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RESEARCH ARTICLE

Transoral Laser Microsurgery *vs* Radiotherapy for Early Glottic Cancer: Study at Tertiary Care Center in India

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ABSTRACT

Aim: To compare laryngeal preservation rates, survival rates, and voice outcomes after treatment of early glottic cancer between transoral laser microsurgery (TLM) and radiotherapy (RT).

Materials and methods: A review of oncologic results was performed on a consecutive series of individuals with early-stage glottic carcinoma (T1 and T2) who were treated between 2011 and 2014 at Kidwai Memorial Institute of Oncology and had received either RT or TLM. Data were collected with a view to assess overall survival, disease-specific survival, laryngectomy-free survival, and laryngeal preservation rates. The Voice Handicap Index-30 (VHI-30) was used as the measure of voice quality after treatment.

Results: Two-year overall survival for TLM group was 93.8% and for RT group was 90.5%, p = 0.643. Disease-free survival (TLM = 90.6% *vs* RT = 76.2%) was not found to be significant (p-value = 0.104). Laryngeal preservation rate was 79.5% in TLM and 71.4% in RT group (p-value = 0.003). Laryngectomy-free survival was better in TLM (TLM = 96.9% *vs* RT = 76.2%, p = 0.003). Substage analysis showed equivalent voice for TLM (VHI = 6–12) and RT (VHI = 6–14) in T1a patients (p = 0.94), whereas voice outcome was better for RT in T1b (VHI = 10–16 for TLM *vs* VHI = 11–18 for RT, p = 0.044) and T2 (VHI = 21–29 for TLM *vs* VHI = 16–23 for RT, p = 0.002) stages.

Conclusion: Transoral laser microsurgery can be considered the treatment of choice for early glottic cancer in view of better laryngeal preservation rate and laryngectomy-free survival with added advantage of low treatment cost and shorter hospital stay compared with RT.

Clinical significance: Laryngeal cancers represent the most common malignancy of head and neck, with estimated worldwide incidence of 120,000 cases annually. Optimal treatment modality has generated significant controversy in literature. External beam RT, open partial laryngectomy, and TLM are various treatment options available. This study depicts TLM as a preferred modality for early glottic cancer.

Keywords: Glottic cancer, Laser, Radiotherapy.

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INTRODUCTION

Laryngeal cancer is a common malignancy of head and neck, with an incidence of 120,000 cases per year worldwide. Due to early appearance of symptoms, large number of cases present in early stage of cancer.[1,2]

Early-stage glottic cancer is highly curable with excellence locoregional control rates of 90%, as regional lymph node metastasis is rare in realms of paucity of lymphatic drainage.[3]

Goals of treatment are cure, preservation of voice quality, and minimization of serious complications. Various treatment modalities for early glottic cancer include radiotherapy (RT), open partial laryngectomy, and conservation in the form of transoral laser microsurgery (TLM).[4,5]

Transoral laser microsurgery, an emerging modality with various advantages, was first performed by Strong and Jako in 1972.[6]

Various advantages of TLM over RT are shorter duration of treatment, less posttreatment morbidity, no contraindication for retreatment after recurrence, relatively lower cost, better laryngeal preservation, better quality of life, while quality of functional outcome, particularly voice quality, is still questionable after treatment by TLM.[7,8]

However, it still remains an issue of concern as there is no appropriate controlled studies comparing both the modalities (TLM and RT) that can produce reliable

Table 1: Voice handicap index (VHI-30)

