

Evaluation of CO₂ Laser Surgery for Early Carcinoma Larynx

¹Vijay K Sharma, ²Ajith Nilakantan

¹Consultant, Department of ENT, Inlaks and Budhrani Hospital, Pune, Maharashtra, India

²Senior Adviser and Professor, Department of ENT, Army Hospital (R & R), Delhi Cantt, New Delhi, India

Correspondence: Vijay K Sharma, Consultant, Department of ENT, Inlaks and Budhrani Hospital, Pune, Maharashtra, India
e-mail:1972.vijay@gmail.com

ABSTRACT

Objective: To evaluate the effectiveness of transoral endoscopic laser surgery in the treatment of early laryngeal cancers in comparison to external radiotherapy.

Method: The patients included in the study were those who reported to the ENT department of a tertiary care hospital with early malignant lesions of the larynx.

Result: Our study revealed a local recurrence rate of 15% in the radiotherapy arm but only 10% in the CO₂ laser arm; however, this difference was not statistically significant. The only parameter in the analysis of voice which showed a statistically significant difference between the two arms was roughness which was better in the radiotherapy arm at 6 months. The major complication following transoral CO₂ laser surgery was persistent hoarseness which was seen in six patients and it resolved completely on continuation of conservative measures. Severe laryngeal edema following treatment was seen in two patients. Statistically significant difference was noted in patient acceptability in favor of CO₂ laser.

Conclusion: Endoscopic CO₂ laser surgery in early laryngeal cancer leads to similar control of the disease as with the traditional methods, with better patient acceptability, low morbidity and good functional results.

Keywords: Early carcinoma larynx, CO₂ laser, Radiotherapy.

INTRODUCTION

As clearly defined by Ferlito et al,¹ early laryngeal carcinoma is an invasive lesion confined to the lamina propria, not involving the adjacent muscles and cartilages but still capable of metastasis to the lymph nodes or distant sites. Clinically, this is usually a glottic neoplasm with full cord mobility. There is a general agreement in grouping Tis, T1 and T2 lesions together for diagnostic and therapeutic purposes.

The ideal treatment of early laryngeal cancers would be one that offer high cure rates and good voice quality, is single staged, does not require prolonged hospitalization and tracheostomy. In early laryngeal cancers, traditional treatment modalities, namely radiation therapy and open-partial laryngectomy, have comparable cure rates. While radiation therapy achieves the goal of preserving laryngeal function, the morbidity associated with prolonged duration of treatment, mucosal radiation reaction and long-term xerostomia are deterrents.

The advent of the CO₂ laser beam coupled with the microscope has revolutionized the treatment of early laryngeal cancers. The magnified view through the microscope and the precision of the laser beam allows the resection to be done with narrow margins. There is no need for a tracheostomy. In case laser therapy fails, the standard treatment modalities (radiotherapy and surgery) are still available to the patient.

The objective of this study was to evaluate the effectiveness of transoral endoscopic laser surgery in the treatment of early laryngeal cancers in comparison to external radiotherapy (the established modality of treatment in these conditions). The study was designed to determine the local control rates, posttreatment quality of voice and to identify the side effects and morbidity of early glottic cancers following transoral endoscopic CO₂ laser surgery and compare them with that following external radiotherapy. Besides, the patient acceptability of this modality of treatment vis-a-vis radiotherapy was ascertained.

MATERIALS AND METHODS

This prospective study was conducted in a sample of 40 consecutive patients treated at a tertiary care center between July 2005 to July 2007, for early carcinoma larynx with either transoral endoscopic CO₂ laser approach or radiotherapy.

The patients included were those with early squamous cell carcinoma of the larynx (glottic and supraglottic) who underwent transoral laser surgery or radiotherapy as the primary modality of treatment, with no cervical metastasis and those willing to participate in the study. Patients presenting with a synchronous second primary lesion of the head and neck, those who had undergone prior treatment in the form of either surgery or radiotherapy, those who failed to complete the minimum postoperative follow-up of 1 year,

those having lesion extending to the anterior commissure of glottis and those who had preoperative diagnosis of benign lesion of the larynx were excluded from the study. Also excluded were those patients who were medically unfit for surgery.

Written informed consent was obtained from all patients after explaining the treatment protocol and study design to them and they were alternately allotted to the surgery or radiotherapy arm.

All patients were worked up as per the MDTC protocol. Fiberoptic laryngoscopy was also done in all patients and findings recorded. Panendoscopy under general anesthesia was performed to evaluate the extent of the tumor and to rule out any second primary lesion.

