

Oncological Outcomes Following Transoral CO₂ Laser Microsurgery for T1 Glottic Cancer

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Abstract The objective of this study is to analyze oncological outcomes for treatment of Tis and T1 glottic squamous cell carcinoma after transoral laser microsurgery. This study is retrospective analysis of previously untreated, suspected lesion of glottis, staged cT1a and cT1b squamous cell carcinoma in a tertiary care hospital and 53 patients were included in the study. End points for analysis were local control, overall and disease specific survival rates. The local control, ultimate local control with laser alone, 3-year overall survival, 3-year disease specific survival and organ preservation rates were 86.7, 90.5, 92.4, 98.1 and 98.1% respectively. The involvement of anterior commissure did not show any significant impact on local control or survival. TLM is safe and effective treatment of early glottis cancer, associated with less morbidity and a high percentage of local control, survival and organ preservation rates.

Keywords Laryngeal carcinoma · Glottis · CO₂ laser · Squamous cell carcinoma · Transoral laser microsurgery

Introduction

The ideal initial management of early glottis cancer should be one which is most likely to result in cure and to preserve a normal voice without impairment of swallowing or breathing and at the same time leaving all modalities of

treatment available for recurrence or second primary cancer. Different options are available for treatment especially when the tumor is identified in early stage: transoral laser microsurgery (TLM), open partial laryngectomy (OPL) and radiotherapy (EBRT) [1, 2].

Since Strong and Jako [3, 4] proposed laser endoscopic surgery for the treatment of larynx cancer in the seventies, transoral laser microsurgery has gained territory in larynx oncology and established itself as an effective option in the treatment of glottis, supraglottis and hypopharyngeal tumors.

In spite of providing good oncological results, OPL has greater detrimental impact on laryngeal architecture and results in poorer functional outcome and longer hospital stay [5]. EBRT achieves better voice and higher laryngeal preservation, but has higher costs and longer time of care [6]. TLM provides oncological benefits similar to open surgery in carefully selected patients and quality of voice is comparable to radiotherapy as well as hospitalization time is reduced.

In this paper; we analyze our experience with TLM in terms of oncological outcomes for treatment of Tis and T1 glottic squamous cell carcinoma. The end point for analysis in this study was local control, overall and disease specific survival and larynx preservation rate.

Materials and Methods

We performed a retrospective analysis of patients previously untreated, with a clinically suspicious lesion of glottis staged-Tis, cT1a or cT1b and clinically negative neck who underwent Transoral Laser Microsurgery (TLM) between 2011 and 2015. Patients who had previous radiotherapy, had distant or nodal metastasis, history of

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previous malignancy of head and neck region were excluded from our study.

Based on the aforementioned criteria, 53 patients (49 males, 4 females; mean age 53 years) operated in the department of otorhinolaryngology-head and neck surgery of our institution for glottis cancer were enrolled in the study. Patient consent for data collection was sought and the study was approved by the ethics committee of our institute.

All the therapeutic options (TLM vs. RT vs. open surgery) and their risks and benefits were discussed with the patient before obtaining informed consent. Preoperative workup included physical examination, routine blood tests, chest radiography, videolaryngostroboscopy (VLS) and flexible fiber optic laryngoscopy (FOL). In addition, a computed tomography (CT) scan of neck with contrast was performed for lesions of anterior commissure, suspected thyroid cartilage involvement, or infiltration of paraglottic space or extension to subglottis or arytenoids. Overall, 12 cases showed evidence of contrast enhancement in anterior commissure region but without thyroid cartilage involvement on CT scan and were included.

All surgical procedures were done under general anesthesia with orotracheal intubation using laser safe tube of inner diameter 4.5 or 5 mm (Laser-Flex, Mallinckrodt Medical, Athlone, Ireland). Suspension laryngoscopy with anterior commissure laryngoscope was done for optimal exposure of lesion and anterior commissure. Counter pressure was applied externally on the cricoid cartilage in case of unsatisfactory exposure of anterior commissure.

