically reviewed.

Transoral treatment strategies

2.3 Larynx

Glottic carcinomas

In the larynx vocal fold carcinomas were first treated by using an transoral access. The combination of transoral endoscopic access path with microscopic oversight led to the development of MLS [12]. This method is still the standard procedure for diagnosis and treatment of benign lesions, benign pseudo-tumors and malignancies.

Using the laser, TES has been increasingly applied in the treatment of early and middle staged tumors of the larynx (T1, T2 and selected T3). This form of treatment has been validated in numerous retrospective and prospective studies. The results of local tumor control of transoral resection of these tumors are comparable with the results of open surgery and radiation therapy, if not even superior.

The recurrence-free survival rate of 230 patients treated at Gießen University with a transoral resection of unilateral carcinoma in situ and pT1a–pT3 vocal fold carcinoma amounted to 96%, none of the patients lost the larynx, only one patient died as a result of mediastinal metastases from irradiated recurrence. In a recent retrospective study by Iro et al., the disease-specific survival after transoral resection of vocal cord carcinoma was 95% [29]. A meta-analysis of 2,436 transoral endoscopically treated T1–T2 vocal fold carcinomas shows a 5-year overall survival (OS) of 82%, a disease-specific survival (DSS) of 96% and local tumor control rate of 89% (Table 1). The advantages of transoral endoscopic in contrast to open transcervical resection consist primarily in a lower intra- and postoperative morbidity. Above all, no tracheotomy is required; dysphagia and aspiration are rarely observed [30], [31], [32], [33], [34], [35], [36], [37], [38], [39], [40].

Dysplastic lesions or pT1a-vocal fold carcinomas should always be resected in one stage procedure during microlaryngoscopy or panendoscopy.

Preoperative stroboscopy for the diagnosis of phonatory movement helps to differentiate between dysplasia and microinvasive cancer [41], [42]. However, the evidence of the mucosal wave only excludes the infiltration of the vocal ligament. Rigid and flexible endoscopes in different angles allow an improved evaluation of the subglottic space or the ventricle. In addition, by the use of fluorescence endoscopy and/or narrow band imaging a more precise delimitation of a precancerous lesion or early carcinoma in contrast to healthy tissue can be performed and the area of resection can be more precisely determined [26], [27], [42].

Intraoperative palpation and hydrodissection are also helpful in assessing whether or not there is an infiltration [43]. For all minimally invasive approaches, access to special instruments and a thorough training and experience of the surgeon is required. Patient and tumor selection is of utmost importance. The exposure of the larynx,
the full clarity of the tumor site and the right tools are essential to the application of TES.

Biopsies in dysplasia, carcinoma in situ and early vocal fold carcinoma should be avoided, since postoperative inflammation with subsequent induration can be caused at the biopsy site and may result in a misinterpretation during cordectomy.

TES has a significantly lower morbidity in contrast to the open transcervical technique [29], [30], [44]. Transcervical technique should be performed for functional reasons only in combination with immediate intraoperative reconstruction, tracheotomy is mandatory [45]. In transoral cordectomy type II and III vocal fold augmentation can be achieved by fat injection during the same intervention [46]. Therefore transcervical resection may be performed in tumors leaving large defects that cannot be augmented by fat injection and require reconstruction. TES can also be performed several times as control microlaryngoscopy including resections without significant increase in morbidity [47], [48]. In contrast to the transcervical resections with glottic reconstruction recurrences are much easier to recognize. Due to cost effectiveness and very good results surgical treatment of early glottic cancer is the treatment of choice (Figure 3).

**Table 1: Meta-analysis T1–T2 vocal fold carcinoma (TES)**

| Study            | n  | OS (%) | DSS (%) | LC (%) |
|------------------|----|--------|---------|--------|
| Iro et al. (2011)| 557| 78     | 95      | 91     |
| Rödel et al. (2008)| 444| 83     | 98      | 82     |
| Motta et al. (2005)| 668| 89     | 93      | 90     |
| Peretti et al. (2009)| 513| 83     | 99      | 93     |
| Eckel et al. (2000)| 254| 70     | 98      | 85     |
| **Total**        | 2,436| 82   | 96      | 88     |

Supraglottic laryngeal cancer

Compared to glottic carcinomas supraglottic carcinomas are usually much further progressed when patients come for treatment, since these tumors grow relatively hidden and cause late onset of symptoms. Mostly, they have already attained a considerable size and are metastasized to regional lymph nodes. Therefore, it is necessary to perform larger resections of these tumors. Regional metastases should be included in the therapeutic strategy. Additionally, functional aspects should play an important role in decision making, e.g. to avoid permanent aspiration.

Transoral endoscopic resection of supraglottic tumors have almost completely replaced transcervical partial resection described by Alonso. This does not apply to the subtotal laryngectomy by Pearson and Moszolewski or Cricohyoidoepiglottopexie that can also be applied to T4 supraglottic carcinomas.

Transoral partial resections respect the position of the larynx in the neck, and swallowing is mostly not impaired. The epiglottis is replaced by the base of the tongue regarding the covering function of the laryngeal entrance.
In comparison to transcervical approaches conservation of at least one superior laryngeal nerve is obtained to a higher degree. This guarantees at least a partial preservation of sensation. Additionally, only in rare cases endoscopic resection of supraglottic tumors requires a tracheotomy.