Part I - F (functional)	*Never*	*Almost never*	*Sometimes*	*Almost always*	*Always*
F1. My voice makes it difficult for people to hear me	0	1	2	3	4
F2. People have difficulty understanding me in a noisy room	0	1	2	3	4
F3. My family has difficulty hearing me when I call them throughout the house	0	1	2	3	4
F4. I use the phone less often than I would like to	0	1	2	3	4
F5. I tend to avoid groups of people because of my voice	0	1	2	3	4
F6. I speak with friends, neighbors, or relatives less often because of my voice	0	1	2	3	4
F7. People ask me to repeat myself when speaking face-to-face	0	1	2	3	4
F8. My voice difficulties restrict personal and social life	0	1	2	3	4
F9. I feel left out of conversations because of my voice	0	1	2	3	4
F10. My voice problem causes me to lose income	0	1	2	3	4
Part II - P (physical)					
P1. I run out of air when I talk	0	1	2	3	4
P2. The sound of my voice varies throughout the day	0	1	2	3	4
P3. People ask, "What's wrong with your voice?"	0	1	2	3	4
P4. My voice sounds creaky and dry	0	1	2	3	4
P5. I feel as though I have to stain to produce voice	0	1	2	3	4
P6. The clarity of my voice is unpredictable	0	1	2	3	4
P7. I try to change my voice to sound different	0	1	2	3	4
P8. I use a great deal of effort to speak	0	1	2	3	4
P9. My voice is worse in the evening	0	1	2	3	4
P10. My voice "gives out" on me in the middle of speaking	0	1	2	3	4
Part III - E (emotional)					
E1. I am tense when talking to others because of my voice	0	1	2	3	4
E2. People seem irritated with my voice	0	1	2	3	4
E3. I find other people do not understand my voice problem	0	1	2	3	4
E4. My voice problem upsets me	0	1	2	3	4
E5. I am less outgoing because of my voice problem	0	1	2	3	4
E6. My voice makes me feel handicapped	0	1	2	3	4
E7. I feel annoyed when people ask me to repeat	0	1	2	3	4
E8. I feel embarrassed when people ask me to repeat	0	1	2	3	4
E9. My voice makes me feel incompetent	0	1	2	3	4
E10. I am ashamed of my voice problem	0	1	2	3	4

result and can decide the superiority of one modality over another.

The present study compares both the modalities (TLM and RT) with special reference to oncological and voice outcomes.

Voice outcome was measured by using Voice Handicap Index-30 (VHI-30), a 30-item self-administered questionnaire that asks an individual to describe their voice and the effects of their voice on their life. Three subscales cover the areas of functional, emotional, and physical aspects of voice disorders (Table 1).[9]

The VHI is a validated and reliable tool for objective assessment of VHI. It requires less time to administer, and is easy to score and interpret. Points from the questions were combined to assign a total score. The severity of dysfunction is graded as mild, moderate, and severe, and shown in Table 2.

Table 2: Severity of dysfunction

Scale	*Mild*	*Moderate*	*Severe*
Functional	>10	>12	>18
Physical	>15	>18	>22
Emotional	>8	>13	>20
Total	>33	>44	>61

MATERIALS AND METHODS

This is a retrospective study done from July 2011 to June 2014 in the Department of Head and Neck Oncology at Kidwai Memorial Institute of Oncology, Bengaluru, India. All patients with early glottic carcinoma (T1 and T2 stage) who were treated by TLM and RT were included in the study. Patients were staged using 90° Hopkins endoscopy and flexible fiberoptic endoscopy and in some cases by computed tomography or magnetic resonance imaging, especially when the tumor was at anterior commissure and in T2 tumors where extent could not be determined on endoscopy. Patients who were lost to follow-up, having other diseases affecting function of upper aerodigestive tract, or who were diagnosed with second head and neck carcinoma were excluded from the study. The data were collected from hospital records of early glottic cancer patients treated by TLM and RT during this time period.

All the patients were followed up for a minimum period of 2 years. During the follow-up period, voice outcome was assessed by VHI of all patients for 2 years following treatment. Validated and translated version of questionnaire in local language (Kannada) was used to assess VHI.[10]

Oncological outcomes including overall survival, disease-free survival, laryngeal preservation rate, and laryngectomy-free survival were analyzed at the end of 2 years.

Statistical Package for the Social Sciences version 21 was used for statistical analysis. Student's t-test was used to analyze continuous, normally distributed variables, and Fisher's exact test was used to analyze nominal variables. All statistical testing was performed using an intention to treat analysis unless otherwise stated in the results. Log-rank (Mantel-Cox) survival analyses were performed for disease-free survival, laryngectomy-free survival, and overall survival. Pearson's chi-square was used to analyze laryngeal preservation rate.

RESULTS

A total of 85 early-stage glottic cancer (T1a, T1b, T2) patients were treated between July 2011 and June 2014 in the Department of Head and Neck Oncology at our institute by TLM (n = 64) and by RT (n = 21). Among all patients treated by TLM, 25 patients were in stage T1a, 18 patients were in stage T1b, and 21 patients were in T2. Whereas among all patients treated by RT, 8 patients were in stage T1a, 6 patients were in stage T1b, and 7 patients were in T2 (Table 3).

