Long Term Oncological Results of Transoral Laser Microsurgery for Early and Moderately Advanced Glottic Carcinoma in Primary and Salvage Settings

Prem Sagar¹ · Rajeev Kumar¹ · Richa Vaish² · Alok Thakar¹

Received: 31 August 2018 / Accepted: 25 September 2018 / Published online: 29 September 2018
© Association of Otolaryngologists of India 2018

Abstract The aim of the study is to document the long term oncological results of trans-oral laser microsurgery (TLM) for early and moderately advanced glottic cancer in primary and salvage settings. In this prospective cohort study 43 consecutive patients of glottic cancer (T1–30, T2–7, and selected T3 with mobile cords-6) were recruited. TLM was performed in these 35 primary and 8 previously treated cases. In our series, the local disease control rate with TLM was 90% (27/30) for T1 disease, 71.4% (5/7) for T2 cancer and 66.6% (4/6) for T3 lesions. The overall disease control rates after subsequent treatment for locoregional recurrences were 100% (30/30), 85.7% (6/7) and 83.3% (5/6) for T1, T2, and T3 glottic cancers respectively. The 5-years disease free survival rate for primary cases was 100% and 50% for salvage cases. The 5-years local disease control rate was 96.4% and 41.67% in primary and salvage TLM settings respectively. The 5-years laryngectomy free rates were 96.3% and 18.75% for primary and salvage cases respectively. TLM offers a minimally invasive and oncologically robust treatment option for early glottic cancer with an overall disease free survival of 100% at 5 years noted for primary untreated cases in this experience. TLM for post radiation salvage cases has however been disappointing and alternate larynx preserving option of open partial laryngectomy needs to be considered in this setting.

Keywords Transoral laser microsurgery · Early glottic cancer · Recurrent glottic cancer · Salvage transoral laser microsurgery

Introduction

With improvement in the survival of patients of laryngeal cancers, the focus has shifted to morbidity due to treatment and quality of life, post-treatment. The concept of conservation surgery has revolutionized the head and neck oncology treatment protocols. Conservation laryngectomy surgery preserves the laryngeal airway, voice and swallowing with good oncologic outcome. Radiotherapy and concurrent chemoradiation preserve the quality of voice, but with multiple complications associated with them. Trans-oral laser microsurgery (TLM) provides the advantages of radiotherapy and open conservation laryngectomy without their associated complications. TLM is performed by trans-oral route and is free of the cosmetic implications of open partial laryngectomies or radiation effects on the skin. Avoidance of dissection of strap muscles and laryngeal framework, rules out the risk of wound dehiscence, pharyngocutaneous and laryngocutaneous fistulas. CO₂ Laser cuts the tissue precisely with excellent haemostasis. After tumour excision the raw area heals by second intention resulting in a mucosalised and sensate post-surgical defect. Resultant intact physiology of swallowing and sensate laryngopharyngeal mucosa leads to early swallowing and faster healing. Magnification provided by microscope gives better delineation of tumour-host interface in all the three dimensions. To the experienced surgeon, the charring characteristics of the tissue cutting with CO₂ laser also helps in the differentiation of tumour and

✉ Alok Thakar
drathakar@gmail.com

¹ Department of Otolaryngology and Head & Neck Surgery, All India Institute of Medical Sciences, New Delhi 110029, India

² Department of Head and Neck Oncology, Tata Memorial Hospital, Mumbai 400012, India

normal tissue during this multi-block tumour excision procedure. All these factors enable close margin excision with normal tissue preservation. Finally, apart from preserving the organ, TLM keeps other treatment modalities in reserve if salvage is needed for recurrence or a second primary cancer.

TLM has proven its role in early glottic cancers [1, 2]. Studies have shown good outcome with advanced glottic cancers [3]. This study reports the outcome of our experience of TLM for primary as well as salvage, early and moderately advanced glottic carcinoma. The oncologic outcome and prognostic factors have been analysed.

