Cerrahpaşa Med J 2023; 47(3): 285-290 ORIGINAL ARTICLE

Does Anterior Commissure Involvement Change the Selection of Treatment Modality in Early-Stage Glottic Larynx Cancer?

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Abstract

Objective: Glottic laryngeal cancers are detected at an early stage at the time of diagnosis. Radiotherapy or transoral laser microsurgery as a local treatment is a choice for early-stage glottic laryngeal cancer. This study aims to investigate the local control rate after radiotherapy or transoral laser microsurgery for early-stage glottic laryngeal cancer with anterior commissure involvement.

Methods: In total, 119 patients with early-stage (Tis-T1-2) laryngeal cancer were treated in our institution with radiotherapy or transoral laser microsurgery between 2009 and 2021. The median follow-up time was 52 months. Seventy-three patients underwent transoral laser microsurgery. Forty-six patients received radiotherapy, and there were 41 patients with anterior commissure involvement.

Results: The 2 and 5 years overall survival rates were 92% and 73%, whereas local failure-free survival rates were 84% and 82% in all groups, respectively. The 2-year overall survival was 88% in the radiotherapy arm and 94% in the transoral laser microsurgery arm, respectively. There was no statistically significant difference between the two treatment groups for overall survival (*P*: .062). According to anterior commissure involvement, 29 underwent transoral laser microsurgery, whereas 12 patients received radiotherapy. A total of 9 local failures occurred in the transoral laser microsurgery group, there was no recurrence in the radiotherapy group (*P*: 0.028).

Conclusion: There was no statistically significant difference between the two treatment groups for local failure-free survival and overall survival. However, in the case of the anterior commissure involvement, 9 local failures occurred in the transoral laser microsurgery group, and there was no recurrence in the radiotherapy group. Radiotherapy might be recommended in early-stage glottic laryngeal cancer, especially in patients with anterior commissure involvement.

Keywords: Radiotherapy, larynx cancer, microsurgery, anterior commissure

Introduction

Laryngeal cancer is one of the most common head and neck malignancies. Glottic laryngeal cancer is the most common subsite in laryngeal cancer and is approximately two-thirds.[1] Since hoarseness is an early symptom, most glottic laryngeal cancers are detected at an early stage at the time of diagnosis. In early-stage disease, lymph node metastasis is rare, with an incidence of clinically positive lymph nodes of nearly none for the T1 stage and < 2% for the T2 stage. Because nodal metastasis is an uncommon situation, local treatment was a choice for early glottic laryngeal cancer.[2] For local treatment, radiotherapy (RT) or transoral laser microsurgery (TLM) is the treatment of choice.[3] Treatment may vary by geographic region, and some studies report that T2 tumor and anterior commissure (AC) involvement are poor prognostic factors for local control (LC). Which local treatment modality is better in tumors with T2 or AC involvement is controversial.[4,5] This study aims to investigate the LC rate after RT or TLM for early glottic laryngeal cancer with AC involvement.

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Methods

Patients

Patients with histologically confirmed in situ and early-stage (T1-2) squamous cell carcinoma (SCC) of the larynx, treated with either RT or TLM, were included in the study. In our series, there were 119 patients treated in our institution between 2009 and 2021. Radiotherapy was performed on 46 (38%) of the patients, and TLM was performed on 73 (62%) of the patients. The median age was 59 (range 36-85), and 95% of the patients were male. Out of 119 patients, 99 had invasive and 20 had in situ carcinoma. Patients' features were examined retrospectively for pathological evaluation and treatment modalities which are listed in Table 1.

Table 1. Patients Characteristics and Pathological Evaluation—Treatment Schedule

Median age	**59 (36-58)**
Sex	
Male	113 (95%)
Female	6 (5%)
T Stage	
Tis	21 (18%)
T1a	77 (65%)
T1b	8 (7%)
T2	13 (10%)
Pathology	
SCC	99 (83%)
In situ carcinoma	20 (17%)
Location	
Right	48 (40%)
Left	52 (44%)
Bilateral	19 (16%)
Anterior commissure involvement	
Involved	41 (34%)
Not involved	78 (66%)
Treatment modality	
Radiotherapy	46 (38%)
Transoral laser microsurgery	73 (62%)
Radiotherapy	
2D conventional RT	3 (7%)
3D CRT-IMRT	43 (93%)

3D CRT, 3D conformal radiotherapy; IMRT, intensity-modulated radiation therapy; RT, radiotherapy; SCC, squamous cell carcinoma.

