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A comparative study of short-term phonatory outcomes in primary cases of early glottic cancer treated with radiotherapy versus laser surgery

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Abstract

Background Early-stage glottic carcinomas can be treated with either laser surgery or radiotherapy. Both approaches have demonstrated similar cure rates. However, the question of which modality is superior in terms of voice outcomes remains a topic of debate.

Methods In our study, we conducted a comparison of short-term phonatory outcomes in patients with primary early glottic cancer who underwent treatment using both modalities. We assessed these outcomes using videostroboscopy and voice analysis software at three time points: immediately following treatment, at 1 month, and at 3 months post-treatment.

Results Voice analysis revealed that laser surgery had a more favorable immediate effect compared to radiotherapy in parameters such as jitter, shimmer, harmonics-to-noise ratio, and fundamental frequency. However, at the 3-month post-treatment mark, both treatment modalities demonstrated similar effects. Additionally, both modalities had comparable effects on maximum phonation time. Videostroboscopy observations showed that mucosal wave forms were more prominent immediately after laser surgery and gradually improved following radiotherapy. Furthermore, patients with incomplete glottic closure experienced recovery after both treatment modalities.

Conclusion Based on the results, there are better outcomes immediately following LS compared to RT. However, after a 3-month period, the outcomes of both treatment modalities become comparable. The treating physicians must consider various factors such as complications, patient-specific considerations, treatment costs, and duration to make informed decisions. A personalized approach considering the individual patient's circumstances is crucial in achieving optimal results in the management of T1 laryngeal cancer.

Keywords Glottic carcinoma, Laser surgery, Radiotherapy, Videostroboscopy, Voice analysis

Background

Early-stage glottic carcinomas are treated with a single modality of treatment, which can be surgery or radiotherapy. All the modalities available offer similar results in treatment of early glottic carcinoma giving a cure rate of approximately 90% [1]. Keeping this in view, post treatment voice quality plays an important role while considering the modality.

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Both surgery and radiotherapy cause some complications to voice. The extent of the surgery will depend on the location and extent of tumor. Surgery can leave a tissue deficit due to the tumor excision and stiffness due to scarring. The deficit may leave a phonatory gap during the adduction of vocal folds resulting in wastage of air, breathy voice, inadequate loudness, and short duration of phonation. The stiffness of the surrounding tissue may lead to impaired mucosal waves due to irregular vocal fold vibration.

Radiation can cause swelling of the mucosa followed by dryness and stiffness of the vocal folds. The long-term effects of radiation include fibrosis of soft tissue, which limits the normal range of mucosal wave formation leading to damage to voice [2].

There is continuing debate whether radiation therapy or surgery is superior in treatment of early glottic cancer in terms of voice outcome. The comparison of voice quality post treatment in early-stage squamous cell carcinoma larynx treated with surgery versus radiation has been studied by researchers and there are numerous studies reporting that voice outcome in patients of glottic carcinoma is comparable whether they are treated with surgery or radiotherapy. However, some researchers have concluded that surgery is the first treatment of choice with good functional and oncological outcomes. On contrary to it, there is also evidence that voice parameters were better in patients treated with radiotherapy. The evidence to date is insufficient to resolve the controversies, particularly because of the paucity of prospective randomized controlled trials.

Keeping all this in view, there is further scope to study and compare the phonatory outcomes objective parameters in patients of early glottic cancer treated with surgery or radiotherapy. In our study, we compared the short-term phonatory outcomes in primary cases of early glottic cancer treated with radiotherapy (RT) versus laser surgery (LS).

Methods

Study design

After approval from the Institutional Ethics Committee, a tertiary-level hospital based prospective observational study was carried out over a period of 2 years from October 2019 to September 2022 at our center. All the patients reporting to our center were screened as per the inclusion and exclusion criteria (Table 1), and the eligible patients were registered. The study was carried out after obtaining written and informed consent.

Detailed ENT examination was done. Videolaryngoscopy was done using Hopkin's telescope to determine the extent of lesion and vocal cord mobility. All the patients underwent contrast-enhanced computed tomography (CECT) of the base of the skull to the mediastinum to determine the extent of lesion, nodal status, and presence of any secondary lesion.