Materials and methods

This was a prospective case series study conducted at the department of Otolaryngology and Head & Neck surgery in a tertiary care referral hospital. Patients with pathologically proven carcinoma of glottis were evaluated and assessed by a team of head and neck surgeons, radiation oncologists and medical oncologists. Staging was done according to the 7th edition of the American Joint Committee on Cancer classification of malignant tumors. Different treatment options with their disease control rate, morbidity, complications, and cost were discussed with the patients and their caretakers. Patients who consented for surgery were evaluated for suitability for TLM. Carcinoma of glottis with T 1, T2 and selected T3 (paraglottic or pre-epiglottic space involvement) with or without history of previous surgery or radiotherapy were considered for TLM.

All cases were operated under general anaesthesia using a laser resistant endotracheal tube introduced transorally. Appropriate laser specific safety measures and precautions were undertaken by the surgeons, anaesthetists as well as other operation theatre staff. Till 2011, Deka CO2 laser system and from 2012 Lumenis UltraPulseSurgiTouchCO2 laser system was used. CO2 surgical laser attached to an operating microscope was adjusted to an output power of 6–10 W in an ultrapulse continuous mode at a spot size of 0.8 mm or a straight line of the length of 1–4 mm. Adequate exposure of the laryngeal structures was done using suspension laryngoscopes of various sizes and designs. Many cases required excision of part of epiglottis or false cords for complete exposure of the tumours. Small tumours were excised “en-bloc” and large tumours were removed in multi-bloc fashion. Surgical specimens were pinned on a board and oriented anatomically along with the resected margins with the help of diagrams to aid thorough histopathological evaluation. European Laryngological Society, 2000 classification of laser cordectomy was used for uniformity and international comparison of results [4]. Neck dissection was performed in cases with positive neck

nodes in the same sitting. Temporary tracheostomy was undertaken for larger resection judged to be at high risk for airway-compromising postoperative oedema or bleeding. Patients, who were not tracheostomised, were vigilantly observed for any airway compromise after extubation.

Late complications in the form of laryngeal web, polyp or stenosis were noted down and were treated if symptomatic. Follow-up time was calculated from the date of first surgery. During each follow-up, patients were evaluated for any loco-regional recurrences by clinical examination, fiberoptic laryngoscopy, and additional radiology, direct laryngology and biopsy if required.

Results

A total of 43 patients underwent TLM for glottic cancer from 2007 to 2013 by a single primary surgeon (author AT). The mean age of patients was 53.2 years with a range of 28–80 years. There were 39 male and four female patients. Majority of patients were in their fourth or fifth decade of life. Out of 43 cases, 35 (81.39%) were primary cases and eight (18.6%) were recurrent. These salvage cases were post-microlaryngeal surgery (three cases) or post-radiation (four cases) or following both these modalities of treatment (one case). The mean follow-up period was 62.4 months and the range was 23–102 months. The tumour (T) staging of all the patients is shown in Table 1. Only one patient had clinically positive neck node (N2) with a primary stage of rT2.

Various cordectomies performed in all the patients is summarised in Table 2. Only one patient (rT2 N2c) underwent same stage neck dissection in the form of ipsilateral modified neck dissection and contralateral level II, III and IV clearance. None of the patients had tracheostomy prior to surgery. Three (6.9%, $n = 3/43$) patients had a temporary tracheostomy in the postoperative period and all those cases had T3 lesions (2 primary and one recurrent).

Histopathological evaluation revealed squamous cell carcinoma in 29 (67.44%) patients, carcinoma-in situ in four cases, adenoid cystic carcinoma in one patient and no evidence of malignancy in remaining 10 (23.25%) cases.

Table 1 Tumour (T) stage-wise patient distribution

T stage	Primary cases (n = 35)	Salvage cases (n = 8)	Total cases (n = 43)
1a	19	3	22 (51.16%)
1b	6	2	8 (18.6%)
2	5	2	7 (16.26%)
3	5	1	6 (13.95%)

Table 2 Summary of the type of cordectomy performed in all the cases

Type of surgery	Primary cases	Salvage cases	Total no of cases
Type I cordectomy	9	1	10
Type II cordectomy	6	1	7
Type III cordectomy	4	1	5
Type IV cordectomy	2	–	2
Type Va cordectomy	4	1	5
Type Vb cordectomy	–	–	–
Type Vc cordectomy	2	2	4
Type Vd cordectomy	8	2	10

Table 3 Significant short term and long term event/surgical intervention in the post-operative period