Treatment

Radiotherapy

Between 2009 and 2010, a 2D conventional scheme of RT was used, whereas patients treated after 2010 received 3D conformal radiotherapy (3D-CRT) or intensity-modulated radiation therapy (IMRT). Patients were immobilized during treatment with a thermoplastic head and neck mask. The median RT dose was 63 Gy (range 58-70 Gy). The fraction dose was 2 or 2.25 Gy. For patients who received conventional or conformal RT, a box field was used. The box field contains a treatment field with the superior border at the top of the thyroid cartilage and the inferior border at the bottom of the cricoid cartilage. For patients treated with IMRT, gross tumor volume (GTV) of the primary tumor was delineated according to clinical and radiological findings. Clinical target volume (CTV) was delineated as GTV plus a 5 mm margin in all directions except anatomical barriers. A 3 mm margin was added in all directions to delineate the planning target volume (PTV).

Surgery

The procedures were performed under general anesthesia by using endotracheal tubes suitable for laser surgery. Following direct laryngoscopic exposition of the larynx, the patients were examined with rigid 0- or 30-degree telescopes and the location and extend of the lesions were noted. According to the location and extent of the tumor, type III-V or type VI cordectomies were performed, while the larynx was directly visible using a 400 mm focus operating microscope.

Follow-up

During RT, we examine patients weekly about head and neck symptoms such as dysphagia and dermatitis. Patients were examined physically and endoscopically every 2 months for the first 2 years, every 6 months between the second and fifth years, and annually after the fifth year. Events of toxicity, relapse, and metastasis were recorded during the follow-up visits.

Statistical Analysis

This study was conducted retrospectively. Local control was defined as the time from the initiation of RT or surgery to recurrence. Kaplan–Meier survival analysis was performed for local failure-free survival (LFFS), disease-free survival (DFS), and overall survival (OS). The computer software SPSS version 21 for Windows (IBM SPSS Corp.; Armonk, NY, USA) was used for all statistical analyses, and $P < .05$ was considered for statistical

Table 2. Distribution of Patients Characteristics

Treatment Modalities n (%)	**RT**	**TLM**	***P***
Mean age	63	61	.52
Sex			
Male	43 (93%)	70 (96%)	.55
Female	3 (7%)	3 (4%)	
T Stage			
Tis - T1a	40 (87%)	58 (79%)	.29
T1b - T2	6 (13%)	15 (21%)	
Pathology			
SCC	39 (85%)	60 (82%)	.71
In situ carcinoma	7 (15%)	13 (18%)	
Anterior commissure involvement			
Involved	12 (26%)	29 (40%)	.12
Not involved	34 (74%)	44 (60%)	
T distribution of patients with anterior commissure involvement			‘
Tis - T1a	2 (17%)	15 (52%)	.84
T1b - T2	10 (83%)	14 (48%)	

RT, radiotherapy; SCC, squamous cell carcinoma; TLM, transoral laser microsurgery.

significance. This study was approved by the local ethics committee (No: 564034).

Results

Patients and Tumor Characteristics

Patients and tumor characteristics are demonstrated in Table 1. Patients' characteristics, such as age, sex, histopathology, T stage, location, and AC involvement, were similar between the 2 groups (Table 2).

Survival

The 2- and 5-year OS rates were 92% and 73%, whereas the LFFS rates were 84% and 82% in all groups, respectively. Totally, 16 patients died, and the cause of death was cancer related in only 5 patients. Three patients died because of secondary malignancy (lung n = 1, esophagus n = 1, and prostate n = 1), 1 patient died because of chronic obstructive pulmonary disease (COPD), and the other 1 died because of aortic dissection. One patient died due to urosepsis. Five patients' deaths were unknown. The 2-year OS was 88% in the RT arm and 94% in the TLM arm, respectively. There was no statistically significant difference between the 2 treatment groups for OS (*P*: 0.062).

Local Control

The median follow-up time was 52 months (IQR 25: 32, IQR 75 : 84). A total of 19 patients had recurrence; 6 patients in the RT arm, and 13 patients in the TLM arm. The major recurrence pattern was local (n = 19), and there was no distant failure. The median recurrence-free time was 10.7 months (IQR 25: 7.34, IQR 75 : 16.68). The 2-year and 5-year LFFS were 86% and 86% in the RT arm and 83%, and 78% in the TLM arm, and there was no statistically significant difference between the two groups (*P*: 0.503). The 2-year and 5-year DFS were 79%, 61% in the RT arm and 80%, 75% in the TLM arm, and there was no statistically significant difference between the 2 groups (*P*: 0.795) (Figure 1 and 2). In subgroup analyses; there were 41 patients with AC involvement. Twenty-nine patients underwent TLM, whereas 12 patients received RT. A total of 9 local failures occurred in the TLM group; there was no recurrence in the RT group (*P*: 0.028) (Figure 3).