In the area of the suprahypopharyngeal epiglottis and vestibular folds transcervical endoscopic resection can be performed in comfortable safety margins. The exposition succeeds to a great extent. In contrast, the depth of infiltration in the infrapharyngeal petiolus region may be difficult to assess. A T1 petiolus carcinoma can easily progress to a T3 stage tumor. Therefore, the exposure to the supraglottic structures for complete endoscopic resection is of vital importance.

If the paraglottic space at the glottic level is not too severely affected, the glottic sphincter can be preserved. Resections going deep down to the vocal fold creating a glottic insufficiency and deterioration of voice quality. Extensive resections involving the arytenoids can lead to a sustained aspiration.

Recent publications have shown that in comparison to laryngectomy the application of partial resection in early supraglottic laryngeal cancer can achieve similar control rates [52]. A meta-analysis of 303 transoral endoscopically treated T1–T2 supraglottic carcinomas shows a 5-year overall survival (OS) of 70%, a disease-specific survival (DSS) of 82% and local tumor control (LC) of 90% (Table 2) [29], [53], [54], [55], [56]. Functional results of TES were superior to transcervical resections [57], [58]. Although the use of TES for advanced laryngeal cancer is controversially assessed, several working groups report similar results compared to open surgery or non-surgical treatment strategies [59], [60]. These studies support further investigation into the use of TES in advanced laryngeal cancer.

Considering TES results functional outcome focusses primarily on breathing and swallowing. Initially postoperative voice quality is of secondary importance, but does have a significant impact on life quality of patients. Despite good voice quality a latent aspiration, due to reduced sensitive vigilance and reduced neuronal function of the upper esophageal sphincter may restrict quality of life significantly secondary to recurrent pneumonia in elderly patients (>70 years) on the one hand. On the other hand, in multi-morbid patients a tumor can be resected without major burden for the patient by a one-stage transoral resection. Accordingly, not only the extent of the tumor but the overall situation of the patient has to be critically taken into account when partial laryngeal resection is considered a treatment option [61].

### 2.4 Hypopharynx

Hypopharyngeal cancers have the poorest prognosis among head and neck malignancies. In 1987 Steiner and Herbst for the first time presented a study with 36 transoral resections of hypopharyngeal carcinomas [62]. The oncological results in hypopharyngeal cancer depend more on the control of regional metastases and cancerous cervical soft tissue involvement than the tumor resection itself. Therefore radical surgical approaches not automatically do lead to improved survival [63]. The majority of patients require a neck dissection and postoperative radiotherapy and/or radio-chemotherapy, i.e. a maximum tumor therapy. Most hypopharyngeal tumors are located in the piriform sinus. They are extremely rare in the postcricoid region, but relatively rare on the posterior wall of the piriform sinus. Therefore latter regions are mentioned briefly. They are only suitable for a transoral endoscopic approach if a sufficient exposure is possible and the tumor growth superficially. Both regions can be involved in cancers of the piriform sinus.

The most important criterion for the selection of hypopharyngeal tumors for transoral resection with preservation of the larynx is the lack of evidence for a deep infiltration. Favorable for a TES is a location of the tumor in the upper level of the piriform sinus (Figure 4, Figure 5). The tumor must be easy to expose with distending laryngoscopes and relocatable against the underlying tissue, i.e. against the lateral and medial wall of piriform sinus (thyroid cartilage, hyoid bone, thyreohyoidal ligament, abductor muscles and cricoid). The ventricular fold should be both, soft and not too arched forward, because this may be related to an infiltration of the upper lateral paraglottic space. Furthermore, the vocal folds should be soft to palpation, not infiltrated and clinically free moving. This means the lower paraglottic space is not affected by the tumor. The arytenoids should be actively and passively free to move. Overall, the apex of the piriform sinus is visible and not exceeded. It is important that the esophagus is free and the whole circumference of the hypopharynx does not have to be resected completely. Otherwise stenosis may develop which is extremely difficult to master.

| Table 2: Meta-analysis T1–T2 supraglottic carcinoma (TES ± RT/RCT) |
|-----------------|-------|-------|-------|-------|
|                 | n     | OS (%) | DSS (%) | LC (%) |
| Ambrosch et al. (1998) | 48    | 76     | 83     | 97     |
| Eckel et al. (1997)   | 46    | 59     | 72     | 90     |
| Iro et al. (2011)     | 137   | 60     | 82     | 91     |
| Rudert et al. (1999)  | 17    | 77     | 80     | 82     |
| Csanády et al. (2011) | 55    | 98     | 91     | 84     |
| Total              | 303   | 70     | 82     | 90     |
What applies to the piriform sinus is also true for rare tumors of the postcricoid region which are especially difficult to expose. Tumors of the posterior wall of the hypopharynx should not invade the anterior longitudinal ligament, i.e. not be fixed to the cervical spine. The superior laryngeal artery and nerve as well as the thyrohyoidal ligament should be free of tumor, otherwise a cervical soft tissue involvement has to be expected and a sufficiently radical resection is no longer guaranteed, especially in the usually performed subsequent neck dissection. The tumor should grow more exophytic and not ulcerate nor undermine the edges. This kind of tumor growth is predominantly found in tumors of the apex of the piriform sinus. Due to the anatomically constricted area, these tumors grow early in the cartilaginous-bony skeleton of the larynx [64].

