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Transoral laser surgery for laryngeal cancer: Outcome, complications and prognostic factors in 275 patients

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Abstract

Aim: Curative treatment options for laryngeal carcinoma include primary radiation therapy, open surgical techniques and transoral laser surgery (TLS). In the last decade, TLS has become an important tool in the treatment of laryngeal cancer and has become the standard approach in many institutions. The aim of this study was to review the experience of a single center institution with TLS for early and advanced laryngeal cancer.
Methods: We retrospectively analyzed 275 patients who underwent TLS in regard to the survival outcome and surgical complications.
Results: The 5-year disease-free survival estimate was 90.3% and the 10-year disease-free survival estimate was 88.2%. The 5-year larynx preservation rate estimate was 88.2% and the 10-year larynx preservation rate estimate was 87.3%. The disease-free survival was significantly worsened by the variables T and N ($p = 0.0003$; $p < 0.001$, respectively). Two percent of all patients required intraoperative tracheostomy and the rate of minor postoperative complications was 17%. There were no fatal complications.
Conclusions: We conclude that TLS is a valid treatment method for early laryngeal carcinoma. Selected cases of advanced carcinomas may also benefit from TLS.

Keywords: Laryngeal carcinoma; Laser; Surgery; Survival

Introduction

Microlaryngoscopic laser surgery or transoral laser surgery (TLS) was initially proposed for the treatment of patients with limited glottic carcinomas.[1,2] Since it was introduced in head and neck oncology, the range of indications for laser surgery of the larynx has been significantly expanded. It has become a commonly used alternative to resection using endoscopic techniques with cold-cutting instruments, to open partial laryngectomy, and also to primary radiotherapy. In addition to glottic carcinomas, also subglottic and supraglottic laryngeal cancers have been successfully treated using laser microsurgery and the use of laser surgery with a curative intent has also been reported in patients with advanced laryngeal carcinomas.[3] Previous reports have shown that laser microsurgery causes minimal morbidity and good functional results and is a cost-effective alternative to open surgical procedures and radiotherapy.[4–7] The aim of this study was to assess the oncologic results and the complications in 275 patients treated with microlaryngoscopic laser surgery for laryngeal cancer of various stages and localizations at a referral center that uses transoral laser surgery as the standard approach to these tumors.

Patients and methods

Patients and treatment selection

In this retrospective chart review, we analyzed 275 consecutive patients with previously untreated squamous cell carcinomas of the larynx treated at the Department of Otorhinolaryngology, University of Cologne, Germany,

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from 1985 to 2005. All of these patients underwent an initial staging endoscopy of the oral cavity, larynx, pharynx and esophagus to facilitate a detailed assessment of the primary tumor stage and to exclude secondary primaries. All of the included patients had a primary tumor extent that was judged to be endoscopically accessible (mainly T1–T2 stages) and were treated with a curative intent. Patients with a malignancy other than squamous cell carcinoma, simultaneous distant metastases, previous or simultaneous second primary, previous treatment to the head and neck region with chemotherapy, radiation, or surgery were excluded. Staging was done according to the 5th edition of the Union Internationale Contre le Cancer/ American Joint Committee on Cancer classification of malignant tumors 1997.

Surgical technique

The surgical technique for the transoral approach to larynx carcinoma used throughout this study has been described in detail previously.[7–11] Briefly, a CO_2 surgical laser was coupled to an operating microscope and was set at an output power of 2–8 W in a super-pulse mode at a spot size of approximately 0.8 mm^2. All patients were intubated transorally before surgery. Different laryngoscopes, including bivalved adjustable laryngoscopes, were used to expose the laryngeal structures. Regarding glottic carcinomas, small, midcordal lesions required a type II resection one vocal cord was completely resected, leaving the anterior commissure and the arytenoid intact. Tumors with anterior commissure involvement were managed by a type III resection, which included the anterior commissure down to the thyroid cartilage, the subglottic region with the cricothyroid membrane and the upper margin of the cricoid cartilage as a borderline. This ''en bloc'' excision extended to the arytenoid cartilage or could even include it, but with preservation of the posterior mucosa. T2 tumors frequently required a type IV (''transglottic'') resection containing all endolaryngeal structures down to the thyroid and cricoid cartilage, the cricothyroid membrane and the ipsilateral arytenoid cartilage, if necessary. The cartilaginous framework of the larynx was always left intact. The resection types of endolaryngeal laser partial laryngectomies have been described in detail previously.[11] Regarding supraglottic tumor sites, tumors of the epiglottis border and the aryepiglottic fold were excised with a safety margin of at least 1 cm.