Event/intervention	Primary cases (35)	Salvage cases (8)	Total no. of cases
Temporary tracheostomy	2	1	3 (6.9%)
Temporary aspiration	1	1	2 (4.6%)
Margin revision	2	1	3 (6.9%)
Laser kashima	0	1	1 (2.3%)
Web release	2	0	2 (4.6%)
Fat injection	2	0	2 (4.6%)
Polyp excision	1	0	1 (2.3%)

Out of five cases (11.62%, $n = 5/43$) with histopathologically positive tumour margin, three patients were subjected to margin revision and in all of them the specimens were negative for tumour tissue. Remaining two cases received adjuvant radiotherapy. Significant postoperative events are briefed in Table 3.

Total 8 patients (18.6%) developed locoregional recurrence during subsequent follow-up with initial period of disease-free status of varying duration. The recurrence rate was 5.7% ($n = 2/35$) in the primary cases in the form of only local recurrence. Similarly the recurrence rate was 75% ($n = 6/8$) in salvage cases and 5 (62.5%) of them had local recurrence whereas one (12.5%) case had nodal recurrence. Total laryngectomy was performed in three (6.9%) patients with local recurrence comprising of one (2.8%) primary and two (25%) salvage cases. In the three patients in the salvage group, who had recurrent disease following previous surgeries, two patients had local recurrence (one received radiotherapy and other underwent revision TLM). The pattern of recurrence, treatment received and subsequent status is depicted in Fig. 1 for primary cases and Fig. 2 for salvage cases.

The mean duration till recurrence was 14.87 months with a range of 2–55 months. This duration was 14 months in the primary cases and 15 months in the recurrent cases. In the recurrent cases, one patient developed recurrence after an extreme of 55 months. Excluding this patient, the average duration for recurrence was 7.2 months in the salvage group. Using logrank and wilcoxon test, the 5 year disease specific survival in our patients is 88.88%, the 5 year local control rate is 64.98%, the 5 year disease free survival is 84.9% and the 5 year organ preservation rate is 79.82%. The separate survival analysis in primary and recurrent cases is shown in Table 4. Using Kaplan–Meier survival estimate the 5 year disease-free survival is 96% for primary cases and 41% for salvage cases (Fig. 3). Univariate analysis (Chi square/Fisher exact test) of various clinical and pathological factors in relation to local disease control is described in Table 5.

Fig. 1 Complete treatment course of all the primary cases of glottic cancer. *DF* disease free, *LR* local recurrence, *TL* total laryngectomy, *RT* radiotherapy

Fig. 2 Complete treatment course of all salvage cases of glottic cancer. *DF* disease free, *LR* local recurrence, *RR* regional recurrence, *TL* total laryngectomy, *RT* radiotherapy, *CT* chemotherapy, *MND* modified neck dissection

Table 4 Survival analysis between in primary and recurrent cases of glottic cancer patients

Survival	Primary cases (n = 34, excluding one case of adenoid cystic disease of histopathology) (%)	Recurrent cases (n = 8) (%)	<i>p</i> value (using Chi square with Yates correction)
5 year disease free survival	100	50	< 0.0001
5 year local control	96.4	41.67	< 0.0001
5 year larynx preservation	96.3	18.75	< 0.0001

Bold values indicate statistically significant

Discussion

The first description of transoral laser microsurgery was in 1972 by Jako as an experimental study on dogs [5]. Subsequently in 1975 Strong and Jako described about the role of CO₂ laser resection for early laryngeal cancers [6]. Since

then, numerous studies have described about the surgical option of TLM, its advantages over conventional open conservation surgery, the indications and contraindications as well as the detailed operative technique [7–9].