All patients in the surgical arm were treated with transoral endoscopic CO₂ laser surgery. A Martin MCO 50 CO₂ laser with an adaptor (Kaps system) for mini point micromanipulator set on a continuous mode (7-50 W, 270 µm spot size) was used. Appropriate endoscopic laser cordectomies were performed as dictated by the extent of the neoplasm as preoperatively and intraoperatively defined. Wherever required the margins were confirmed with frozen section. For histopathological examination the specimen was oriented by staining the superior edge with marking ink and examined after formalin fixation and paraffin embedding.

Radiotherapy was done with teletherapy machine – THERATRON 780 E (Theratronics, Canada). The treatment plan was studied on contiguous CT slices of 5 mm thickness with a 3D convolution algorithm. Simulator (SIMULIX HP – 1200, Nucletron, Holland) was also used for planning and designing radiotherapy. The dose was prescribed to the ICRU point and ranged from 66 to 70 Gy. Conventional fractionation of 1.8 to 2.0 Gy was used.

Twenty patients who underwent transoral laser surgery and 20 patients who underwent radiotherapy were included in the study. All patients were followed up postoperatively at 2 months, 4 months, 6 months, 9 months and at 1 year. The cases recruited earlier were followed up at 18 months and 2 years also.

Local control rates were compared between the two arms and results statistically analyzed using Chi-square test. p-value of < 0.05 was considered significant. Any residual tumor present was treated with either radiotherapy (for CO₂ laser group) or by salvage surgery (radiotherapy arm).

All patients received assessment of voice both before and after intervention. Audio tape recordings of a running speech voice sample were made in a sound proof cubicle, using a 4-channel tape recorder (Sony). Recordings prior to treatment, and at 6 months and 12 months after complete treatment were analyzed by an otolaryngologist and a speech therapist, neither of whom were directly involved in treatment. Perceptive evaluation was performed with the GRBAS (Grade, Roughness, Breathiness, Asthenicity and Strain) evaluation system. A four-point rating scale (0 to 3)

was used to identify the grade of vocal handicap, for each of the five parameters. Scores at both 6 months and 1 year were compared between the two arms and analyzed statistically. Statistical evaluation of phonatory functional results was performed using Mann-Whitney test.

Side effects and morbidities related to either treatment modality were recorded at each follow-up visit. Patient acceptability was evaluated based on the convenience, complications, cost, etc. Since the treatment was given free of cost, other miscellaneous expenditure and loss of daily wages were taken into account. A questionnaire was given to the patient at the completion of treatment and was later analyzed for patient acceptability. The patients were grouped as per the scores obtained from the questionnaire into three grades, good (10-14), fair (15-19) and bad (20-24). Patient acceptability for the two arms was compared statistically using Mann-Whitney test.

RESULTS

This study group consisted of 40 patients (34 males and 6 females, mean age - 64.2 years), equally divided into the two arms. All patients were heavy users of tobacco and alcohol. The average tobacco consumption was for 20.65 years (range 10-35 years). None of these patients were a professional voice user.

The tumors were classified as carcinoma *in situ* (Tis) four patients (10%); T1 30 patients (75%); T2 six patients (15%). All the tumors in this study group were localized to the glottis and there were no case of lymph node or distant metastasis, i.e. N0 M0. Histopathologic examination of specimen obtained following CO₂ laser surgery showed a well-differentiated carcinoma (G1) in 16 patients and moderately differentiated carcinoma (G2) in four patients. Tis, T1 and T2 lesions were equally divided between the surgery and radiotherapy groups (Table 1).

A minimum of 1-year follow-up was done. Follow-up of these patients revealed recurrence in five patients, three in the radiotherapy arm and two in the CO₂ laser arm. Two of the recurrences were in patients with T1 tumor and three with T2 stage. There was no case of cervical or distant metastasis (N0 M0) during the follow-up period. Salvage surgery was done in cases of recurrence following radiotherapy, whereas radiotherapy was given to those cases where recurrence was following CO₂ laser surgery. Histopathological examination of the specimen following CO₂ laser excision revealed all to be squamous cell carcinoma.