The TLM was performed using CO₂ laser (Sharplan 40C, Lumenis) with scanner (SurgiTouch) and coupled with micromanipulator (AcuSpot 712) in continuous superpulse mode (4–8 weeks). The tumor was removed with a margin of 1–3 mm en bloc in case of small tumors and piecemeal resection was done in case of bulky tumors or inadequate exposure. Laser vestibulectomy was performed when the lateral or anterior portion of tumor was hidden by ventricular fold. The extent of tumor was evaluated by visualization under high magnification through operating microscope and by palpation with microforceps. The cordectomies were classified according to the European Laryngological Society classification of endoscopic cordectomies [7].

In all cases, laser photocoagulation of the surgical margins was performed after resection. The procedure consisted of vaporizing the microscopically healthy tissue in adjacent surgical area using CO₂ laser to destroy any residual cancer cell and to minimize local recurrence. No frozen section was performed.

The Voice Handicap Index (hindi version) [8] was used for subjective analysis of voice by each patient, which comprised 30 questions in 3 categories and patients were

asked to fill it up preoperatively (day before surgery), post-operatively during routine follow-up at 3 months, 1 year and 3 years respectively.

Followup

Each patient was examined every 4 weeks for first year and thereafter every 3 monthly. We did not evaluate the margin status so every patient was rigorously followed up and flexible fiber optic laryngoscopy was done each time. Biopsy was done in case of suspicious lesion on follow-up and if positive for recurrence, a CT scan of neck was done. We included the patients who were followed up for at least 36 months in the study.

Statistical Analysis

Statistical analysis was performed with SPSS program for Windows, version 23. We evaluated oncologic outcomes including overall survival, specific survival, local control with laser and organ preservation using the Kaplan–Meier survival analysis. The overall survival was defined as interval between the date of surgery and last consultation or the date of death. Disease specific survival was considered from time of surgery until death caused due to tumor or until the performance of total laryngectomy. Local recurrence was defined as carcinoma occurring after completion of primary treatment independent of the localization in the glottis area. Regional recurrence was defined as any manifestation of cervical lymph node metastasis from squamous cell carcinoma. The statistical significance was calculated using χ^2 or student-*t* test. A $p < 0.05$ was considered statistically significant.

Results

Of the 53 consecutive patients who underwent TLM, 49 were male and 4 were female, and the mean age was 53 ± 10.79 years (range 30–77 years). The tumor stages of the patients: 13pTis (24.5%), 28pT1a (52.8%) and 12pT1b (22.6%) (Table 1). All the patients were clinically node negative (N0) on physical examination and there was no case of distant metastasis. The mean follow-up was 51.49 months (min. 4/max. 77). The types of TLM performed were as follows: 16 Type 1, 5 Type 2, 20 Type 3, 2 Type 4, 4 Type 5 and 6 Type 6 (Table 1). Surgical excisions were tailor made as per the extent of the tumor guided by microscopic evaluation and laser tumor interaction.

None of the patients required tracheostomy for exposure or for compromised airway. No patients developed post-operative bleeding, infection, aspiration or subcutaneous emphysema. One patient suffered a dislocation of tooth

Table 1 Type of cordectomy according to ELSOC classification

Type of cordectomy	Tis	T1a	T1b	Frequency	Percent
1	10	6	0	16	30.2
2	1	4	0	5	9.4
3	1	17	2	20	37.7
4	0	1	1	2	3.8
5	0	0	3	3	5.7
6	0	0	1	1	1.9
9	1	0	5	6	11.3
Total	13	28	12	53	100.0

ELSOC European Laryngological Society

during surgery. The mean hospital stay was 1.5 days (range 1–3 days), most patients in our institution are discharged the next day of surgery. The discharge was delayed for patients with extensive cordectomies or with swallowing difficulty. These patients were started on anti-reflux therapy (intravenous proton pump inhibitors) but none of the patients required nasogastric (NG) feeding. Oral intake was started same evening. In late postoperative period, no patient had complications associated with surgical technique such as aspiration pneumonia, chondritis of thyroid cartilage, among others. Late complications affected 2 of our patients: one patient developed glottis web and another developed vocal cord granuloma. The glottis web was excised using CO₂ laser and a silastic keel was applied while the vocal cord granuloma subsided with the use of proton pump inhibitors.