At diagnosis most patients show an advanced tumor stage. 70–85% of patients present with stage III or IV [65], [66], [67], [68], [69], [70], [71]. The oncological results of experienced surgeons in TES of selected hypopharyngeal carcinomas are comparable to those of open techniques. They present a high degree of local control and organ preservation (90%), a 60% disease-specific survival rate and a 5-year overall survival rate of 50–70% for stages I–II and 40–50% for stages III–IV [72], [73]. Primary polychemo-radiotherapy is applied especially to advanced, but also to smaller tumors [74]. Studies in recent years show very good oncological and functional results for transoral endoscopic treatment of early hypopharyngeal carcinomas [75], [76]. They indicate a disease-specific survival of 68.9% and highlight the need to complete tumor resection and the benefits of adjuvant therapy. A meta-analysis of 292 transoral endoscopically treated T1–T2 hypopharyngeal cancers show a 5-year overall survival (OS) of 59%, a disease-specific survival (DSS) of 77% and local tumor control rate of 80% (Table 3) [20], [29], [77], [78], [79], [80], [81].

Clinically or histologically proven metastases are no contraindication for transoral resection of hypopharyngeal tumors. They do not affect the incidence of local recurrence in the larynx, but a potential tumor recurrence in the soft tissues of neck or distant metastases may develop in the course of time. Even with extensive metastasis to the deep supraclavicular, paratracheal and parajugular lymph nodes as well as extranodal tumor growth the respective primary tumor, which meets the above mentioned selection criteria, can be excised transorally and the larynx can be preserved. In these cases, the fate of the patients will be determined by metastatic recurrences and not by the threat of local recurrence in the preserved larynx. The quality of life of these patients with a very poor prognosis is significantly improved by the preservation of the larynx till the end of their life. Preservation of the larynx does not mean an additional risk to the patient’s already threatened life [82].

Only in extensive transoral endoscopic resections of hypopharyngeal cancer postoperative dysphagia can be observed leading to the placement of a nasogastric tube or in some cases to the installation of a PEG. Steiner et al. reported about 27% of patients being able to be feed via naturales on the first postoperative day. In the same study, the feeding tube was removed after nine days on average [18].

Tracheotomy is usually not necessary as long as the resection does not include extended supraglottic areas or aspiration as well as severe swelling is not to be expected. In supraglottic or hypopharyngeal resections phonation is usually not affected because of the preserved neurovascular supply and the intact glottic sphincter. Only if the resection includes the posterior half of the medial wall of the piriform sinus, vocal problems may occur secondary to the involvement of the arytenoid or the posterior cricoarytenoid. Furthermore, the inferior laryngeal nerve can be injured when penetrating to the posterior paraglottic space during transoral endoscopic resection [25]. Postoperative scarring and fixation of the piriform sinus rarely affect voice quality.

2.5 Oropharynx

Similar to the treatment of laryngeal and hypopharyngeal carcinoma transoral access with endoscopic-microscopic resection of oropharyngeal tumors is an elegant and
conserving treatment method. Tumor selection, surgical experience and patient selection are primary considerations. Regardless of tumor stage and location recommended resection margins should amount to 1 cm. Defects at T1–T2 oropharyngeal carcinomas usually heal without major reconstruction. Larger defects in the area of the soft palate caused by TES may lead to a velum insufficiency. In these cases, the resulting defect may be covered by a free radial forearm flap in order to restore function. Tumors of the posterior wall of the oropharynx are well suited for transoral endoscopic resection. Furthermore, small tumors of the lateral oropharyngeal wall are easy to expose and resect by a transoral endoscopic approach. The surgeon should be aware of the proximity to large vessels. The lateral towards the tonsil running vessels are the palatinal, ascending pharyngeal and lingual artery as well as the external carotid artery itself. Especially exposed large vessels are a potential source of danger and should be covered by a microvascular flap. Inadequate endoscopic exposure of the tumor is predominantly found in tumors of the base of the tongue, making the use of the laser more difficult. This is especially true

|                | n  | OS (%) | DSS (%) | LC (%) |
|----------------|----|--------|---------|--------|
| Iro et al. (2011) | 118| 51     | 72      | 85     |
| Mori et al. (2000) | 16 | 87     | 87      | 94     |
| Martin et al. (2008) | 61 | 68     | 96      | 73     |
| Rudert et al. (2003) | 27 | 37     | 50      | 70     |
| Huang et al. (2009) | 24 | 75     | 79      | 82     |
| Eckel et al. (2001) | 46 | 61     | 76      | 73     |
| **Total**       | 292| 59     | 77      | 80     |
in salvage surgery and metachronous second cancers in previously irradiated head and neck area [83]. Beside the postcricoid region the base of the tongue is very difficult to expose during transoral endoscopic surgery. In these cases robotic-assisted surgery is clearly more of advantage (Figure 6, Figure 7, Figure 8).

Despite these limitations in the indications several research groups have published oncological results of selected patients which are comparable to those of open surgery and nonsurgical treatments [83], [84], [85], [86], [87].

In addition, postoperative morbidity (nasogastric tube, tracheostomy, length of hospital stay) is significantly reduced by the transoral endoscopic approach in comparison to the transcervical approach [83], [84], [85]. The endoscopic approach in combination with the one-or two-stage Neck dissection can be applied in selected patients which are comparable to those of open surgery and nonsurgical treatments [83].