The following parameters were analyzed at the end of the study:

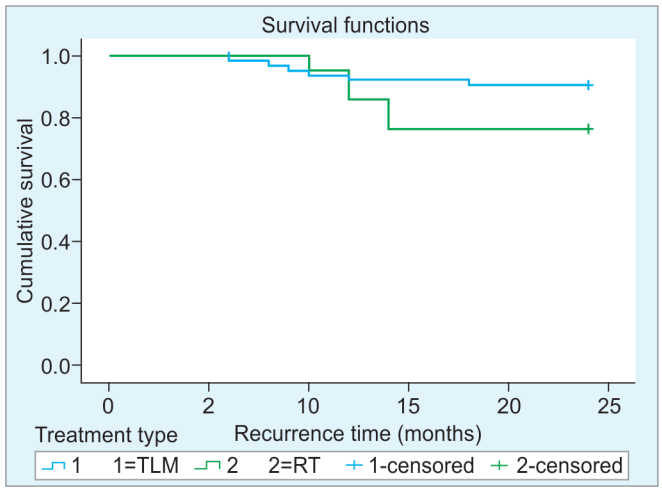
- Recurrence

  Six patients recurred between 6 and 18 months in TLM group; of this 3 patients were treated by RT, 1 patient by TLM, and 2 patients by laryngectomy as secondary treatment.

  Five patients recurred between 10 and 14 months in the RT group, of which all patients underwent laryngectomy as a secondary treatment. Disease-free survival was calculated between two groups (TLM = 90.6% *vs* RT = 76.2%) and was not found to be significant (p-value = 0.104). A substage analysis for disease-free survival was also insignificant between the two groups (Graphs 1 and 2A to C).

Table 3: Stage distribution between two groups

Treatment	*Number of patients*	*Stage distribution*
Transoral laser microsurgery group	64	T1a = 25(39%) T1b = 18(28%) T2 = 21(33%)
Radiotherapy group	21	T1a = 8(38%) T1b = 6(28%) T2 = 7(34%)



Graph 1: Disease-free survival

- Survival

  Four patients died in TLM group between 13 and 20 months, of which 1 patient was in T1b, and 3 patients were in T2, whereas 2 patients died in RT group at 20 and 22 months after initial treatment, both patients were in T2 stage. Two-year overall survival for TLM group was 93.8% and for RT group was 90.5%; p = 0.643, not significant (Graph 3).

  On substage analysis for 2 years, overall survival between the two groups was also not significant (Graphs 4A and B).