A Cochrane review of the published data on TLM, external beam RT and open partial surgery, was unable to

Fig. 3 Kaplan–Meier estimate of disease-free survival for primary and salvage cases of glottic cancer **Table 5** Univariate analysis of the impact of various clinicopathologic factors with local disease recurrence

Factors	Recurrence rate	<i>p</i> value
Primary/salvage		
Primary	2/35 (5.7%)	0.0011
Salvage	5/8 (37.5%)	
Age		
< 60 years	3/33 (9%)	0.0399
> 60 years	4/10 (40%)	
Sex		
Male	6/39 (15.38%)	0.5227
Female	1/4 (25%)	
T stage		
T1a	2/22 (9%)	0.3956
T1b	1/8 (12%)	
T2	2/7 (28.5%)	
T3	2/6 (33.33%)	
Anterior commissure involvement		
Yes	1/5 (20%)	1.0000
No	6/38 (15.78%)	
Supraglottis involvement		
Yes	3/10 (30%)	0.3249
No	4/33 (12.12%)	
Subglottis involvement		
Yes	2/4 (50%)	0.1177
No	5/39 (12.8%)	
Margin status		
Negative	6/39 (15.38%)	0.5227
Positive	1/4 (25%)	

Bold values indicate statistically significant

provide definite recommendation regarding the treatment of early glottic lesions [10]. The EaStER trial (Early Stage Glottic Cancer: Endoscopic Excision or Radiotherapy) concluded that TLM is the preferred treatment option for early laryngeal cancer [11]. However, factors like patient preference, treatment associated morbidity, voice quality and cost of treatment are to be considered while deciding the treatment plan for individual patients with glottic cancer [7, 12]. In a meta-analysis, Higgins et al. [13] found a trend towards improved post-treatment voice quality with radiotherapy when compared to that after TLM for early glottic lesions. Carlos et al. in a clinical review concluded that the oncologic and functional outcome of TLM for early glottic cancer appears to be comparable to those of radiotherapy. However, the cost of treatment with radiotherapy is 2- to 5-fold higher than the cost of surgery [14]. Studies show local control rates at 5 years as 78–94% for T1 lesions, 47–91% for T2 lesions and 86.3% for T3 lesions [3, 15, 16]. The laryngeal preservation rate is 93–100% for T1 glottic cancers, 76–93% for T2 and 51% for T3 lesions [3, 17]. Our experience of TLM for T1, T2 and limited T3 glottic carcinoma (primary and salvage) showed the 5 year disease specific survival as 88.88%, the 5 year local control rate as 64.98%, the 5 year disease free survival as 84.9% and the 5 year organ preservation rate as 79.82%.

Bocciolini et al. [18] in their series of 79 patients with early stage glottic cancers achieved a 97.5% overall survival, 89.9% disease free survival, 92.4% ultimate local control rate and 97.4% laryngeal preservation rate, at 3 years. Lester et al. [19] in their cohort of 53 patients with T1 or T2 glottic cancers reached a 5 year disease free survival rate (including salvage) of 96.2%, 5 year overall

survival rate of 88.8% and 5 years laryngectomy free survival of 98.1%. In a series of 575 patients with T1–T3 glottic cancers, Peretti et al. [20] observed a disease specific and disease-free survival, local control rate with laser, and organ preservation rate of 99%, 81.3%, 92.7%, and 97.1% respectively. In our series, in the primary cases ($n = 35$), the 5 year disease free survival rate was 100%, the 5 year local control rate was 96.4%, and the 5 year larynx preservation rate was 96.3%.

Salvage TLM after radiotherapy for early glottic lesions (Tis–T2) had been reported to result in 24–60% recurrence rate and 25%–53% total laryngectomy rates [21–25]. Outzen et al. [26] in their study of salvage TLM for T1–T4 glottic carcinoma in 16 patients reported a local recurrence rate of 25% and total laryngectomy rate of 13%. Steiner et al. reported a local recurrence rate of 59% after salvage TLM in 34 patients with glottic lesions (T1–T3) who had received radiotherapy previously for the same disease. The median interval between salvage TLM and local recurrence was 8 months and 21% of patients required total laryngectomy in spite of one or multiple salvage TLM procedures in their series [27]. Roedel et al. studied the effect of repeated TLM in the case of failure after primary laser resection of glottic cancer in 56 patients with early local recurrence ($n = 44$) and advanced local or locoregional recurrence ($n = 12$). The 5-year overall survival rates in patients with early and advanced recurrences were 61.6% versus 25.8%, respectively. The 5 year locoregional control rate were 63.6% and 27.5% in patients with early and advanced recurrences respectively. This significant difference prompted the authors to conclude that in cases of early local recurrence after primary laser resection of early glottic cancer, further laser resection seems to be justified as an organ-preserving treatment option. Whereas, salvage laryngectomy should be considered early for patients with advanced local or locoregional recurrence, as per the authors' opinion [28]. Peretti et al. [29] remarked that superficial recurrence of T1–T2 tumours can be managed successfully with TLM in > 75% of the cases, whereas submucosal recurrence with cartilage invasion are not amenable to repeat laser surgery. Huang et al. in their study on 50 cases of salvage TLM for early recurrent glottic carcinoma following primary laser treatment faced a local recurrence rate of 36% and regional recurrence rate of 2% [30]. However, 70% of total patients were successfully resalvaged with TLM. The 5 year local control rate and 5 year disease specific survival rate were 62.3% and 97.9% after the first salvage TLM. In our series, salvage TLM was performed in 8 patients and five of them were post-radiotherapy. In this salvage group the local recurrence rate was 62.5% ($n = 5/8$), regional recurrence rate was 12.5% ($n = 1/8$) and the total laryngectomy rate was 25% ($n = 2/8$). These discouraging results have led us to now prefer