Several studies have highlighted the importance of the HPV virus pathogenesis and prognosis needs further evaluation [92], [93], [94]. Unfortunately, the evidence for routine use of TES is based on retrospective and not prospective findings but studies of experienced head and neck surgeons are in progress. The results show that in selected patients as well as in the hands of experienced surgeons TES is a good alternative to both open organ-preserving surgery with reconstruction by microvascular anastomosed flaps as well as polychemo-radiotherapy.

3 Transoral robot-assisted surgery (TORS)

Surgical robot-systems have the ability to perform minimally invasive surgery in the head and neck. These systems were introduced in clinical use around the middle 80s [95]. The DaVinci-System currently well known in many clinical fields was approved by the FDA in 2000. This type of technology which was at first available at big centers was progressively adopted by many hospitals. It is made up of a console to be generally placed in the surgery room and equipment with four active robotic arms acting directly on the patient, which is controlled by the console. Three arms are dedicated to surgical applications. The fourth arm is used to control the endoscopic camera with two objectives, which allows the surgeon at the console to have a complete stereoscopic or 3D-visualization (Figure 6).

The DaVinci-System scales, filters and translates the hand movements of the surgeon in precise micro movements of the driven instruments and the physiological tremor may be completely avoided. The ergonomic drawbacks of the transoral endoscopic surgery would be completely avoided by the use of a comfortable console to control the robotic arms that, in addition, do not require the surgeon to be next to the patient. Theoretically the system even permits the surgeon to work outside of the operating theatre. The bleeding-related risks may be minimized by the use of electo cautery and other hemostatic instruments as well as the flexible endoscopic CO₂-Laser [96]. It is important to note that the electro cauterizer is still...
considered the most important instrument of TORS for tissue resection providing increased thermal damage during tumor resection in comparison to CO₂-Laser [97]. The 3D 90° telescope, the flexible laser system and the instruments designed to respond to specific tasks have many advantages. The 3D endoscope allows special perspectives on the surgical field which are impossible to achieve by microscopic view. The robotic system in combination with the flexible laser system constitutes a system that can manipulate the tissue and allows precise sutures making it possible to perform complex surgical resection and reconstructions.

It is important to consider that the surgical robotic equipment was not primarily developed for use in the head and neck area. Therefore these surgical instruments can be either to large or inflexible. Accordingly these tools must still be optimized and adapted to our small surgical field. Another disadvantage is the lack of haptic abilities of the surgeon when using the robotic system during oncologic surgery. However, different authors were able to demonstrate that this potential drawback can be compensated by optimized exposure and excellent view of the surgery zone and manipulation of the tumor as well as of the surrounding healthy tissue. A complete resection of the tumor with free margin is possible [98], [99], [100].

In current literature the treatment of oropharyngeal squamous cell carcinomas with TORS as first-line curative treatment is described. In both pro- and retrospective studies it is demonstrated that TORS comparable to TES represents a safe technique with low morbidity in terms of the need of tracheotomy, feeding tube and hospitalization duration in comparison to transcervical surgery [100], [101], [102], [103]. From an oncological point of view, it can be shown that the use of TORS provides similar results in terms of local controls, tumor remission and survival rate in comparison to current treatment strategies. On the other hand application of TORS in selected T1- and T2- tumor patients has achieved excellent results in terms of local controls and functionality [104], [105], [106], [107]. Until now no prospective and randomized study has been published comparing surgical therapies vs. radio chemotherapy in the treatment of small and medium size oropharyngeal carcinomas.

The primary treatment of oropharyngeal tumors can easily be performed with TORS, which allows a minimally invasive access to specific types of tumors that before its development could exclusively have been treated by transcervical surgery [95] (Figure 7, Figure 8).

These results support the extension of the indications to small as well as middle size tumors and the improvement of functional results. The greatest advantage of this surgical technique in comparison to TES is its use in the resection of tongue base tumors. These tumors were more or less exclusively treated by open surgery secondary to their difficult exposure [95]. This surgical protocol resulted in a decrease of radio- and radio chemotherapies in selected patients. Moreover, in a recent study with 50 patients, the application of TORS was combined with a personalized adjuvant therapy. In this study there was no detectable difference between HPV- positive or negative oropharyngeal carcinoma patients in terms of oncologic results and so supports the assumption that in case of HPV-negative tumors this surgical method may provide better oncologic results [98]. The observation that HPV-positive and negative tumors have different oncologic outcomes if treated by polyradiochemotherapy likely depends on the tumor responsiveness to radiotherapy. These special biological differences have no impact on the outcome of surgical treatment. Minimally invasive resection with application of robotic tools in the oropharynx, especially in case of salvage situations, may require further reconstruction [101].

There is a lack of information in the literature concerning the oncologic and functional outcome of TORS in the treatment of laryngeal carcinomas. MLS as the standard transoral access to the larynx is, in general, easily performed and well established. In contrast, the exposure by a transoral access remains difficult for the big robotic arms in the treatment of laryngeal diseases. Initial studies were able to demonstrate that it is possible to perform a minimally invasive supraglottic partial resection with TORS [108].