All patients who were clinico-radiologically T1a/T1bN0M0 underwent pretreatment assessment of phonation using videostroboscopy and voice analysis software. Objective analysis of voice was done using the "Praat" software. The patient was asked to take a deep breath and phonate a vowel and sustain it to the maximum. The voice was recorded using the Logic Pro software via Focusrite Scarlett 2i2 audio interface and mic in a soundproof room. Parameters like jitter, shimmer, harmonics-to-noise ratio, fundamental frequency (F0), and maximum phonation time (MPT) were measured using the Praat software. Videostroboscopy was done using Karl Storz 70° rigid telescope and Invisia Highlight Basic model stroboscope. The videostroboscopy study included the analysis of parameters like glottic closure and mucosal wave.

Both videostroboscopy and voice analysis were done prior to biopsy, as biopsy can alter pre-treatment phonation status. The patients underwent hematological and biochemical investigations, chest x-ray, electrocardiogram, ultrasound abdomen, and pre-anesthetic checkup. After getting fitness for surgery, all the patients underwent microlaryngoscopy, mapping of disease, and biopsy from the lesion for histopathological examination. Staging of the disease was done after confirming the

Table 1 Criteria for selection of patients

Inclusion criteria	• Patients with previously untreated primary glottic cancer (T1a/T1b N0M0)
Exclusion criteria	• All advanced cases of glottic cancer (T2, T3, T4, N+, and M+) • All recurrent cases • Cases with prior exposure of radiation to neck • Cases with pre-existing vocal cord palsy • Cases with central speech pathology • Patients on tracheostomy • All patients with poor pulmonary reserve

histopathology. Patients underwent treatment after the decision of the joint tumor board of the hospital as per standard guidelines in consultation with the patients.

Surgical arm

Transoral laser cordectomy was performed in patients who underwent LS. Lumenis Acupulse 40ST CO2 laser machine was used. Endoscopic laser cordectomy was performed using 4 W continuous CO_2 laser, super pulse mode, as dictated by the extent of the neoplasm. Specimen was then sent for histopathological examination.

Radiation arm

RT was given by Theratron-1000E, Cobalt 60 teletherapy machine (Siemens). Treatment plan was made on Radiotherapy Simulator Siemens 3000. Target volume encompassed the larynx, sparing the suprahyoid epiglottis. Lateral parallel-opposed photon fields were used: superior border—top of the thyroid cartilage for T1 lesion and supraglottic extension for T2 lesion; anterior border—approximately 1 cm fall off; posterior border—anterior margin of vertebral bodies; and inferior border—lower margin of the cricoid. The dose given in T1 lesions was 63 Gy in 28 fractions, and for microscopic disease, it was reduced to 60 Gy with 30 fractions.

Post operative follow-up

All patients were be followed up post treatment. Fifteen cases who underwent RT were categorized to group A, and 15 cases who underwent LS were categorized to group B. Phonatory outcomes were assessed objectively using videostroboscopy and voice analysis software respectively at immediate (0) and 1 and 3 months following the treatment.

A comparison of the short-term phonatory outcomes at immediate (0) and 1 and 3 months following the treatment with RT versus LS was made. Qualitative and quantitative data obtained from the two study groups were corelated for significant statistical differences.

Results

Acoustic analysis of voice

Acoustic analysis of voice was done at pre-treatment, immediate post treatment, and 1 and 3 months post treatment. The quantitative included jitter, shimmer, harmonics-to-noise ratio (HNR), maximum phonation time (MPT), and fundamental frequency (F0). A repeated measures ANOVA with a Greenhouse–Geisser correction was used. The difference between time points and the interaction effect between time and treatment are determined. Post hoc analysis with a Bonferroni adjustment was done to study the effects of individual treatment. Comparison of values at different time points under laser surgery versus radiotherapy was done using Welch two sample *t*-test.

In our study, voice analysis showed immediate increase in jitter and shimmer values following RT compared to pre-treatment. Then, the values reduced gradually. However, at 3 months post treatment, both the modalities have almost same effects (Figs. 1 and 2). HNR decreases immediately after radiotherapy. At the same time, laser surgery shows a consistent increase in HNR over time. At 1 month and 3 months, both the modalities give similar effects on HNR (Fig. 3). Both the modalities showed similar effects on MPT (Fig. 4). There is a significant difference between LS and RT in the pre-treatment F0 values. There is no immediate effect from laser surgery on F0. But a gradual decrease to normal values can be observed after 1 month and 3 months. Radiotherapy showed an immediate increase in fundamental frequency which gradually normalized by 3 months (Fig. 5).