open partial laryngectomy for salvage of most patients with post radiation recurrences of early glottic cancer.

The disappointing results in post radiation settings may be attributed to many factors. Such recurrences are known to be multicentric as radiation does not always lead to a centrifugal shrinkage of tumour and may lead to more than one residual site of viable tumour. Further, tumour failing radiation may represent a biologically more aggressive cancer. Additionally, post radiation tissue oedema may have impact on laser-tissue interaction and make surgical assessment of tumour margin more difficult.

Post cordectomy histopathology was negative for malignancy in 23.25% of our cases. This can be explained by the small size of the tumour which might have been excised during biopsy. Laser causes partial or complete denudation of surface epithelium, leaving only the lamina propria. The later can be assessed for the presence or absence of invasion, but not dysplasia [31]. Moreover when margin was revised in three cases, the specimens did not reveal any tumour tissue. This may be attributed to tissue shrinkage after excision which might have falsely been reported as close margin after first TLM. Makki et al. in their prospective randomized blinded study on 45 patients demonstrated that CO₂ laser causes a significant degree of artifact that can interfere with accurate margin assessment in TLM for early glottic cancer. Preuss et al. [32] reported that only 46% of margin revision surgery cases demonstrated residual carcinoma in the histopathology.

In our series, 6.9% ($n = 3$) of patients required temporary tracheostomy, 4.6% ($n = 2$) patients experienced temporary aspiration. Lester et al. did not perform tracheostomy in any of their patients ($n = 53$) and all the patients tolerated normal diet on the day following surgery. However, one patient (1.8%, $n = 1/53$) required reintubation due to breathing difficulty in the immediate post-operative period [19]. Grant et al. [33] mentioned the temporary tracheostomy rate as 9% and post-operative nasogastric tube feeding rate as 17% in their prospective study on 76 patients of glottic cancer. Similarly Preuss et al. [32] mentioned post-operative tracheostomy rate as 2% and aspiration in 6% of cases in a retrospective study on 275 patients.

Total 13.95% ($n = 6/43$) of our patients required post-TLM non oncologic procedures for either breathing difficulty or voice improvement. In their series of 53 patients with early glottic cancers, Lester et al. [19] reported requirement of emergency tracheostomy in one (1.8%, $n = 1/53$) patient who developed significant delayed hemorrhage. Grant et al. [33] encountered supraglottic stenosis in 3% patients. Preuss et al. noticed laryngeal synechia in 10% of the cases. However they have not mentioned about the surgical intervention performed for the same in their study.

The mean duration between surgery and recurrence was 7.2 months in the salvage group (excluding one patient

with an extreme of 55 months of disease free status) as compared to that in the primary cases as 14.87 months. So, the recurrence was earlier and rate was higher in the salvage group. The average interval to recurrence has been documented as 37.5 months by Peretti et al. [34] in 140 cases of primary TLM for early glottic carcinoma. Huang et al. [30] mentioned the mean time to loco-regional recurrence as 18.8 months in their salvage TOLM cases following primary laser treatment.