If possible, specimens were resected in one piece and oriented anatomically after removal to facilitate histopathological examination of the margins. The patients were closely observed after extubation for airway control. An elective ipsilateral neck dissection was performed in cases of supraglottic primaries. In all other cases, neck dissections were only performed in patients with clinically positive neck nodes. Indications for adjuvant radio(chemo)-therapy changed over the study period. In general, they included advanced neck disease (pN2/3), extracapsular tumor spread, infiltration of lymph vessels, or incomplete removal of the primary tumor (R+). In cases of histopathological diagnosis of positive margins, a re-resection for the inadequate margins was performed.

Assessment of complications

Complications were recorded as intraoperative complications during the procedure, postoperative complications were defined to occur during the postoperative hospital stay and late complications occurred after the inpatient period. Follow-up data were collected at periodic visits in 3–6 months' intervals at our outpatients department. Follow-up time was defined as the time from the date of the first tumor operation until the date of the last visit or the date of an event (death, death due to laryngeal cancer, recurrence, laryngectomy).

Statistical analysis

Statistical analysis of the data was performed using SPSS software for medical statistics. The overall survival, the disease-free survival, the disease-specific survival and the larynx preservation rates were calculated using the Kaplan–Meier method. The statistical relationship of following variables on the survival parameters was analyzed: sex, tobacco intake, localization of the primary tumor, T stage and N stage. For univariate analysis, the log-rank statistic was used to detect differences between strata and corresponding survival data. For all tests two-sided p values of less than 0.05 were interpreted as statistically significant.

Results

Clinical details

The clinical details of the included 275 patients are listed in Table 1. The mean follow-up time was 59.2 months with a minimum of 2.1 months and a maximum of 233.1 months. Eighty-two percent of all patients were active smokers and 55% of all smokers permanently quit smoking after the diagnosis of laryngeal cancer.

The resection status (R0–R2) is listed in correlation to the stage of the primary tumor in Table 2. Positive resection margins significantly correlated with advanced primary tumor stages ($p < 0.001$). Positive margins lead to revision surgery in 93 patients of whom 83 underwent a second transoral procedure and 10 a transcervical, open resection. In 46% of these revision surgery cases, residual carcinoma was found in histopathological examination. Sixteen patients underwent two revision surgeries with the histological proof of residual carcinoma in 75% of these cases and three patients required a third procedure of whom two patients showed residual carcinoma on histology. In the course, a total of 14 patients subsequently required a total

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Table 1
Clinical characteristics of the patients

Characteristic	No. of patients	N (total)
Sex		
Male	241	275
Female	34	
	Age: median 62 years (range 19–88)	
Primary site		
Supraglottic	50	275
Glottic	204	
Subglottic	4	
Transglottic	17	
T stage		
1	153	275
2	105	
3	13	
4	4	
N stage		
0	249	275
1	12	
2	12	
3	2	
M stage		
0	275	275
1	0	
Treatment		
Transoral laser	275	275
Neck dissection	84	
Postoperative radiotherapy	35	

laryngectomy (5%). The most frequent reason for a prolonged hospital stay was the need for revision surgery due to positive margins.

Complications

The complications after the lasersurgical procedures are listed in Table 3. In 94% of all cases there were no intraoperative complications. Two percent of all patients required intraoperative tracheostomy. The rate of postoperative complications was 17% as was the rate of late complications with the main late complication of laryngeal synechia. There were no fatal intra- and postoperative complications.

Survival outcome

The 5-year overall survival estimate was 67.6% and the 10-year overall survival estimate was 45.7%. The median overall survival was 130.3 months. The 5-year disease-free survival estimate was 90.3% and the 10-year disease-free survival estimate was 88.2%. The median disease-free survival was 209.8 months. The 5-year disease-specific survival estimate was 96% and the 10-year disease-specific survival estimate was 95%. The median disease-specific survival was 223.5 months. The 5-year larynx preservation rate estimate was 88.2% and the 10-year larynx preservation rate estimate was 87.3%.