Our study reveals a local recurrence rate of 15% (3/20) in the radiotherapy arm, 10% (2/20) in the CO₂ laser treated arm (Table 2). However, there was no statistically significant difference between the two arms, on applying Fisher's exact test and Chi-square test. On analysis of voice, the only parameter which showed a statistically significant difference between the two arms was 'Roughness', which was better

Table 1: Clinical staging/treatment

	<i>Tis</i>	<i>T1</i>	<i>T2</i>
Surgery (laser) (n = 20)	2	16	2
Radiotherapy (n = 20)	2	14	4

Table 2: Local control (at 1 year follow-up)

	<i>Tis</i>	<i>T1</i>	<i>T2</i>
Surgery (laser) (n = 20)	0/2	0/16	2/2
Radiotherapy (n = 20)	0/2	2/14	1 /4

in the radiotherapy arm at 6 months. However, this difference was not maintained at 1 year (Table 3).

Radiation resulted in progressive hoarseness, dysphagia and sore throat in six patients that increased during the 6 weeks course of treatment, but these improved on follow-up. Grade I mucositis was seen in 18 out of the 20 patients undergoing irradiation and most of these patients also had mild-to-moderate laryngeal edema. Conservative measures such as antibiotics, steroids, voice rest and smoking cessation resolved these ailments. Severe laryngeal edema persisting more than 3 months after treatment occurred in six patients. All of them were biopsied, which showed tumor recurrence in three patients. These were subjected to salvage surgery, whereas in the remaining three patients laryngeal edema resolved completely on continuation of conservative measures.

Table 5: Patient acceptability

	<i>Good</i>	<i>Fair</i>	<i>Bad</i>
Surgery (laser) (n = 20)	14	6	0
Radiotherapy (n = 20)	2	15	3

The major complication following transoral CO₂ laser surgery was persistent hoarseness which was seen in six patients and it improved on continuation of conservative measures. Severe laryngeal edema persisting more than 3 months after treatment was seen in two patients. These patients were biopsied which showed tumor recurrence. They were therefore subjected to radiotherapy. Temporary tracheostomy had to be performed in one patient who had developed postoperative laryngeal edema and stridor. Other minor complication like aspiration pneumonia was seen in one patient; it resolved on medical management (Table 4).

Statistical comparison of the scores of the questionnaire for evaluation of patient acceptability by Mann-Whitney test revealed that patients in the CO₂ laser arm showed greater acceptability. The difference was seen to be statistically significant (Table 5). It was interesting to note that the average duration of hospital stay in the surgical arm was 2.2 days. Three patients in the radiotherapy arm who had local recurrence, considered the treatment poor.

DISCUSSION

We have followed the existing accepted convention regarding the definition of early laryngeal cancer, which limits it to Tis, T1 and T2 glottic and supraglottic cancers

Table 3: Assessment of voice

Average values of perceptive evaluation GRBAS scale	<i>At 6 months</i>					<i>At 12 months</i>				
	G	R	B	A	S	G	R	B	A	S
Surgery (laser) (n = 20)	1.2	1.1	0.8	1.0	0.8	0.4	0.4	0.6	0.5	0.5
Radiotherapy (n = 20)	0.8	0.2	0.2	1.0	1.0	0.5	0.3	0.3	0.3	0.5

Table 4: Side effects and morbidity

	<i>Mucositis</i>	<i>Edema (>3 months)</i>	<i>Persistent hoarseness</i>	<i>Temporary tracheostomy</i>	<i>Others</i>
Surgery (laser) (n = 20)	0	2	6	1	1
Radiotherapy (n = 20)	18	6	6	0	0

with node negative neck (N0). However, no supraglottic cancer meeting these characteristics could be enrolled in the study. Thus, all the tumors in this study group were localized to the glottis, and there were no case of lymph node or distant metastasis, i.e. N0 M0.

CO₂ laser surgery for early carcinoma has been shown to be oncologically effective, as per several studies, showing a local control rate varying from 87 to 96%.^{2,3} Other treatment modalities such as radiotherapy and open neck procedures offer similar results.⁴ Our study shows 90% local control rate in the laser group and only 85% in the radiotherapy arm; however, this difference is seen not to be statistically significant. Thus, our results are similar when compared with the previously published reports.²⁻⁴

Involvement of the anterior commissure seems to reduce the likelihood of local tumor control for both radiotherapy⁵ and especially for transoral CO₂ laser excision, but this finding is not universally accepted. In any case, our study excluded all patients with anterior commissure involvement. Reduced cord mobility in T2 lesions may negatively influence treatment outcome. This was seen in three patients, where initial evaluation revealed impaired cord mobility and later on during follow-up recurrence was noticed.