On analysing the association of clinicopathologic factors with local disease control, factors like T stage, involvement of anterior commissure, supraglottis or subglottis involvement or margin positivity had no statistically significant association. The recurrence rate was statistically higher in salvage group patients and patients aged 60 years and above. Peretti et al. [34] retrospectively analysed 140 patients with early glottic disease and found that involvement of anterior third of vocal cord or false cord or infiltration of vocalis muscle has a significant negative impact on the disease-free survival. In their study the factors which did not affect the disease-free survival were sex of the patient, smoking status, anterior commissure involvement, ventricle involvement, margin positivity and adjuvant treatment. When Huang et al. analysed 50 salvage cases of TLM following primary laser surgery, second local recurrence showed a significant negative impact on disease-specific survival rate and larynx preservation rate. Histological grading showed a significant influence on the laryngeal preservation rate in their study.

Conclusion

TLM offers a minimally invasive and oncologically robust treatment option for early glottic cancer. In our experience of early glottic and moderately advanced primary untreated glottic cases, the 5 year local control rate was 96.4% and the overall disease free survival was 100%. However, results of TLM as an salvage option for recurrent glottic cancers was disappointing. Hence, alternate larynx preserving option of open partial laryngectomy needs to be considered in this setting.

Compliance with Ethical Standards

Conflict of interest Prem Sagar, Rajeev Kumar, Richa Vaish and Alok Thakar declares that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with institutional ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

References

1. Feng Y, Wang B, Wen S (2011) Laser surgery versus radiotherapy for T1–T2N0 glottic cancer: a meta-analysis. *ORL* 73(6):336–342
2. Schrijvers ML, van Riel EL, Langendijk JA et al (2009) Higher laryngeal preservation rate after CO₂ laser surgery compared with radiotherapy in T1a glottic laryngeal carcinoma. *Head Neck* 31:759–764
3. Vilaseca I, Bernal-Sprekelson M, Luis Blanch J (2010) Transoral laser microsurgery for T3 laryngeal tumors: prognostic factors. *Head Neck* 32(7):929–938
4. Remacle M, Eckel HE, Antonelli A et al (2000) Endoscopic cordectomy. A proposal for a classification by the Working Committee, European Laryngological Society. *Eur Arch Otorhinolaryngol* 257:227–231
5. Jako GJ (1972) Laser Surgery of the vocal cords; an experimental study with carbon dioxide lasers on dogs. *Laryngoscope* 82:2204–2216
6. Strong MS (1975) Laser excision of carcinoma of larynx. *Laryngoscope* 85(8):1286–1289
7. Ambrosch P (2007) The role of laser microsurgery in the treatment of laryngeal cancer. *Curr Opin Otolaryngol Head Neck Surg* 15(2):82–88
8. Cabanillas R, Ortega C, Rodrigo JP, Llorente JL, Ortega P, Suarez C (2005) Functional outcomes of transoral laser surgery of supraglottic carcinoma. *Acta Otorhinolaryngol Esp* 56(4):156–160
9. Rubinstein M, Armstrong WB (2011) Transoral laser microsurgery for laryngeal cancer: a primer and review of laser dosimetry. *Lasers Med Sci* 26:113–124
10. Dey P, Arnold D, Wight R, Kelly CG, McKenzie K (2002) Radiotherapy versus open surgery versus endolaryngeal surgery (with or without laser) for early laryngeal squamous cell cancer. *Cochrane Database Sys Rev* 2:CD002027
11. Birchall MA (2008) Early stage glottic cancer: endoscopic excision or radiotherapy—feasibility study. Cancer Research, London
12. Back G, Sood S (2005) The management of early laryngeal cancer: options for patients and therapists. *Curr Opin Otolaryngol Head Neck Surg* 13:85–91
13. Higgins KM, Shah MD, Ogaick MJ, Enepekides D (2009) Treatment of early stage glottic cancer: meta-analysis comparison of laser excision versus radiotherapy. *J Otolaryngol Head Neck Surg* 38:603–612
14. Suarez C, Rodrigo JP, Silver CE, Hartl DM et al (2012) Laser surgery for early to moderately advanced glottic, supraglottic and hypopharyngeal cancers. *Head Neck* 34:1028–1035
15. Sjogren EV, Langeveld TPM, Baatenberg de Jong RJ (2008) Clinical outcomes of T1 glottic carcinoma since the introduction of endoscopic laser surgery as treatment option. *Head Neck* 30:1167–1174
16. McCoul ED, Har-El G (2009) Meta-analysis of impaired vocal cord mobility as a prognostic factor in T2 glottic carcinoma. *Arch Otolaryngol Head Neck Surg* 135:479–486
17. Mendenhall WM, Werning JW, Hinerman RW, Amdur RJ, Villaret DB (2004) Management of T1–T2 glottic carcinomas. *Cancer* 100:1786–1792
18. Bocciolini C, Presutti L, Laudadio P (2005) Oncologic outcome after CO₂ laser cordectomy for early-stage glottic carcinoma. *Acta Otorhinolaryngol Ital* 25:86–93
19. Lester SE, Rigby MH, Taylor SM (2011) Transoral laser microsurgery outcomes with early glottic cancer: the Dalhousie University experience. *J Laryngol Otol* 125:509–512
20. Peretti G, Piazza C, Cocco D et al (2010) Transoral CO(2) laser treatment for T(is)–T(3) glottic cancer: the University of Brescia experience on 595 patients. *Head Neck* 32:977–983