Two retrospective studies showed that swallowing function was diminished secondary to TORS treatment of laryngeal carcinomas in comparison to other regions of the head and neck. Still the amount of data is insufficient to draw a clear conclusion. The difference in swallowing function is likely to depend on different localizations [100], [103]. TORS was also described in the treatment

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**Table 4: Meta-analysis T1–T2 oropharyngeal carcinoma (TES ± RT/RCT)**

| Study            | n   | OS (%) | DSS (%) | LC (%) |
|------------------|-----|--------|---------|--------|
| Moncrieff et al. (2009) | 92  | NS     | NS      | 87     |
| Cosmidis et al. (2004)  | 53  | 73     | 100     | 13     |
| Eckel et al. (1995)    | 79  | NS     | 81      | NS     |
| Iro et al. (2011)      | 134 | 60     | 78      | 89     |
| Röosli et al. (2009)   | 53  | NS     | 81      | NS     |
| Valvekar et al. (2008) | 49  | NS     | 83      | NS     |
| Galati et al. (2000)   | 30  | NS     | 90      | NS     |
| Hicks et al. (1998)    | 20  | NS     | 88      | 86     |
| **Total**            | 418 | 63.68/187 | 83.64/418 | 72.53/299 |
of hypopharyngeal carcinoma but sufficient data are still missing [109].
In conclusion TORS can be considered a safe and efficient method in the treatment of tumors of the upper aerodigestive tract [110].
Initial evaluation showed a limited morbidity in patients treated by TORS. Prospective studies still in progress suggest that results with TORS are comparable, if not superior, to those obtained by radiotherapy. It is still necessary to further optimize costs, efficacy and availability of robot-assisted surgery [111]. An increasing number of patients requiring a follow-up after TORS will help to evaluate these facts more precisely. The initial high investment in robotic equipment and the high cost of disposables may be minimized by the reduction of the costs for care providers due to a shorter hospitalization that, in turn, causes a long-term reduction of morbidity and of psychosocial drawbacks [112].
In the near future technical developments will create smaller robotic devises. Additionally, instruments and hemostatic equipment will be generated for multifunctional transoral application in the treatment of laryngeal and hypopharyngeal tumors allowing an easier access to such zones [95].

4 Transoral endoscopic and minimally invasive surgery of the thyroid and superior mediastinum, Natural Orifice Transluminal Endoscopic Surgery (NOTES)

4.1 Thyroid

In the last years new minimally invasive accesses have been established based on the NOTES concept and especially upon the development of new endoscopes. The advantage of this costly surgical technique is the ability to preserve body integrity as much as possible. At the beginning of the 20s interest in the use of endoscopes was not just focused on natural orifices but extended to closed body cavities. For this reason the abdomen and the thorax became very interesting regions of investiga-
tion. Dmitrij Oskarovic Ott is considered the pioneer of the NOTES-laparoscopy [113]. He performed the so called culdoscopy through a small vaginal incision and introduced a cystoscope in the abdomen of the patient to diagnose special diseases with special focus on the ovaries. In 1901 the gastroenterologist Georg Kelling inspected the abdominal cavity through a cystoscope by using air insufflation with a special filter mechanism. He named this procedure celioscopy [114]. Complete endoscopic accesses through chest, axilla, mastoid or mouth with or without CO₂-insufflation were performed by some groups in the treatment of benign thyroid diseases [114], [115], [116], [117], [118], [119], [120], [121]. These accesses do not aim at minimizing the scars or extension of subplatysmal dissection, but transfer them to other less visible regions. Initial studies demonstrated that complete thyroid resection by endoscopic techniques can be effectively applied in the treatment of early thyroid carcinomas by experienced head and neck surgeons [122]. The technical development during the last two years in regard to endoscopic video-assisted surgery has opened new horizons in thyroid surgery. The growing worldwide use of video-assisted thyroid surgery is due to its improved cosmetic outcome gaining increasing acceptance by surgeons. Since 1997 more than 20 different minimally invasive endoscopic techniques have been introduced in surgery of the thyroid gland [123]. Techniques can be differentiated in minimally invasive procedures of the neck creating visible scars or invasive techniques with small access routes from outside the neck with small hidden scars. In two short published metaanalyses of 18 publications in total involving 613 patients, extra cervical procedures required extra surgery time and caused more significant post-operative pain [123], [124]. In order to increase the quality of surgery in particular regarding the cosmetic outcomes for the patient while decreasing the pre-operative preparation, it is important to choose an access as close to the thyroid as possible. Sonographic evaluation of the transoral access route by Wilhelm et al. presented the same distance between the thyroid and the floor of the mouth compared to the jugulum [125]. This demonstrates that the preparation surface used by transoral and conventional access are identical. While in the transcervical procedure the skin, the platysma, the neck fascia and in some cases the neck muscles have to be cut in order to reach the thyroid, transoral technique dissects from the oral cavity through the subplatysmal anatomical surface to the pretracheal space. At this level the thyroid is as exposed and mobilized as during the conventional transcervical treatment. The skin, platysma, and neck fascia remain completely untouched. The smooth and subtle preparation with 3 mm instruments underlines the minimally invasive character of this procedure. Since the access penetrates through the mucosa of the floor of the mouth the healing process will be concluded with a Restitutio ad integrum. This surgical technique is expected to leave just a small visible scar. The cosmetic result is therefore optimal. Because of the special lighting and the optical magnification of the surgery zone it is possible to perform a more subtle preparation, displaying all the needed anatomic details. The inferior laryngeal nerve can be delimited and safely counterchecked by neuromonitoring. Thus minimal invasiveness and optimal cosmetic outcome is not obtained at costs of the patient’s safety. At present, thyroid surgery without scars is impossible. Witzel et al. described a transoral access in combination with an incision of 3.5 mm, performed 15 mm below the larynx [126], Benhidjeb et al. [120], [121], [123], [125] described the technique of a complete transoral thyroid resection. Extra cervical accesses allow extraction of specimens by subcutaneous tunneling up to 70 ml volume. In transoral surgery extractable specimen size is limited by the anatomical conditions of the floor of the mouth. At present the extension of the
oral incision without drawbacks for the patient is under evaluation since being of high relevance for the further development of the technique. An isolated removal of a thyroid node can easily be achieved by the transoral endoscopic technique. This may be in contrast to the requirements of endocrinological surgery. Potential risks implied in the transoral procedure regard the injury of the mental nerve as well as marginal mandibular nerve during the placement of the 3 mm bivestibular trocars. In order to minimize such risks, the incisions have to be performed at the level of the first molars, and the mental nerve has to be identified and kept under control. Another point to be clarified is the outcome of manipulation at the floor of the mouth followed by scar formation and secondary reduction of tongue mobility causing speech and swallowing problems. Another potential complication may be caused by an infection of the neck wound by bacteria of the oral cavity. Hong and Yang were able to demonstrate that transoral submandibular resection has an infection rate of 2.6% in contrast to 7.3% in transcervical resection [127]. Therefore an accurate desinfection of the oral cavity and a prophylactic antibiotic treatment may minimize such risk.