Table 2
T-classification in correlation to resection status

Resection	pT			
	pT1	pT2	pT3	pT4
R0	60.1%	37.1%	30.8%	50%
R1	29.4%	50.5%	46.2%	50%
R2	0.7%	1.9%	15.4%	0%
RX	9.8%	10.5%	7.7%	0%
Overall	100%	100%	100%	100%

Table 3
Surgical complications

Intraoperative complications	N
None	259
Significant bleeding	5
Tracheostomy	5
Dental injury	2
Unexpected difficult resection	3
Other	1
Postoperative complications	
None	227
Dysphagia/aspiration	17
Bleeding	8
Dyspnoea	7
Infection	5
Other	11
Late complications	
None	227
Laryngeal synechia	23
Dysphagia	9
Hoarseness	9
Dyspnoea	3
Fistula	2
Pain	2

In univariate analysis, the overall survival was affected by the factors N stages ($p = 0.0345$). Patients who did not quit smoking after the diagnosis of laryngeal cancer had a significantly reduced overall survival ($p = 0.0271$). The disease-free survival was significantly declined by the variables T and N ($p = 0.0003$; $p < 0.001$, respectively). Continuing smoking did not significantly affect the disease-free survival rates. The disease-specific survival was only affected by the factor N stage ($p < 0.001$). The larynx preservation rates were affected by the T stages and N stages ($p < 0.001$; $p < 0.001$, respectively). The factor primary tumor site did not significantly affect the survival rates (Fig. 1).

Discussion

Curative treatment options for laryngeal carcinoma are primary radiation therapy, open, surgical techniques and transoral laser surgery (TLS). In the last decade, TLS has become an important tool in the treatment of laryngeal cancer and has become the standard approach in many institutions.[3]

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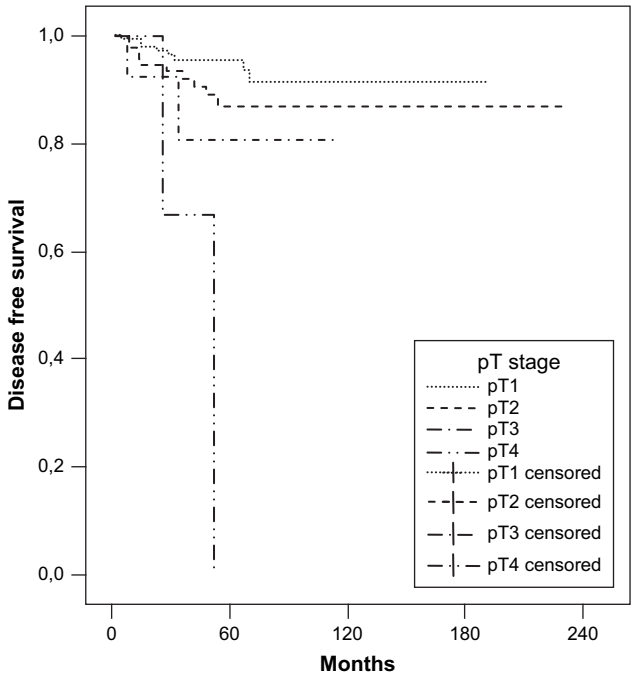

Fig. 1. Disease-free survival stratified to T-classification (log-rank; $p = 0.0003$).

Current treatment modalities

Radiotherapy is the most frequently used treatment modality for early glottic carcinoma in the United States, Canada and northern Europe.[12] Its main advantage is voice preservation, subject to the condition that the initial treatment is successful. Generally, radiation therapy for laryngeal carcinomas carries some important disadvantages: First, in a considerable number of patients with early glottic carcinomas the tumor is completely removed with the diagnostic biopsy.[13] Therefore, giving these patients radiotherapy carries the risk of overtreatment. Second, the event of local tumor recurrence in irradiated patients frequently leads to a total laryngectomy as it is rarely possible to perform partial laryngectomies in these cases. Third, radiotherapy usually cannot be repeated in previously irradiated patients who develop a recurrent tumor or a second primary tumor in the head and neck region. Furthermore, compared to radiation therapy with treatment durations of 6–7 weeks, TLS provides a less long treatment period and is also more cost-effective.[6,14] Several reports analyzed the costs of therapeutic options for laryngeal cancer. It was calculated that the costs of CO_2 laser surgery for T1 vocal cord tumors were approximately 50% of those for open-procedure hemilaryngectomy or for radiation therapy.[6] These data have been confirmed in part showing that the costs of CO_2 laser surgery and radiation therapy for the treatment of T1 glottic tumors are substantially identical if postlaser radiation therapy, in the case of histologically positive margins, is associated.[15]

