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Clinical Outcomes of Definitive Radiation Therapy for Early Glottic Cancer Using Different Techniques: A Seven-Year Experience at a Tertiary Care Center in North India

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Abstract

Aim

The aim of this study was to evaluate overall survival (OS) in patients with early-stage glottic cancer treated with definitive radiation therapy (RT) and to assess local control (LC), disease-free survival (DFS), prognostic factors, and acute toxicity.

Materials and methods

This retrospective cohort study included 50 patients with early-stage glottic cancer treated with definitive RT between January 2018 and December 2023. Follow-up continued until December 2025. Twenty patients received intensity-modulated RT (IMRT), and 30 received three-dimensional conformal RT (3DCRT). The median prescribed dose was 66 Gy. OS was the primary endpoint. Secondary endpoints were LC, DFS, prognostic factors, and acute toxicity.

Results

The median follow-up was 32 months (range, 1-66 months). Complete response was reported in 48 patients (96%), partial response in one patient (2%), and disease progression in one patient (2%), who developed brain metastasis. Locoregional recurrence occurred in one patient, and distant metastasis occurred in one patient. In univariate analysis, anterior commissure (AC) involvement and tumor stage were significantly associated with DFS and OS. In multivariable analysis, AC involvement was also significantly associated with LC. Median OS was 34 months. No grade 2 or 3 radiation toxicity was reported.

Conclusions

Definitive RT was associated with a high complete-response rate, and few recurrences were reported in this cohort. The study describes outcomes among patients treated with 3DCRT or IMRT but does not establish the superiority of either technique.

Categories: Radiation Oncology
Keywords: early glottic cancer, intensity-modulated radiotherapy (imrt), local control, three-dimensional conformal radiotherapy (3d-crt), toxicity

Introduction

Laryngeal cancers are among the most prevalent head and neck cancers and constitute 1% of all cancers globally. By definition, glottic cancer is a cancer arising from the true vocal cords and the anterior and posterior commissures of the larynx. According to the eighth edition of the American Joint Committee on Cancer staging system, early glottic cancer is defined as T1N0M0 and T2N0M0 tumors [1]. Smoking and excessive alcohol consumption have been associated with the occurrence of glottic cancer. Smokers have been reported to have 15-30 times higher rates of glottic cancer than nonsmokers [2]. Of all laryngeal cancers, glottic squamous cell carcinoma (SCC) accounts for over 75% [3]. Early glottic cancer carries the most favorable prognosis among laryngeal cancers. The five-year overall survival (OS) rate for early glottic cancer ranges from 70% to 90% [4,5]. The treatment goals for early glottic cancer are cure and preservation of voice quality. Various treatment options for early glottic cancer include transoral laser microsurgery (TLS), open partial laryngectomy, and definitive external beam radiation therapy (RT). All treatment modalities yield comparable results in terms of survival [6-8]. However, RT yields better voice quality compared with TLS [9].

Traditionally, two-dimensional or three-dimensional conformal RT (3DCRT) planning is used to deliver RT for early-stage glottic cancer using parallel opposing fields that include the whole larynx. Intensity-modulated RT (IMRT) is an alternative to conventional RT, offering a more conformal radiation dose distribution and thereby reducing the dose to organs at risk (OARs). Thus, IMRT is widely accepted as the standard of care in the therapeutic management of head and neck cancers [10].

This retrospective cohort study evaluated OS in patients with early-stage glottic cancer treated with definitive RT. Secondary outcomes included local control (LC), disease-free survival (DFS), prognostic factors, and acute treatment-related toxicity. Outcomes were also described according to RT technique (3DCRT or IMRT); however, the study was not designed to establish the superiority of either technique.

Materials And Methods

Study type

This was a retrospective cohort study evaluating treatment outcomes, survival, LC, and acute toxicities in patients with early-stage glottic cancer treated with definitive RT using 3DCRT or IMRT.

Sampling technique

Consecutive sampling was used to include 50 eligible patients with early-stage glottic cancer treated between January 2018 and December 2023. Of these, 30 patients received 3DCRT, and 20 received IMRT, based on the availability of complete medical records.

Inclusion and exclusion criteria

Patients with histopathologically confirmed early-stage glottic cancer (T1N0M0 or T2N0M0) who received definitive RT and had adequate clinical, treatment, and follow-up records were included in the study. Patients with stage III or IV glottic cancer, incomplete medical records that precluded meaningful outcome assessment, or inadequate follow-up information were excluded from the study.

Confounders

The potential confounders in this study included age, sex, tumor stage (T1 vs. T2), anterior commissure (AC) involvement, histopathological characteristics, and the RT technique used (3DCRT vs. IMRT).

Study location

The present study was conducted in the Department of Radiation Oncology, Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Srinagar, India, after obtaining ethical approval from the Institutional Ethics Committee of SKIMS (IEC protocol no. RP 18/2021, dated April 24, 2021).