Patterns of Failure

The recurrence rate was 13% in the RT group, while it was 17% in the TLM group. In the RT group, a total of 5 local failures, and only 1 locoregional failure was observed. After recurrence; 1 patient who developed locoregional relapse was considered inoperable and referred for systemic treatment. And 2 patients underwent partial laryngectomy. One of them underwent TLM after the first relapse, but no treatment could be applied to him for the second relapse. After local recurrence, 3 patients died because of rapid progression.

In the TLM group, 12 local failures and 1 locoregional failure occurred. Seven of them underwent TLM again and 6 of them had no recurrence after treatment. One patient underwent 2 other TLM operations after recurrence. Three patients underwent partial laryngectomy (right hemilaryngectomy n = 2, supracricoid laryngectomy n = 1). One of the patients who underwent partial laryngectomy underwent 3 TLM operations before PL. One patient underwent total laryngectomy, and 1 patient received RT. All of these patients' salvage treatments were successful in the TLM arm.

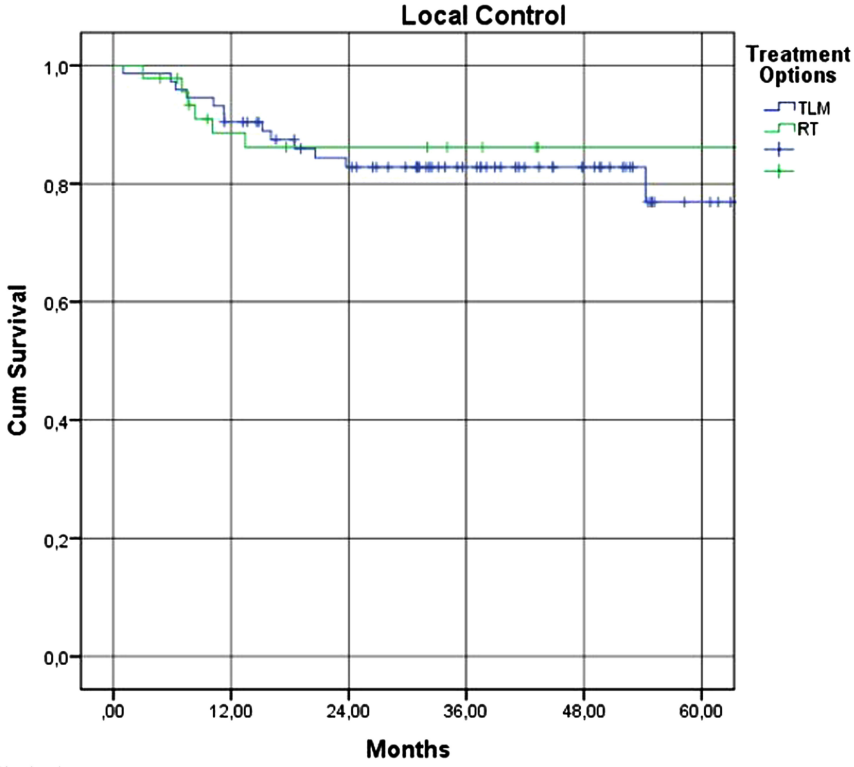
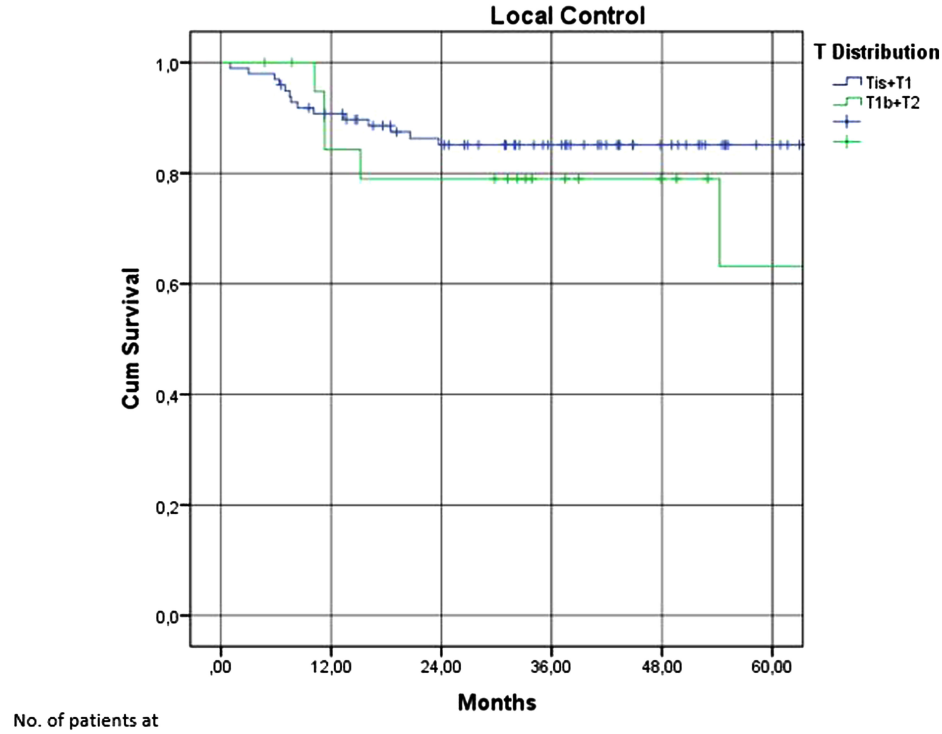
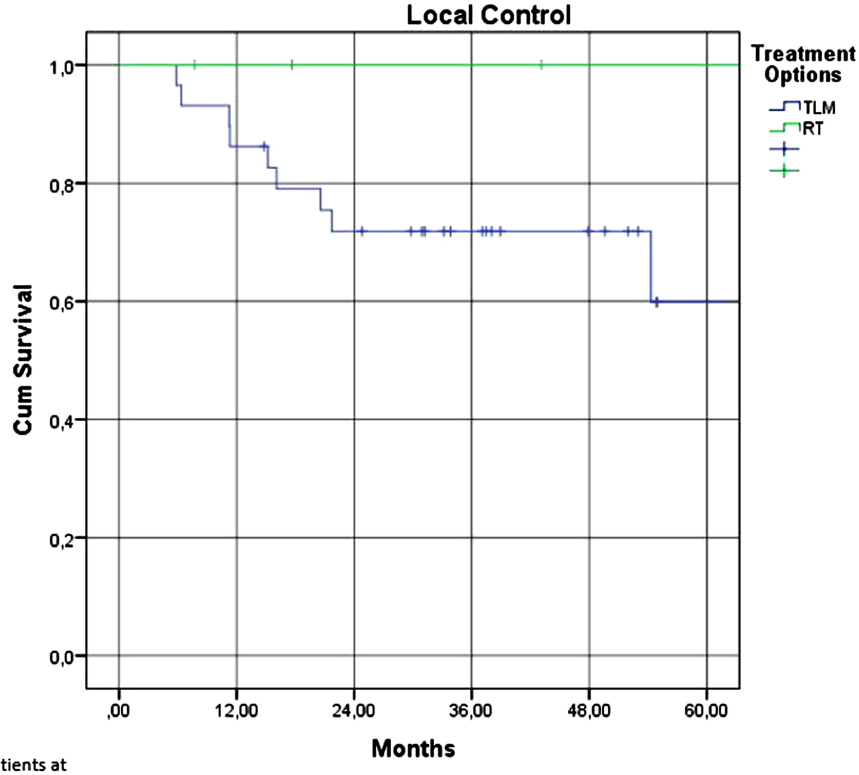


Figure 1. Local control for the whole group.



No. of patients at risk (months)						
Tis+T1a	98	89	84	84	84	84
T1b+T2	21	18	17	17	17	16

Figure 2. Local control in T-stage distribution.



No. of patients at risk (months)						
TLM	29	25	21	21	21	20
RT	12	12	12	12	12	12

Figure 3. Local control for TLM and RT in patients with anterior commissure involvement.

Only 1 patient required total thyroidectomy plus level 6 neck dissection after progression and thereafter received RT. The patient died because of rapid progression.

Discussion

There are a lot of studies in the literature related to early-stage glottic laryngeal cancer (ESLC). Different treatment modalities can be administered in ESLC. Conflicting results were reported in studies comparing RT and TLM. We demonstrated that there was not a statistically significant difference between the two treatment groups for LC, DFS, and OS. Although patients with anterior involvement had better LC in the RT arm (*P*: 0.028), patients with local recurrence were treated better in the surgery arm. Local control could not be accomplished in 5 patients who underwent salvage treatment. Four patients were in the RT arm, whereas 1 patient was in the TLM arm.