Analysis of videostroboscopy observations

Videostroboscopy analyzed qualitative parameters including mucosal wave and glottic closure. The McNemar test was done to study the effect of treatment as well as the comparison of both the modalities. On videostroboscopy, mucosal wave was absent in all patients prior to treatment, and it immediately forms after laser surgery and gradually after radiotherapy. Patients with incomplete glottic closure pretreatment immediately recovers after both laser surgery and radiotherapy (Fig. 6).

Discussion

Laryngeal carcinoma is the second most common malignancy in the respiratory tract after lung carcinoma. It accounts for 30–50% of all the malignant head and neck tumors and 1–2% of all malignancies in the body. In terms of histopathology, 95–98% of all laryngeal cancers are squamous cell carcinoma (SCC) [3]. The age of our patients ranged between 50 and 69 years. The mean age was 61 years. In our study, 46% specimens were reported to be differentiated SCC on HPE, and 54% were moderately differentiated SCC, which is similar to the results obtained in studies by De Stefani et al. [4].

Early glottic carcinoma is treated with a single modality treatment, which generally includes RT or surgery. Both the modalities have shown excellent loco-regional control and survival rates, which are comparable in both the arms of treatment. In a meta-analysis by Yan Feng et al. in 2011, eleven studies involving 1135 patients were included, and the cure rate did not differ between patients receiving LS versus RT. Hence, post treatment phonation plays an important role in deciding the management option. The results regarding voice preservation were inconclusive [5].