In our study 7 patients (13.2%) developed local recurrence after a mean period of 33.29 months. None of the patients in our study developed regional or distant metastasis. Out of these 7 patients, 2 patients underwent salvage TLM, 4 patients were treated with RT and 1 with total laryngectomy. One of these patients developed second recurrence and underwent repeated TLM. 12 out of 53 (22.6%) patients had anterior commissure involvement at the time of surgery. The involvement of anterior commissure neither had impact on recurrence of disease ($p = 0.162$) nor the cure rates after TLM ($p = 0.950$).

We achieved local control with first surgery in 46 (86.7%) patients, in that 100% (13/13) were Tis, 82.14% (23/28) were T1a and 83.3% (10/12) were T1b. The ultimate local control only with TLM was 90.5%. Three year overall survival was 92.4% (Fig. 1) and three year disease specific survival was 98.1% (Fig. 2). Overall survival according to T stage was 92.3% (Tis), 100% (T1a) and 75% (T1b), with no statistically significant difference between them ($p = 0.590$) (Table 2). In our cohort only 1 patient required total laryngectomy achieving organ preservation rate of 98.1%.

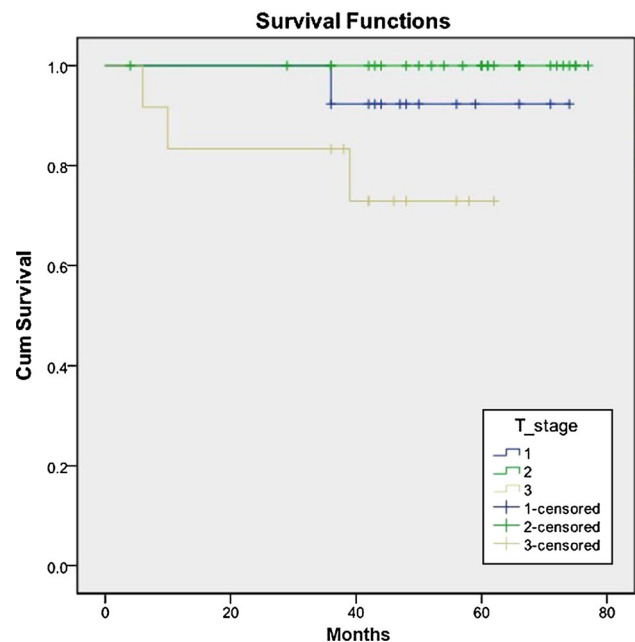


Fig. 1 Kaplan–Meier 3 year survival according to tumor stage and for all causes of death

The mean value on Voice Handicap Index-10 scores pre-operatively was 40.71 ± 18.94 . Post-operatively at 3 months mean VHI-10 score was 45.08 ± 19.30 ; at 1 year- 23.85 ± 8.58 ; and at 3 years- 21.63 ± 11.62 respectively.

During follow-up 4 patients died, 3 of unrelated causes while 1 death was reported due to disease itself. None of the patients in our study developed second primary.