Complications and associated morbidity

Compared to open surgical procedures, TLS has some significant advantages: Tracheotomies have a substantial negative impact on postoperative adjustment and quality of life in patients following open partial surgery and are usually not required with TLS.[7,10,16–18] Furthermore, the intraoperative and postoperative complications and the associated morbidity of TLS are reported to be low.[18,19] Deglutition is usually not affected, while extended partial laryngectomies in the open technique frequently lead to varying degrees of prolonged aspiration.[20] These complications of open surgery often cause a prolonged hospital stay, ranging from 22 to 35 days on average.[21–23] An interesting study retrospectively compared functional results in patients treated with a transoral approach with those of a comparable series of patients who underwent a transcervical approach. The authors could show that the main advantage of the transoral approach was the lower incidence of temporary tracheotomies.[43] In our patients, a minority of 2% of all patients required a tracheostomy. We observed a median postoperative hospital stay of 10 days which is in line with previous publications of a short hospitalization. In our patients, the main complaint after surgery was initial dysphagia and aspiration in 6% of all cases which resolved in about 50% of these patients in the further course.

Survival outcome

Regarding the survival outcome, it is evident that TLS can be used to successfully treat patients with early-stage glottic carcinoma.[14,24–27] The local control rates with radiotherapy as the initial treatment range from 86% to 94% for lesions classified as T1 and from 64% to 77% for T2 lesions in recent publications.[28–32] Improved therapeutic results with high-dose radiation therapy were reported with a 5-year local control and overall actuarial survival of 89–95% for T1 tumors and 86.7–100% for T2 tumors.[33,34] More recently, a report of radiation therapy alone for patients with T1–T2 glottic tumors showed 5-year local control rates ranging from 70% to 95%.[35] However, given these data, the survival rates of radiation therapy are less successful than those reported for partial laryngectomies. Vertical partial procedures and supracricoid partial laryngectomy have repeatedly been reported to produce local control rates exceeding 90%.[20,29,36–38] The reported 5-year adjusted survival for open approaches range from 80.1% to 95.6%[15] and the 5-year overall survival varies from 68% to 90.8%.[20,39,40] A lesser variability can be found in the 5-year local control, reported to range between 98.2% in T1–T2 tumors and 94.6% in T2 to T3 tumors and laryngeal preservation rates ranging between 100% and 95.5%.[40,41] However, as pointed out before these excellent oncologic results of the open approaches are associated with various problems that severely interfere with the postoperative course.

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Randomized studies on the survival outcome of the different treatment modalities have not been presented so far. Comparing the results of radiotherapy vs. conservative surgery at a single institution, Rucci et al. reported on patients with T1–T2 glottic tumors involving the anterior commissure.[42] Conservative open surgery provided higher rates of local control (86%) than radiation therapy did (74%). Superior oncologic results were observed for local recurrences that occurred after surgery compared to recurrences occurring after radiation therapy (ultimate local control, 97.5% vs 82%, respectively). Our results demonstrate a 5-year disease-free survival rate of 90.3% for all patients and for T1/T2 cases of 91.9%. The disease-free survival rates were significantly affected by the factor T stage. The outcome of T3 lesions still reach an estimated 5-year disease-free survival of 80.1%. However, the value of these data is limited since the patients with advanced disease were few, selected cases. Furthermore, we found high disease-specific survival rates with 5-year rates of 96%. In our study, there was a relatively high rate of histopathological positive margins. This might be explained with the fact that we did not routinely perform intraoperative frozen section histology of the margins. Frozen section histology in TLS carries some disadvantages like difficulties in interpretation due to inadequate small biopsies, unsubtle sectioning and heat artefacts with subsequent false negative results. We therefore used permanent section pathology to verify complete tumor resection and performed a re-resection in cases of positive margins. Interestingly, patients who stopped smoking permanently after the diagnosis of cancer had a superior overall survival but did not have better disease-free survival rates compared to patients who continued smoking.

Conclusion

Microscopic laser surgery is a valid approach to T1 and T2 laryngeal carcinoma. In selected, advanced laryngeal cancers, the results of TLS in patients is comparable to those of open partial laryngectomy and better than the results published for primary radiotherapy in regard to local control and survival rates. Therefore, besides the superior results for early laryngeal carcinoma, TLS may also produce good oncological results in selected cases of T3 laryngeal cancer, with a short postoperative course, low risk of complications and limited health-care costs.

We conclude that TLS can be considered an established therapeutic modality for treatment of early-stage laryngeal cancer based on oncologic, functional, and economic considerations. Selected cases of advanced laryngeal cancer may also benefit from TLS treatment.

Conflict of interest

This manuscript has been read and approved by all authors. There was no financial support and no conflict of interest during the preparation of this article.

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