4.2 Mediastinum

Wilhelm et al. developed a transoral access for endoscopic surgery of the mediastinum. In preclinical studies regarding feasibility and safety of the technique they performed cadaver dissections. Taking the same sublingual incision described above an optical scissor was passed through a 6.0 mm trocar to the pre-tracheal region and applied to dissect the tissue. Two additional trocars were placed via bivestibular incisions. During this surgical experiment the trachea could be exposed down to the main bronchi (Figure 9). Paratracheal and subcarinal lymph nodes were bilaterally dissected. Biopsies were removed through the working canal. The anatomical preparation allowed a nice assessment of potential drawbacks. In all cases the target region could be reached endoscopically. Landmarks such as the brachiocephalic trunk, the azygos vein and pulmonary artery were visible and uninjured. The surgical field in the mediastinum could be enlarged by insufflation of CO\(_2\) with 6–8 mm Hg. Mediastinal biopsies could be removed through the working canal. The anatomical dissection of the cervical path and of the mediastinum did not present any disadvantages. Results regarding pain and feeding were normal up to three days after the surgery. No local infection was detected. The intraoperative gas exchange was not remarkable and the CO\(_2\)-insufflation did not affect blood analysis. Complete resection of the paratracheal and subcarinal lymph nodes could be achieved in a well-defined and visible surgical field. These preclinical studies demonstrate that the mediastinum can be reached through a transoral endoscopic access. Studies demonstrating the safety of the method in the clinical routine are still missing [128].

5 Transoral-transpalatal surgery

5.1 Parapharyngeal space

Gehrking et al. [129] describe tumors of the parapharyngeal space as a heterogeneous group that constitute about 0.5% of head and neck tumors. About 70–80% is benign and mostly originates in the salivary glands. Pleomorphic adenomas represent the biggest tumor entity and likely originate from the ectopic salivary gland tissue, in lymph nodes or in the small salivary glands [130]. Further on they can originate in the deep lobe of the parotid gland and extend secondary to the parapharyngeal space. They generally reach a certain size before first symptoms arise. Radiologic evaluation is essential for diagnosis and therapy. As a matter of fact there are four different access paths to the parapharyngeal space: transoral-transpalatal, transcervical-submandibular, transparotideal and transmandibular. A broad access to the prestyloid space can be achieved through a medial incision of the mandible and a dissection through the floor of the mouth in the glossoalveolaric sulcus. Because of its invasiveness and morbidity this access may be reserved for very large adenomas. Mostly transcervical-submandibular access offers a sufficient overview to the parapharyngeal space. Parotic inner lobe tumors can be removed transparotideal or through an access path that combines it with the submandibular one. Adenomas positioned medially are preferentially removed through a transoral-transpalatal way [129], [131]. In the past tumors located in the parapharyngeal region were not considered to be resectable and were generally the target of radiotherapy. Since they are rather insensitive to radiotherapy, surgical resection is the preferential treatment [131], [132]. The transoral-transpalatal access is the least invasive of all. It allows an easy and direct access to the prestyloid space and is considered the preferential choice for selected tumors growing anteromedially with no or little contact to the big neck vessels [129]. A latero-vertical incision of the soft palatal tissue...
and the lateral pharyngeal wall preserves the palatine nerves and vessels [133]. The resulting space for tumor removal is significantly larger in comparison to transcervical procedures, thus excessive pressure on the tumor can be minimized [134]. Current new endoscopic surgical techniques allow a precise resection of parapharyngeal tumors. Therefore this type of access is also suitable for the removal of large tumors. Prestyloid tumors should not be biopsied [129]. Some authors suggest that the use of transoral access can cause damages of nerves and vessels and thus constitute an infection way opened towards the deep neck fascia [131], [134], [135]. Contrarily Goodwin and Chandler [136] observed limited bleeding and little complications using this access. In this way it was possible to fully extract a tumor without cracking the tumor capsule. Through a transoral access it is possible to expose the oropharynx and incise the soft palatal tissue transmural in a vertical-lateral direction. If the tumor capsule is attached to the pharyngeal muscles, it ought to be definitely detached from the surrounding tissue. The deep preparation should generally be achieved with blunt instruments, such as bent instruments, and using the fact that the prestyloid adenoma in the depth is only loosely attached to the surrounding connective tissue. The wound ought to be primarily closed with absorbable thread. In the post-operative strategy of large tumors, the possibility of a wound dehiscence shall be taken into account. The transoral-transpalatal access is suitable for large tumors. When a lateral tumor dissection is impossible, the transoral access can be combined with a transcervical-submandibular path [134], [137].