- Laryngeal Preservation Rate

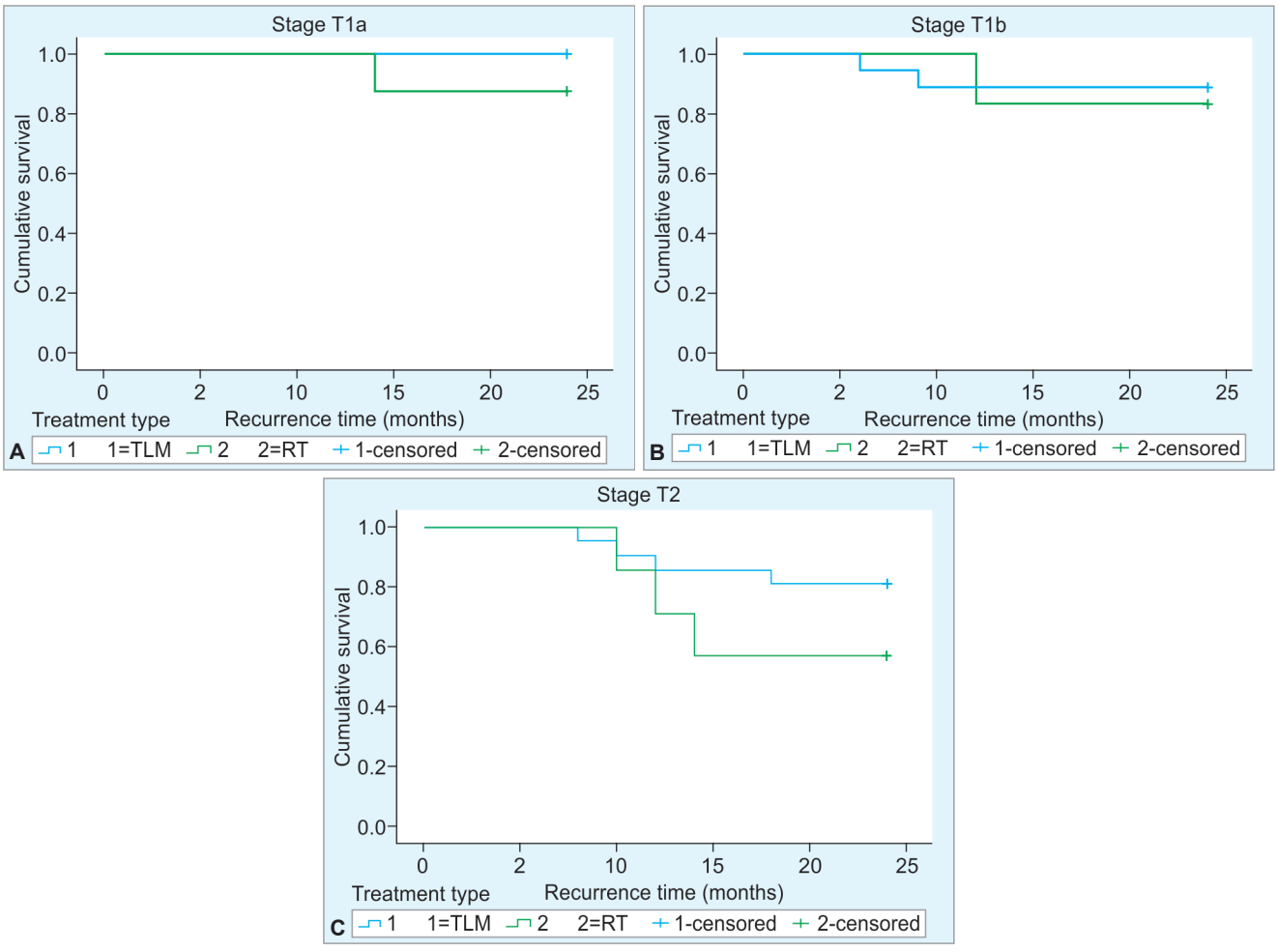
  Among the TLM group, 2 patients underwent laryngectomy following recurrence, whereas in RT group all 5 patients were treated by laryngectomy following recurrence. Laryngeal preservation rate was 79.5% in TLM and 71.4% in RT group (p-value = 0.003, significant). Laryngectomy-free survival was found to be better among patients treated by TLM (TLM = 96.9% *vs* RT = 76.2%, p = 0.003, significant) (Graph 5).

- Voice Outcome

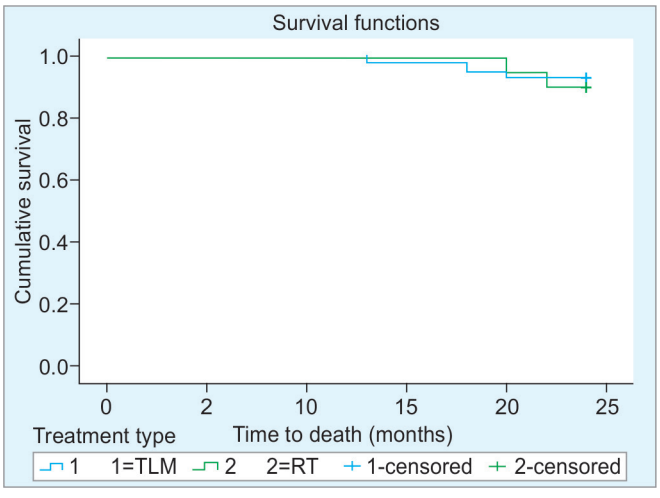
  Voice outcome was calculated in all patients by using VHI at 2 years after initial treatment. On substage analysis, it was found that voice outcome was equivalent for TLM (VHI = 6–12) and RT (VHI = 6–14) for T1a patients (p-value = 0.94). However, voice outcome was better for RT in T1b (VHI = 10–16 for TLM *vs* VHI = 11–18 for RT, p = 0.044) and T2 stages (VHI = 21–29 for TLM *vs* VHI = 16–23 for RT, p = 0.002), reaching statistical significance.