Discussion

Early stage glottis cancer can be managed by OPL, RT or TLM and all of these methods provide good oncological results. So, the choice of treatment should be related to costs, time of hospitalization, rate of complications and

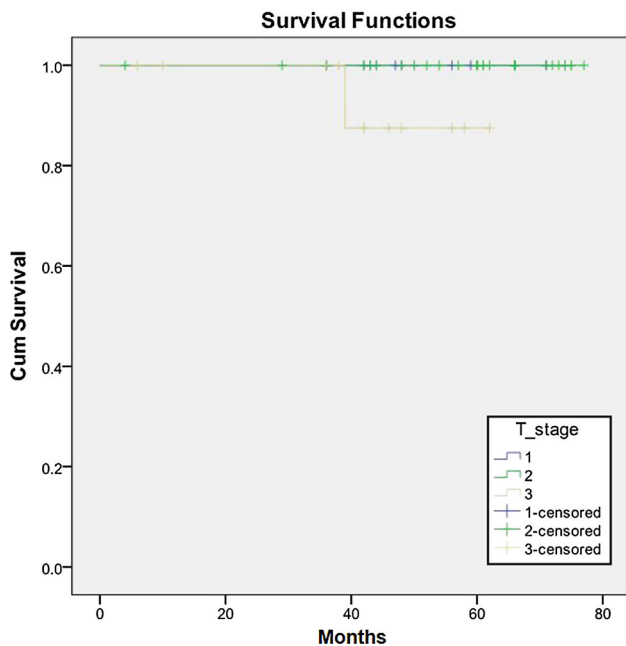


Fig. 2 Kaplan–Meier 3 year specific survival according to tumor stage

functional results. As a general rule, early stage laryngeal tumors should be approached by a single modality treatment [9, 10]. This allows preserving the chance of a second, different treatment in case of recurrence and also provides better functional results, since combined approaches are associated with worse functional outcome.

In our study, the laryngeal carcinoma was more common in men (male:female ratio of 12:1), as is well known in literature [11]. This is due to more prevalence of smoking and alcohol consumption in male population. The mean age at the time of surgery (56.3 years) was also similar to those described by other authors [12]. Hospital stay in our study ranged from 1 to 3 days, in which most of the patients were discharged next day and in case of type 5 and type 6 cordectomies, the mean hospital stay increased upto 3 days in many patients due to swallowing difficulty.

Early postoperative complications include bleeding, dysphagia, subcutaneous emphysema etc. Subcutaneous emphysema occurs when the excision of tumor reaches cricothyroid membrane [13]. Dysphagia and aspiration

pneumonia mostly occurs when the excision involves part of supraglottis i.e. aryepiglottic fold or arytenoids. The rate of these complications ranges from 3 to 19% in all the stages in literature [14–16]. None of the patients in our cohort suffered from these complications or postoperative bleeding. One of the greatest advantages of TLM over OPL is the reduced need of prophylactic tracheostomy [17]. Preuss et al. reported that around 1.9% of patients required prophylactic tracheostomy [16]. In our study, none of the patients required prophylactic tracheostomy as this may be due to strict patient inclusion criteria and experience of the operating surgeon to work in limited field. In our study, 2 patients developed late postoperative complications which included anterior glottis web and vocal cord granuloma. Anterior glottis web are clinically relevant as they shrink the glottis inlet. The glottis web was excised using CO₂ laser and a silastic keel was applied for 4 weeks. Vocal cord granulomas arise when the endoscopic resection reaches the inner perichondrium, especially in the patients with a history of gastro-esophageal reflux disease. One patient in our study developed granuloma and was started on proton pump inhibitors therapy combined with logopedic rehabilitation. The granuloma subsided and didn't require further treatment.

The impact of anterior commissure involvement on oncologic outcomes remains controversial, insignificant for some authors [10, 18–23], or implying poorer results for others [24–28]. One of the important causes of increased recurrence is the inadequate exposure during surgery. To accomplish this, a bigger laryngoscope should be used to achieve best exposure and ventricle fold resected whenever required, to completely expose anterior commissure or ventricle. Hakeem et al. [29] reported no statistically significant difference in local control in patients with and without anterior commissure involvement. In a retrospective study on 110 patients with early glottis cancer, Mortuaire et al. [30] also reported that the local control and anterior commissure are not associated. In our cohort we found that involvement of anterior commissure does not affect recurrence and thus local control rates.