5.2 Nasopharynx, clivus and sphenoid bone region

For the treatment of nasopharyngeal tumors, transoral-transpalatal, endonasal, transpharyngeal and transmaxillary access paths are available. The transoral-transpalatal access is restricted to the nasopharynx, nasal cavity, and sphenoid sinus, since it is not possible to achieve a complete lateral exposure of the tumor. Transoral-transpalatal access can routinely be used for nasopharyngeal tumors. This surgical access can be combined with a sublabial, transantral access to tumors of the nasal cavity and/or of the sphenoid [138], [139], [140]. These accesses are principally used for the treatment of juvenile nasopharyngeal angiofibromas. In literature there is no agreement on the best surgical access, although endoscopic resection becomes more and more important [141]. Volume of the tumor, grade of exposure and complete resection influence the decision making for the most appropriate access. The endoscopic variant is a valid option for limited tumors in stage I or II according to Fisch. The transoral-transpalatal path is the preferential choice for tumors limited to the nasopharynx, and in all cases does not significantly affect the nasal sinuses or the pterygopalatinal fossa. This access allows a good exposure of the tumor with low morbidity and good cosmetic results [139], [140]. The selective embolization of angiofibroma significantly reduces strong intraoperative bleeding. So this technique does not only allow the reduction of the intraoperative bleeding, but also simplifies tumor resection. Surgical access primarily depends on the extension of the lesion, the experience of the surgeon and the preoperative selected arterial embolization. In case of large tumors of the sphenoid, clivus, atlas and axis transoral access path with or without incision of the palate has proven to be a reliable access. Merely the soft palate is to be incised or even the dorsal part of the hard palate and the nasal septum should undergo a resection, depends on the localization of the tumor. If beside the clivus, it is necessary as well to reach the sphenoid, the resection of the soft as well as of the hard portion of the palate is required. For further caudal located processes the incision of the soft palate is sufficient. A transpalatal cranial access path to the clivus requires a resection of both soft and hard portion of the palate to ensure an optimal exposure. The access path is suitable for large processes, in particular for those that are localized above the clivus and extend to the sphenoid. For tumors of the clivus it is necessary to resect the posterior part of the hard palate in addition to the incision of the soft palate. Complications may occur, e.g. to be listed are fistulas between the oral cavity and the nose, impaired mobility of the soft palate, instability of the atlas-axial joint, and injury of the internal carotid artery or the optical nerve. Moreover injury of the basilar artery and even of the dura mater as well as a retropharyngeal abscess may occur too [142].

6 Midfacial degloving

In 1974 Casson et al. described the “Midfacial degloving” as an attractive esthetic alternative to the transfacial access path [143]. According to Götze [144] transoral access can be classified as transoral sublabial rhinotomy and offers a well arranged bilateral access to the nasal cavity and sinuses, the nasopharynx, the retromaxillary space and the frontal base as well as to the clivus. Intraoperative a transfixion incision in the nasal entrance together with an intercartilage incision may be combined with a circumvestibular incision and an incision in the oral vestibule [145]. The limitations of this technique depend on the proximity to the internal carotid artery, the mandible, the hard palate and the skin of the glabella. Incisions in the vestibule of the oral mucosa should not result in any visible scar [146], [147], [148], [149], [150], [151].

In 1986 Maniglia published a 15-year experience describing the results of midfacial degloving in 30 patients. Postoperative occurrence of oroantral fistulas, stenosis of the nasal accesses and epistaxis were listed as drawbacks of the procedure. After 1–2 months problems with infraorbital sensitiveness disappeared. An increasing crust development can be seen for about 3 months [152]. The crust formation could be observed only in presence
of large resection cavities as well as extended mucosal resection. In 1988 Price published results of 48 patients treated with "Midfacial degloving". In the first postoperative month transient sensitiveness problems could be detected. Furthermore increased crust formation and, in two patients, a stenosis of the nasal accesses were described [153], [154]. The complication of a postnasal stenosis of the nasolacrimal duct also depends on the midfacial degloving technique and develops secondary to the performed osteotomies. Cited papers demonstrated that midfacial degloving is a transoral surgical technique with good esthetic result and limited post-operative complications, which can be applied on children and adolescents as well. Midfacial degloving alone or in combination with other procedures is also a valuable option in case of malignant tumors of the nasopharynx or tumor recurrence in oncological surgery. Since there is no evidence of increased recurrence in comparison to other surgical techniques "Midfacial degloving" should be considered a preferential method for tumor surgery whenever an endonasal micro- and endoscopic procedure is not considered a realistic option [154].