- Cost Analysis

  Overall cost of treatment by laser surgery at our institute comes to approximately 200-300 USD. And treatment by three-dimensional conformal RT and intensity-modulated RT comes to around 750 to 1000 USD and 1500 USD respectively.



Graphs 2A to C: (A) Disease-free survival of stage T1a; (B) disease-free survival of stage T1b; and (C) disease-free survival of stage T2



Graph 3: Overall survival

In laser surgery, the patient is discharged on the next day, whereas duration of treatment with RT is approximately 1.5 months, which further increases the cost of treatment.

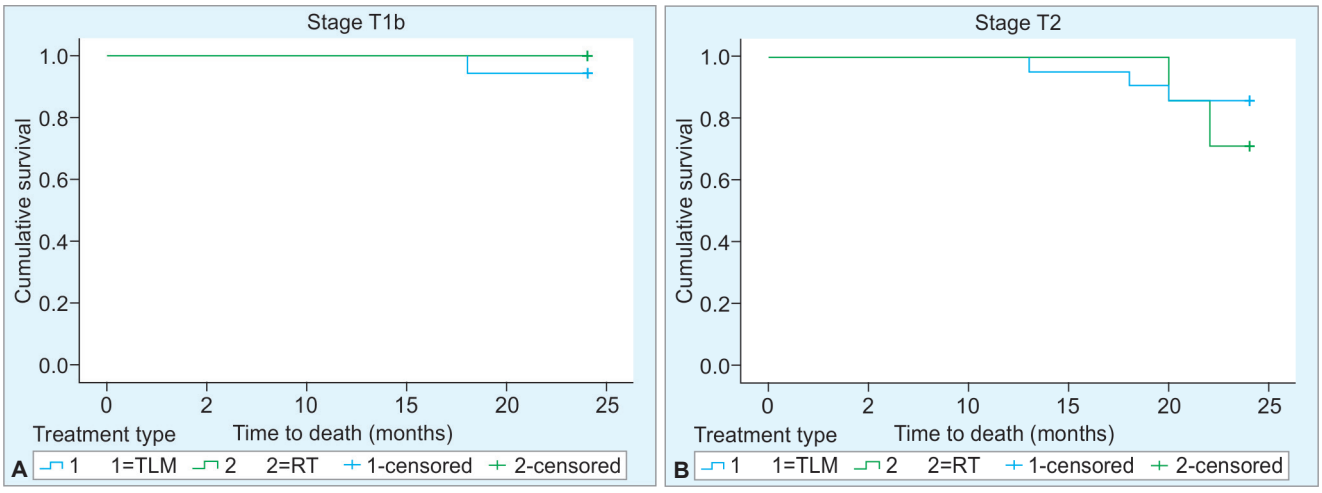
DISCUSSION

Various options for treatment of early glottic cancer include open partial laryngectomy, transoral laser (TOL) excision, and RT. Choice of treatment depends on T-stage of the disease, patient preference, surgeon preference, policy at the institute, and availability of resources. Out of these three modalities, RT and laser excision are equally recommended.[11] The utility of TLM in glottic cancer was popularized by Steiner in the 1980s.[12,13]

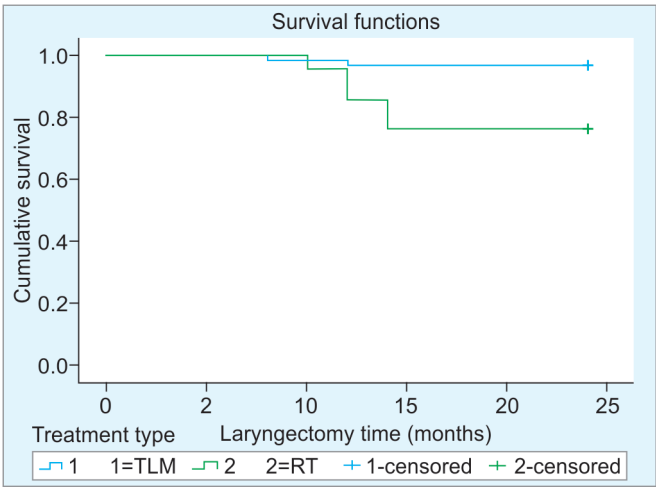
Major advancement in laser surgery was coupling of binocular operating microscope with a laser delivery system. CO_2 laser is the most commonly used laser for laryngologic surgeries, provides very precise resection due to small aiming beam's spot size, and hence, the tissue destruction is monitored carefully. Another added advantage of CO_2 laser is availability of both continuous wave and pulse wave mode, which can be used for both coagulation and cutting mode.