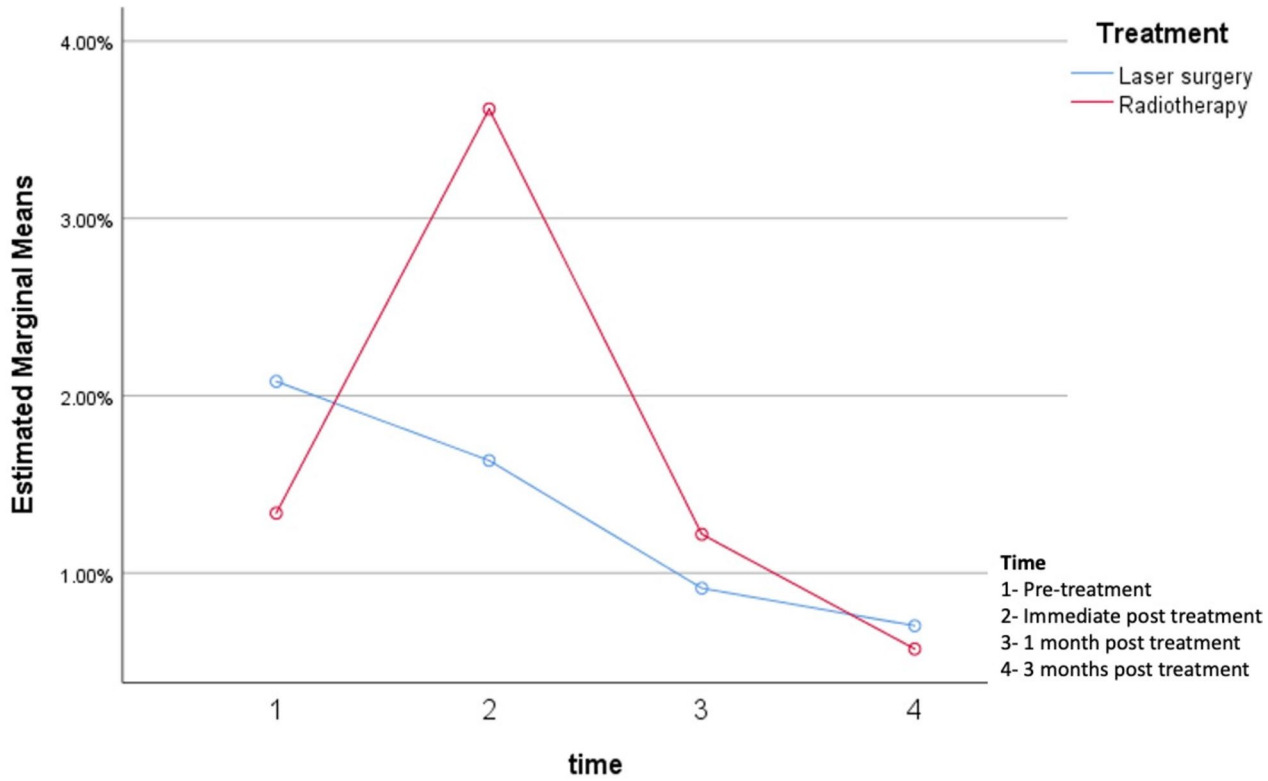

Fig. 1 Comparison of treatment effects on jitter

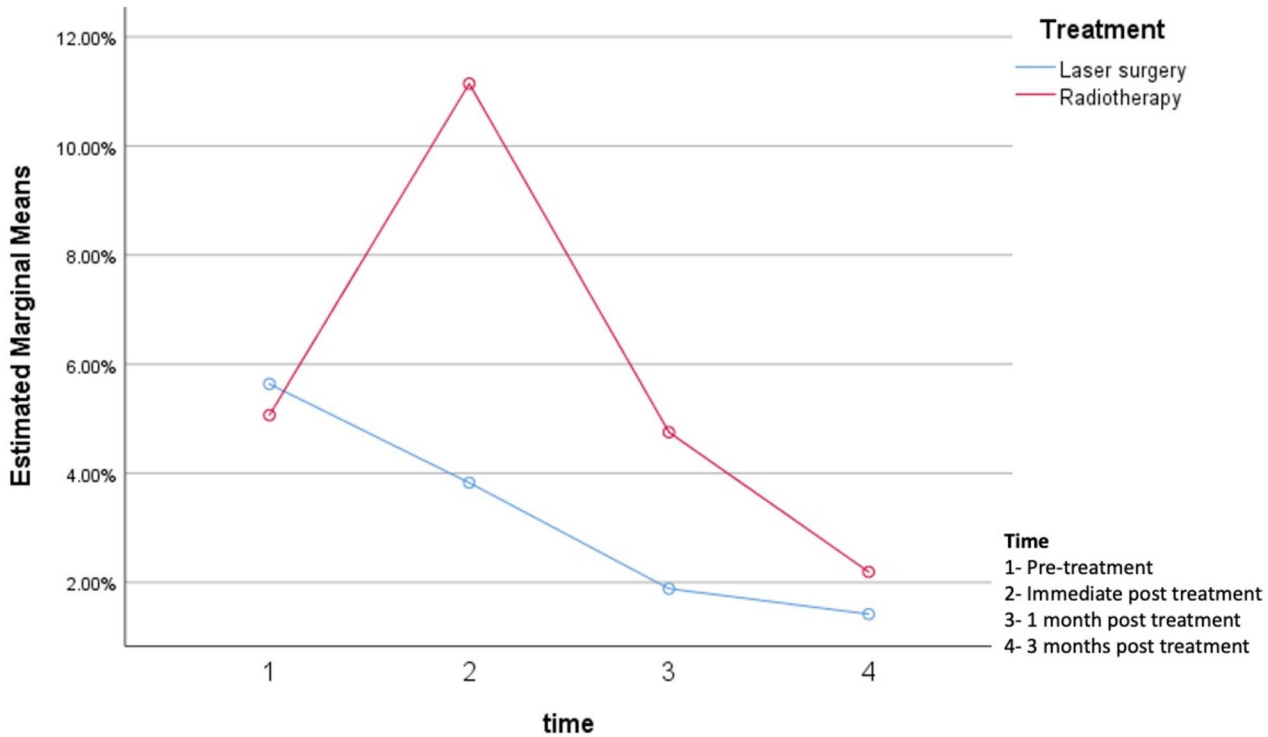

Fig. 2 Comparison of treatment effects on shimmer

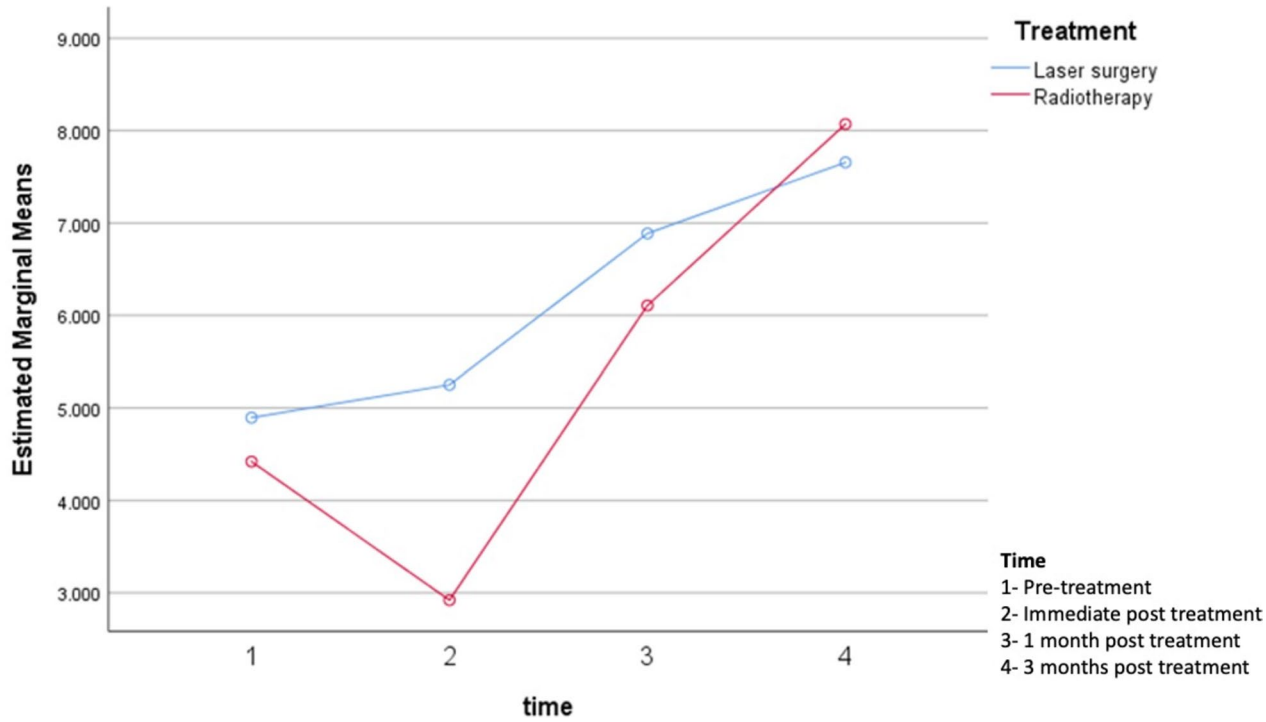

Fig. 3 Comparison of treatment effects on harmonics-to-noise ratio

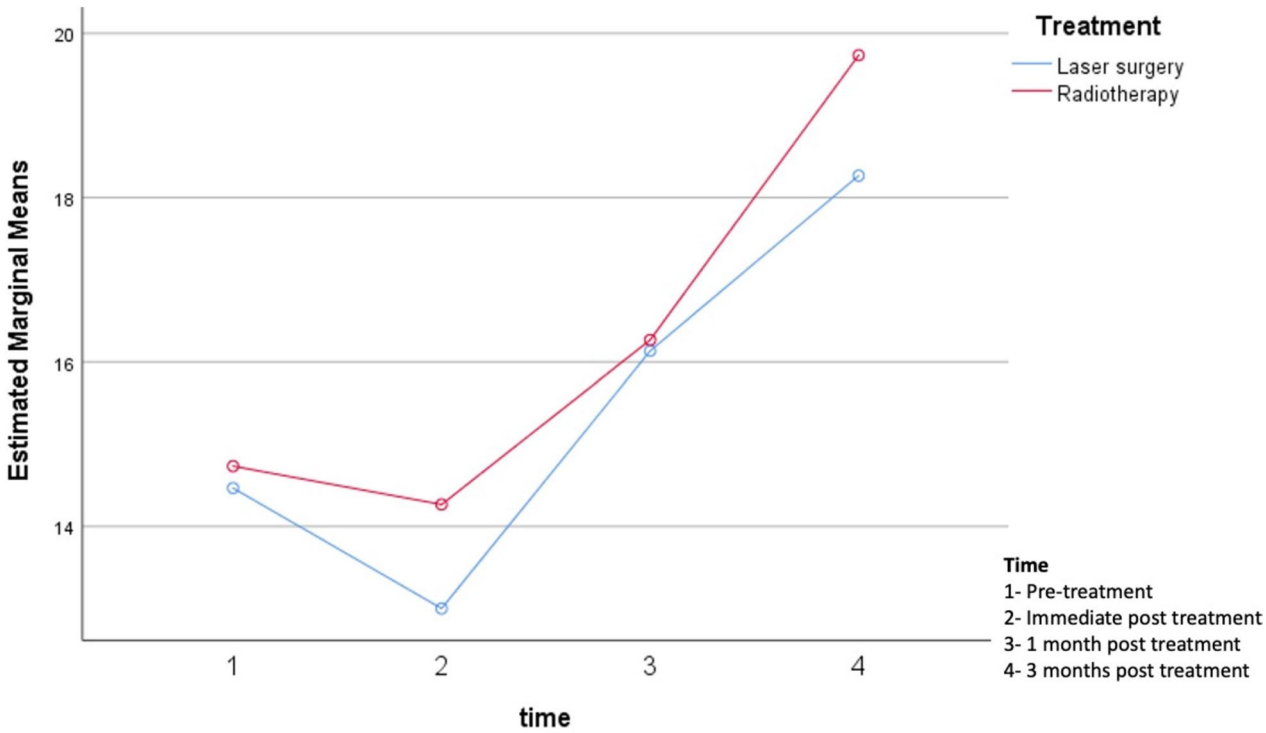

Fig. 4 Comparison of treatment effects on maximum phonation time

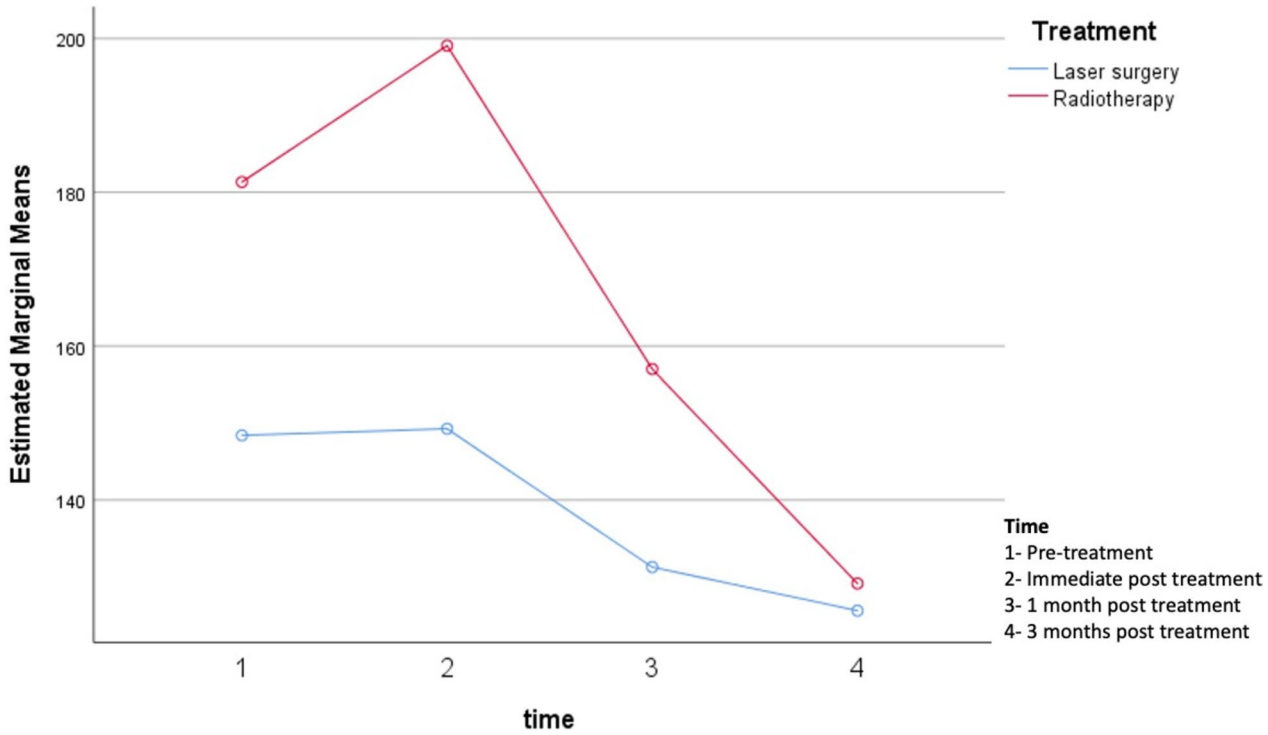

Fig. 5 Comparison of treatment effects on fundamental frequency

In a literature survey by Michael Luscher et al., of the six studies dealing with voice quality, RT was found to be more effective in preservation of the voice in three, while in the other three studies, no significant difference could be detected. With respect to costs of treatment, in