7 Conclusions

The development of transoral access for minimal invasive surgery in the treatment of head and neck tumors achieved to reduced morbidity and duration of hospitalization. Owing to a decreased burden for the patient and its cost effectiveness, this method gained wide acceptance. But the further development of new as well as of already existing transoral surgical methods requires the definition of new standards, particularly in terms of peri- and intra-operative procedures. Therefore a careful selection of patients and tumors is of high importance (Table 5). At present no clear guidelines exist that can offer a valid help in the decisional process behind the choice of the specific therapeutic approach.

Table 5: Different transoral accesses and target organs

| Transoral access                  | Target organ                                      |
|----------------------------------|---------------------------------------------------|
| transoral endoscopic surgery     | oropharynx, hypopharynx, larynx                   |
| transoral robotic-assisted surgery | oropharynx, upper hypopharynx and larynx          |
| NOTES                            | thyroid gland and mediastinum                     |
| transoral-transpalatal surgery   | parapharyngeal space, clivus, nasopharynx, sphenoid region |
| midfacial degloving              | clivus, nasopharynx, nasal cavity, paranasal sinuses, retromaxillary space, frontal skull base |

Most types of transoral endoscopic techniques take the favorite approach for the treatment of small to medium size tumors into consideration. The requirements in terms of technical equipment and surgical instruments however may represent a potential limitation for the use of such methods. Moreover special technical equipment and surgical instruments are mandatory for optimal performance of transoral endoscopic surgery. Standard duration time of transoral endoscopic surgery can be increased if preparation of special equipment and patient is taken into account. Therefore costs of this kind of surgery can increase beside the technological and equipment investment. But the additional complexity of the process and costs may be absorbed in the long run by the positive effects in term of morbidity. The oncologic and functional outcome depends primarily on the expertise of the surgeon. In this respect the learning curve shows a quite steep rise. A complete resection with free margin is an oncologic principle that has also to be respected in minimally invasive procedures. In general a tumor free margin of about 5 mm shall be maintained in order to guarantee the resection including potentially undetectable tumor portions [155], [156]. An exception is constituted by the vocal cord carcinoma. If applicable, an appropriate adjuvant therapy should be used whenever it is thought necessary in order to improve oncologic results. These principles allow experienced surgeons to reduce the morbidity of surgical resection without affecting oncologic results.

In this way an expansion of the indication spectrum and an increasing development of relevant techniques and special equipment is expected in the next years. The primary advantage of minimally invasive surgery of the head and neck region is the minimization of the surgical trauma. Moreover the patients suffer of less post-operative pain, and an improved post-operative functionality is expected. Therefore a faster post-operative recovery as well as shorter hospitalization time is expected. A prompt return to the common house-keeping and job activities as well as to sports can be anticipated. Additionally, in most cases minimal invasive surgery will lead to better cosmetic results. A direct comparison in terms of oncologic and functional outcome with non-surgical procedures is difficult and may be biased due to pre-selection patients and tumors. With the increasing use of individualized treatments the comparison of therapeutic approaches in large groups will become more difficult. In comparison with the polychemoradiotherapy, transoral minimally invasive surgery offers certain advantages. The treatment duration is significantly shorter, more cost effective and better tolerated by the patient. Its functional effects are at least comparable with those obtained by polychemoradiotherapy or radiotherapy alone. Furthermore successful tumor therapy by polychemoradiotherapy is difficult to proof by histology, and residual disease is only documented during the post therapeutic follow-up. With the minimally invasive surgery the tumor is immediately removed, and it is possible to repeat the treatment.
on the same organ for several times. In radiotherapy, depending on the circumstances, several weeks may be required to reach a tumor-affecting dose. Primary surgical therapy alone offers all treatment options in the treatment of metachronic secondary carcinomas in the head and neck region. A long-term toxicity as in the case of radiotherapy should not be expected, thus leading to a better quality of life. For these reasons it is important to know the potential risks of each therapy and evaluate them against the potential benefits. The complication rate or the lethality of a surgical procedure cannot alone constitute the pivotal reason to reject it without considering its qualities. Risky surgeries or those that show significant drawbacks should not be immediately rejected in case of unfavorable prognoses in order to give a “last chance” to the patient. Applying a risky therapy to patients with a better prognosis considered a sign of superficiality, if not negligence. The introduction of transoral endoscopic surgery has brought a significant change in the treatment of head and neck tumors. Thus a new epoch of technical and computer development in our field has start that increases the dynamic of the entire system. Further progresses in mechanics, nanotechnology and endoscopy will support the trend of endoscopic therapy as a preferable means to optimize the organ function while decreasing morbidity. Transoral, minimally invasive surgery shows optimal oncologic and functional results in patients selected on the basis of specific tumor types. It is expected that in the near future the technological advance represented by the miniaturization of the surgical instruments accompanied by the increasing experience with the minimally invasive techniques will enlarge the fields of application of such type of surgery.

Notes

Competing interests

The author declares that he has no competing interests.

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