21. Blakeslee D, Vaughan CW, Shapshay SM, Simpson GT et al (1984) Excisional biopsy in the selective management of T1 glottic cancer: a three year follow-up study. *Laryngoscope* 94:488–494
22. Annyas AA, van Overbeek JJM, Escajadillo JR, Hoeksema PE (1984) CO₂ laser in malignant lesions of the larynx. *Laryngoscope* 94:836–838
23. Casiano RR, Cooper JD, Lundy DS, Chandler JR (1991) Laser cordectomy for T1 glottic carcinoma: a 10 year experience and videostroboscopic findings. *Otolaryngol Head Neck Surg* 104:831–837
24. Quer M, Leon X, Orus C, Venegas P, Lopez M, Burgues J (2000) Endoscopic laser surgery in the treatment of early laryngeal carcinoma. *Head Neck* 8:520–523
25. de Gier HHW, Knegt PPM, de Boer MF, Meeuwis CA, van der Veldon L, Kerrebijn JDF (2001) CO₂-laser treatment of recurrent glottic carcinoma. *Head Neck* 3:177–180
26. Outzen KE, Illum P (1995) CO₂-laser therapy for carcinoma of the larynx. *J Laryngol Otol* 109:111–113
27. Steiner W, Vogt P, Ambrosch P, Kron M (2004) Transoral carbon dioxide laser microsurgery for recurrent glottic carcinoma after radiotherapy. *Head Neck* 26(6):477–484
28. Roedel RM, Matthias C, Wolff HA, Christiansen H (2010) Repeated transoral laser microsurgery for early and advanced recurrence of early glottic cancer after primary laser resection. *Auris Nasus Larynx* 37:340–346
29. Peretti G, Piazza C, Bolzoni A et al (2004) Analysis of recurrences in 322 TS, T1, or T2 glottic carcinomas treated by carbon dioxide laser. *Ann Otol Rhinol Laryngol*. 113:853–858
30. Huang J, Yu Z, Fang J, Chen X et al (2013) Salvage transoral laser microsurgery for early recurrent glottic carcinoma after primary laser treatment. *Acta Otolaryngol* 133:531–537
31. Makki FM, Rigby MH, Bullock M, Brown T et al (2014) CO₂ laser versus cold steel margin analysis following endoscopic excision of glottic cancer. *J Otolaryngol Head Neck Surg*. 43:6
32. Preuss SF, Cramer K, Klusmann JP, Eckle HE, Lichius G (2009) Transoral laser surgery for laryngeal cancer: outcome, complications and prognostic factors in 275 patients. *Eur J Surg Oncol* 35(3):235–240
33. Grant DG, Salassa JR, Hinni ML, Pearson BW, Hayden RE, Perry WC (2007) Transoral laser microsurgery for untreated glottic carcinoma. *Otolaryngol Head Neck Surg* 137(3):482–486
34. Peretti G, Nicolai P, Zinis LOR, Berlucchi M et al (2000) Endoscopic CO₂ laser excision for Tis, T1, and T2 glottic carcinomas: cure rate and prognostic factors. *Otolaryngol Head Neck Surg* 123(1):124–131