three out of four studies, LS was found to be the more economical treatment option [6]. In our study, 15 patients underwent RT, and 15 patients underwent CO_2-assisted laser cordectomy. Treatment was given to all patients free of cost.

In our study, voice analysis showed no immediate effect from LS on jitter and shimmer values. But to certain extent, a significant improvement in the values can be observed after 1 month and 3 months following treatment. However, there is immediate increase following RT compared to pre-treatment. Then, the values reduce gradually over a period of 3 months post treatment.

Even though there is an increase in jitter as well as shimmer immediately following radiotherapy, after 3 months, we can observe that both treatments have almost same effects, a result similar to a study by Sharma et al. [7].

HNR decreases immediately after RT. At the same time, LS shows a consistent increase in HNR over time. After 1 month and 3 months, we can observe that both treatments give similar effects. Studies by Kinshuck A showed similar HNR outcomes in both radiotherapy and laser surgery [8]. Both LS and RT give similar effects in terms of MPT which was in line with studies by Mc Guirt et al. [9] and Hirano M et al. [10].

There is a significant difference between LS and RT in the pretreatment values of fundamental frequency (F0). However, there is no immediate effect from LS on F0. But a gradual decrease to normal values can be observed after 1 month and 3 months. RT shows an immediate increase in fundamental frequency, but the values gradually decrease by 1 month and reduce to normal at 3 months. A study by Battala FN [11] showed no significant difference in fundamental frequency.

On videostroboscopy, mucosal wave was absent before treatment in all patients, and it immediately forms after LS and gradually after RT. RT takes almost 3 months for complete recovery, whereas LS effect can be seen in just 1 month. Patients with incomplete glottic closure immediately recovers after both LS and RT. That implies that both the treatments are equally efficient in treating incomplete glottic closure. In a study on 32 patients of T1a mid-cord glottic carcinoma by Sjogren et al., statistical analysis showed no significant difference between LS and RT in videostroboscopy parameters including glottic closure and mucosal wave [12].