The role of margin status in transoral laser microsurgery for early glottis carcinoma is still not clear. This may be due to the definition of margin is variable: some authors

Table 2 Oncological outcomes according to tumor stage

parameters	Tis (%)	T1a (%)	T1b (%)	Cumulative (%)
3 year overall survival	92.3	100	75	92.4
3 year disease free specific survival	100	100	91.6	98.1
Local control with TLM	100	82.1	83.3	86.7
Ultimate local control only with TLM	100	89.2	83.3	90.5
3 year laryngectomy free survival	100	96.4	100	98.1

routinely use 3 statuses i.e. negative, close and positive [21, 24, 31], whereas others use only positive and negative groups and consider close margin as positive [10]. The limit between positive margins and suspicious margins is difficult to establish because the edge of specimen is carbonized after laser surgery. Crespo et al. [19], Ansarin et al. [32] and Peretti et al. [33] found that positive margins were associated with high local recurrence whereas many other series [10, 20, 21, 24, 31, 34, 35] did not found any association. Hartl et al. [24] suggested that suspicious margins can be managed with a wait and watch approach and positive or suspicious margins were not related to increased rate of recurrence. It was also suggested by Lee et al. [10] that positive or suspicious margins especially in case of piecemeal resection do not mean residual disease. In study conducted by Michel et al. [34], concluded that the margin considered positive after resection do not significantly impact oncologic course, while still requiring close surveillance. Based on these we did not get the margins evaluated by our pathologist and solely depended on the expertise of the surgeon to give oncologically safe margins which in turn depends on the laser tissue interaction under high magnification. The magnification used in micro-laryngoscopy allows for very close analysis of lesion boundaries. In our study, we kept every patient under close follow-up with monthly endoscopies for first year and thereafter every 3 months. During follow-up if endoscopy showed suspicious lesion, patients were re-operated and biopsies were taken. Margin photocoagulation was done after excision of the tumor to reduce the risk of local recurrence in concurrence with the study of Lucioni et al. [36]. They concluded in their study that surgical margin laser photocoagulation increases disease local control in case of close and superficial margin positivity and no further treatment seem to be required in laser photocoagulation patients.

In different published studies, the 5 year local control rate ranged from 78 to 94% for T1 tumors [38] using the three modes of treatment previously described. The 3 year overall survival rate in our study was 92.4% for all causes of death while the 3 year disease specific survival was 98.1%. The ultimate local control only with laser was 86.7 reaching 90.5% after revision surgery and the laryngeal preservation rate was 98.1% comparable to the results reported in literature. Lee et al. [10] achieved a 5 year survival rate of 87.9%, an ultimate local control only with laser of 94.2%, a 5 year specific survival rate of 99 and 96.2% of laryngeal preservation. Galli et al. [37] reported 3 year disease specific survival, disease free survival and laryngeal preservation rates of 98.6, 84.7 and 97.2% respectively. Lucioni et al. [36], in turn, reported an overall survival rate of 90.8%, an ultimate local control only with laser of 94.3%, a disease specific survival rate of 98.8%,

and 97.7% of laryngeal preservation with a minimum follow-up of 24 months. Hartl et al. [24] also reported similar results in their study. The voice outcomes of this study were in accordance with those of previous longitudinal studies which demonstrated deterioration in immediate post-operative period (< 3 months) and improvement and stabilization in late post-operative period [39, 40].

Finally we must note the limitations of our study. The retrospective design, as well as inclusion of a single surgeon's experience without any internal comparison group, is a weakness of this study.

Conclusion

Several studies support the use of TLM in the treatment of T1a, T1b as well as T2 and well selected advanced laryngeal tumors. Our results are similar to those given in literature, showing that TLM is a safe and effective treatment of early glottis carcinoma. It is associated with less morbidity and a high percentage of local control, survival and organ preservation.

Compliance with Ethical Standards

Conflict of interest All authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in the study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any study with animals performed by any of the authors.

Informed Consent Informed consent was obtained from the participant included in the study.

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