The study conducted by Lin and Prisman[14] showed laser surgery as an effective alternative for RT and partial laryngectomy for treatment of early glottic cancer. They observed better oncological and functional outcome.

Another study by Ansarin et al[15] on 460 patients of TLM for early glottic cancer showed significantly better result with respect to outcome, local disease control, feasibility and postoperative morbidity and



Graphs 4A and B: (A) Overall survival T1b; and (B) Overall survival T2



Graph 5: Laryngectomy-free survival

concluded that TLM should be offered as an alternative to conventional RT.

The meta-analysis performed by Higgins et al[16] showed no significant difference in local control and oncologic outcomes between patients treated with external radiotherapy (XRT) and those treated with TOL surgery, whereas voice outcomes were found to be better in RT treatment group.

Other studies done by McGuirt et al[17] and Wedman et al[18] showed no difference in voice quality between both the groups when subjective and objective measures were analyzed.

Similarly, the study of Kerr et al[19] showed equivalent oncologic outcomes in both the groups in stage 1 and stage 2 glottic cancers, while organ preservation rate was trending toward CO_2 laser group.

Mendenhall et al[3] described three criteria for deciding the modality: Local control, voice quality, and cost. Their meta-analysis showed local control rate of 80 to 90% for T1 and 70 to 85% for T2 by laser resection, 90 to 95% for T1, and 70 to 90% for T2 by open partial laryngectomy, 85 to 94% for T1 and 70 to 80% for T2 by RT. They recommended to treat all T1 and T2 with XRT while T1a may be given the option of TOL resection.

The study conducted by Agrawal and Ha[20] showed trends toward decrease in open procedures and improved rates of local control with laser surgery and XRT. Their results showed local control rate including salvage therapy of 97 to 98%, laryngeal preservation of 90 to 99%, and 5-year disease-specific survival of 90 to 98% by TOL resection, whereas local control rate including salvage therapy is 90 to 96%, laryngeal preservation is 83 to 95%, and 5-year disease-specific survival is 95 to 98% by RT. They concluded that laser resection and radiation therapy are equally effective.

Meta-analysis done by Cohen et al[21] regarding voice-related quality of life included six studies with 208 patients (6 T1b and 202 T1a) treated with carbon diode laser excision (CLE) and 91 patients (6 T1b and 85 T1a) treated with external beam radiotherapy (EBRT). The posttreatment VHI scores were similar for the EBRT- and CLE-treated patients ($p = 0.1$).

This study shows that laser and RT are equivalent as far as overall and disease-free survival are concerned. However, it was noted that laryngeal preservation rate and laryngectomy-free survival were better following TLM as compared with RT; this is in consonance with few recently published studies. Previous studies comparing voice quality between both modalities have shown mixed outcomes, with most of them trending in favor of RT, whereas substage analysis in this study revealed that for stage T1b and T2, RT was significantly better than TLM for voice outcome, but for stage T1a TLM it was found equivalent to RT.

CONCLUSION

Transoral laser microsurgery can be considered as the treatment of choice for early glottic cancer in view of

better laryngeal preservation rate and laryngectomy-free survival, with added advantage of low cost of treatment and shorter hospital stay as compared with RT.

Limitation of our study is that it is a retrospective analysis with shorter duration of follow-up. However, a large, controlled study will be more helpful to draw effective conclusion.

CLINICAL SIGNIFICANCE

The present study shows that TLM is superior to RT, because of better laryngeal preservation rate and laryngectomy-free survival with equivalent disease-free and overall survival. Substage analysis also concludes that TLM is equivalent to RT for voice outcomes. It also depicts that the cost and duration of treatment is significantly less with TLM as compared with RT.

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