Comparison with Previous Studies

Before using CT scans, patients were treated by using 2-D plain film x-rays for drawing fields based on bony landmarks. After using CT scans, the radiation technique advanced from large opposed lateral fields to IMRT, which optimally protects adjacent normal tissues. Today, single-cord treatment is used for early glottic laryngeal cancer with IMRT, especially stereotactic body radiotherapy (SBRT) or hypofractionated RT. In the last decade, SBRT has treated small-volume diseases with image guidance in various anatomical sites with high curative doses. For ESLC, some studies demonstrated high LC with SBRT.[6,7] In terms of RT dose, hypofractionated treatment was the standard; however, SBRT has recently been used.[7-10] Before TLM, open partial laryngectomies were considered the standard surgical treatment. After the first results supporting endoscopic CO_2 laser-assisted resection of glottic cancer, TLM was considered the standard surgical treatment for ESLC.[11]

In studies comparing RT and TLM; Chung et al[12] showed that RT had better LC and DFS than cordectomy. Five-year LC rates were 89.9% and 73.2%, whereas DFS rates were 83.7% and 68.0%, in favor of RT.[12] O'Hara et al[13] published a review evaluating 36 publications. This review demonstrated that there was no statistical difference in LC between RT and transoral laser surgery. The 3-year LC rates were 89.3% and 88.9% for RT and transoral laser surgery for stage IA tumors and 86.2% and 76.8%, respectively, for stage IB tumors.[13] Another comprehensive systemic review by Yoo et al[14] also demonstrated that there is no scientific evidence proving the superiority of either treatment modalities. In our study cohort, there was not any statistically significant difference found in terms of LC, OS, and DFS as well.

Because the AC is close to the visceral spaces of the larynx, microscopic spreads may affect LC.[15,16] Anterior commissure involvement was thought to be a negative predictive factor for LC, and its prognostic significance has been investigated in several studies. These studies demonstrated conflicting results. Hendriksma et al[5] evaluated RT studies for ESLC in a review. In 23 out of 34 studies, AC involvement had a significant impact on LC, whereas it did not have a significant impact in 10 studies. On the other hand, 18 out of 24 surgery studies did not identify AC involvement as a significant factor for LC. Some studies are recommended RT for AC involvement. However, in another study it was demonstrated that there is no statistical difference between RT and TLM.[5] In our study, LC rates for TLM patients with or without AC involvement were 69% and 91%, respectively (*P*: 0.023). Also, a total of 9 local failures occurred in the TLM group, there was no recurrence in the RT group (*P*: 0.028).

In the event of any treatment failure, TLM remains more advantageous because it can be performed repeatedly. In the majority of cases with RT failure, the salvage treatment is either total laryngectomy or partial laryngectomy, and voice quality is affected.[11] In our study, 1 patient underwent total laryngectomy, and 2 patients underwent partial laryngectomy after local recurrence. All 3 patients were salvaged successfully. In the surgery group, 6 of 13 patients with local failures underwent TLM again and were salvaged successfully. But 1 patient underwent PL after 3 MLC. Because of the lack of voice quality data in the surgery group we couldn't compare voice quality between them.

Post-treatment follow-up of ESLC is an important issue. According to guidelines, a physical examination including an endoscopic examination is recommended every 1-3 months in the first 2 years after treatment.[17,18] Because most recurrences are observed in the first 2 years. And in our study, all the recurrences were seen in the first 2 years. The median recurrence time was 11.3 months (IQR 25: 6.92, IQR 75: 19.53 months).

Limitation

Our study has several limitations. First, the study is retrospective and has a small sample size. Second, a short follow-up period limits the evaluation of chronic side effects and recurrence. Third, the voice handicap index and voice-related quality of life were not assessed.

Conclusion

There was no statistically significant difference found between the two treatment groups for LC, DFS, and OS. However, in the case of AC involvement, 9 local failures occurred in the TLM group, and there was no recurrence in the RT group. When the groups were compared, there was a statistically significant difference. Radiotherapy might be recommended in ESLC, especially in patients with AC involvement.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of İstanbul University-Cerrahpaşa (Approval no: 558466, Date: 12.12.2022).

Informed Consent: Written and verbal informed consent was obtained from the patients who agreed to take part in the study.

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