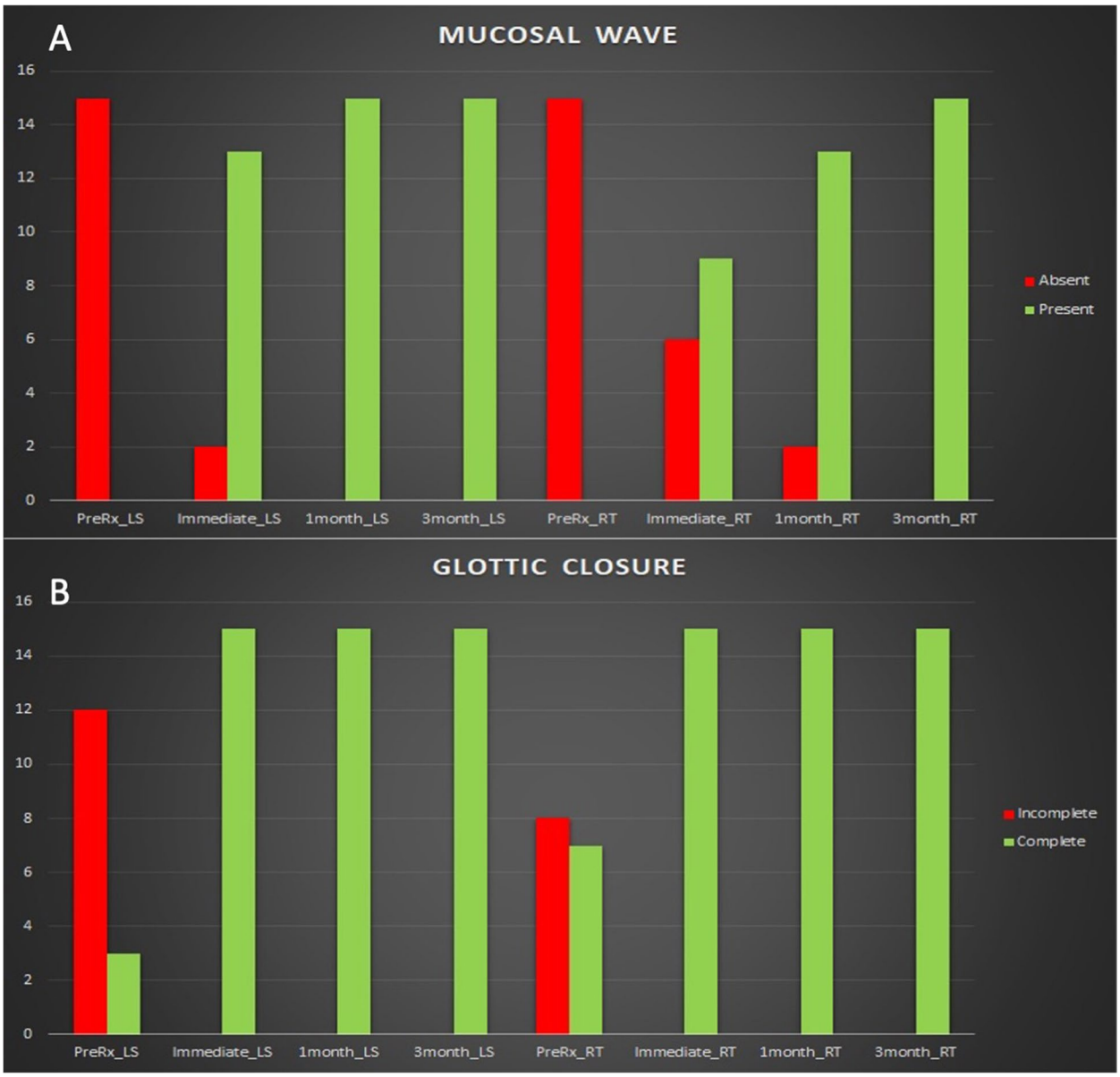

Fig. 6 Comparison of treatment effects **A** mucosal wave and **B** glottic closure

Conclusion

In conclusion, the preservation of the larynx is a primary objective when treating T1 laryngeal cancer patients. The functional and quality of life outcomes associated with radiotherapy and transoral laser microsurgery play a crucial role in planning effective management strategies. However, neither treatment modality demonstrates clear superiority in terms of post-treatment vocal function. To make informed decisions, treating physicians must consider various factors such as complications, patient-specific considerations, treatment costs, and duration. It is important to finalize the treatment plan through comprehensive discussions with the patient, weighing the advantages and disadvantages of both options and seeking guidance from the joint tumor board of the respective hospital. In our study, immediately following treatment, laser surgery tends to yield better outcomes in parameters like jitter, shimmer, harmonics-to-noise ratio (HNR), and mucosal wave, potentially due to glottic edema and the impact on the contralateral vocal cord following radiotherapy. However, after a 3-month period, the outcomes of both treatment modalities become comparable. Overall, a personalized approach considering the individual patient's circumstances is crucial in achieving optimal results in the management of T1 laryngeal cancer.

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Authors' contributions
DKG—design, analysis, interpretation, draft. MR—design, analysis, interpretation, draft, revision. SKS—design, revision. RC—data collection, interpretation, draft. RR—revision. SG—interpretation, draft. HS—revision. BP—data collection. SY—data collection. SB—data collection. All authors have read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Approved by the Institutional Ethics Committee, Army Hospital Research and Referral, Delhi, India vide no. 71/2019 dated 10 October 2019.
Informed written consent to participate in the study was provided by all participants.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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