The controversy about voice results after transoral CO₂ laser excision versus radiotherapy is still ongoing.^{6,7} The rationale given for selecting radiotherapy rather than surgery for the treatment of early carcinoma larynx is that this modality can better preserve voice quality. This assumption is based on subjective voice assessments made by either the patient or a health care provider. Kaiser et al⁸ evaluated the voice quality of 102 patients who had undergone radiotherapy and observed that 59% had good voices, 5% had fair voices and 36% had poor voices. This report was in contrast to a study by a group of radiation oncologists at Mayo clinic⁹ who reported on their voice assessment of 57 patients treated with radiotherapy. A physician subjectively determined the voice quality to be excellent in 9%, good in 70%, fair in 18% and poor in 4%. The problem with subjective voice studies is that they may be insensitive to small voice changes and that they may be subject to biases on the part of those who do the judging.

In our study, quality of voice after laser surgery was inferior to that after treatment with full dose radiotherapy, as assessed by perceptual variables, a finding consistent with those of some earlier studies.^{8,9} However on statistical analysis with Mann-Whitney test, the only parameter which showed a statistically significant difference between the two arms was 'Roughness' which was better in the radiotherapy arm at 6 months. But this difference was not maintained at 1 year. There was no significant difference as far as grade, breathiness, asthenia and strain are concerned. Overall, these results may be taken to show slightly inferior voice quality after laser surgery compared to radiotherapy.

It has been demonstrated that radiotherapy involves the unaffected cord, producing irregular vocal folds and

decreased vibrations and this too contributes to jeopardized postoperative voice outcome.⁷ Furthermore, altered microcirculation of the vocal folds, loss of salivary glands, mucositis, fibrosis, and edema may result from radiotherapy and negatively affect the voice.

In contrast to radiotherapy, transoral CO₂ laser excision preserves the contralateral vocal fold and the mucous secreting glands that are important for vocal fold lubrication. In transoral CO₂ laser excision, the postoperative voice outcome depends upon having a straight postoperative vocal fold for glottic closure and intact vibration from the contralateral vocal fold.

Eighteen of our patients developed radiation-induced mucositis, while six developed hoarseness. These subsided with conservative treatment. Many irradiated patients have mild or moderate laryngeal edema following treatment. Severe laryngeal edema persisting 3 months after treatment occurs in 1.5 to 4.6% of cases and could be a sign of persistent or recurrent tumor, and biopsy must be done if edema persists.¹⁰ Persistent edema beyond 3 months was seen in six of our patients. Biopsy was done which revealed tumor recurrence at the primary site in three cases.

In a review of 39 transoral CO₂ laser excision patients, Pearson and Salassa sent 12 patients home on the day of procedure, performed 11 temporary tracheostomies and hospitalized patients for an average of 3.3 days.¹¹ Wolfensberger and Dort reported persistent hoarseness in 1/3 of the 52 transoral CO₂ laser excision patients they resected. In a review of transoral CO₂ laser excision from Barcelona, complications were identified in 18.9% of 275 patients. These complications included local infection (0.7%), emphysema (1%), cutaneous fistula (0.3%), postoperative bleeding (8%), dyspnea (1.8%) and aspiration pneumonia/swallowing difficulty (6.1%).¹² As the pattern of complications was expected to be different in the two arms, no attempt at statistical comparison of the complication rates was made. However, our results show a similar rate of complications as compared with other studies, in both the arms.

A questionnaire based on the criteria of convenience, cost, loss of wages, etc, was used in our study to determine patient acceptability of a treatment modality. As cost was not a major factor, and treatment was given free of cost to all patients, duration of hospitalization and loss of wages played a leading role. Besides radiotherapy involved 27 to 33 visits, whereas transoral CO₂ laser excision involved on an average 2.2 days of hospitalization. Statistical comparison of the scores of the questionnaire by Mann-Whitney test revealed that patients in the CO₂ laser arm showed greater acceptability. The difference was seen to be statistically significant. However, some patients in our study favored radiotherapy because they could continue working full time during the entire course of treatment. Three patients in the radiotherapy arm, who had local recurrence, considered the treatment poor.

CONCLUSION

The stated advantages of an endoscopic transoral CO₂ laser excision approach over other modalities are a good oncologic result with reduced surgical trauma, conservation of the cartilaginous skeleton, rapid postoperative recovery period with a short hospital stay and extremely low incidence of intra- and postoperative complications. From our study, we conclude that the endoscopic CO₂ laser approach leads to similar control of the disease as with the traditional methods, with better patient acceptability, low morbidity and good functional results.

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