Study duration

The study included patients treated between January 2018 and December 2023, with follow-up conducted from the date of diagnosis until December 2025, covering an overall study period from January 2018 to December 2025. A complete staging workup was performed, including history and physical examination, fiber-optic laryngoscopy, direct laryngoscopy with biopsy, chest X-ray, contrast-enhanced CT (CECT) of the head and neck, and MRI of the head and neck. Data were collected from the regional cancer center files and follow-up records. The collected data included patient characteristics, cancer characteristics, RT details, and treatment outcomes.

Treatment

All patients were treated with definitive RT. Of the 50 patients, 20 received RT using the IMRT technique with 6-MV photon beams following immobilization with thermoplastic masks. The remaining 30 patients were treated with 3DCRT using two opposing oblique beams with 6-MV photon energy and 45° wedges.

For 3DCRT, the treatment field extended superiorly from the thyroid notch to the inferior border of the cricoid cartilage, with the anterior border positioned 1 cm anterior to the thyroid cartilage and the posterior border extending to the posterior aspect of the arytenoid cartilages. For IMRT, the clinical target volume (CTV) encompassed the true and false vocal cords, arytenoid cartilages, aryepiglottic folds, laryngeal ventricle, and subglottic region for T2 disease. The planning target volume was created by adding 5-10 mm craniocaudal and 3-5 mm mediolateral and anteroposterior margins to the CTV.

A dose of 66 Gy in 33 fractions was prescribed for T1 lesions, and 70 Gy in 35 fractions was prescribed for T2 glottic cancer. CT simulation for all patients was performed using a slice thickness of 2-3 mm, covering the region from the base of the skull to the carina. The dose constraints for OARs were defined as follows: maximum spinal cord dose (Dmax) of less than 45 Gy, mean parotid dose (Dmean) of less than 26 Gy, and mean thyroid dose (Dmean) of less than 35 Gy. A seven-field IMRT plan using 6-MV photons was generated

with the Eclipse 13.2 treatment planning system. Throughout treatment, patients were assessed for acute toxicity in the toxicity clinic.

Follow-up

All patients were assessed twice weekly during treatment. After completion of the prescribed RT, patients were followed weekly until acute radiation toxicity subsided, then monthly for three months, every three months for one year, every six months for two years, and annually thereafter. Treatment response was evaluated six to eight weeks after completion of the prescribed treatment through history-taking and physical examination, direct laryngoscopy, and CECT.

Outcome measures

OS was the primary endpoint of the study. The secondary endpoints included LC rate (LCR), DFS, factors affecting OS, and the incidence of acute treatment-related toxicities. OS was defined as the time from diagnosis to death from any cause. LC was calculated from the time of diagnosis to the occurrence of local recurrence or death from any cause. DFS was defined as the interval from diagnosis to the first disease-related event, including locoregional or distant recurrence, development of a second primary cancer, or death from any cause. The Common Terminology Criteria for Adverse Events, version 5.0, was used for toxicity grading [11]. Treatment compliance was evaluated based on the median radiation dose delivered, the overall duration of the RT schedule, and the proportion of patients who completed the prescribed radiation dose.

Statistical analysis

Data were entered into Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) and analyzed using IBM SPSS Statistics for Windows, version 26.0 (released 2018; IBM Corp., Armonk, NY, USA). Continuous variables were expressed as the mean ± SD or median with IQR, depending on the data distribution. Frequencies and percentages were used to express categorical variables.

OS, DFS, and LC were estimated using the Kaplan-Meier method. The log-rank test was used to compare survival between the treatment groups. Univariate analysis using the log-rank test was performed to evaluate factors associated with OS. Study variables with a p-value of less than 0.01 on univariate analysis were entered into a multivariable analysis. Acute toxicities were compared between the treatment arms using the chi-square test. A two-sided p-value of <0.05 was considered statistically significant for all analyses.

Results

Baseline characteristics

A total of 50 patients with early-stage glottic cancer (T1 and T2) were enrolled between January 2018 and December 2023 and followed up until December 2025. Of these, 30 patients were treated with 3DCRT, and 20 were treated with IMRT. The median age at presentation was 58 years. Among the 50 patients, 48 were male, and two were female. Thirty-three patients were smokers, and 17 were nonsmokers. All patients had an Eastern Cooperative Oncology Group performance status of 0-1. Twenty-three patients had no underlying comorbidities, whereas 27 had underlying comorbidities. All patients presented with hoarseness of voice, and the majority presented within six weeks. Thirty-eight patients had T1 disease, 10 had T2 disease, and two had Tis disease. In the majority of patients, the AC was not involved. Histopathological examination predominantly revealed well-differentiated SCC (Table *1*).

Parameter	Category	n	%
Demographics			
Age (years)	Mean ± SD	-	58 ± 9.36
Sex	Male	48	96
	Female	2	4
Smoking status	Smoker	33	66
	Nonsmoker	17	34
Clinical presentation			
Primary symptom	Hoarseness of voice	50	100
	Tis	2	4

Clinical stage	T1aN0	24	48
	T1bN0	14	28
	T2N0	10	20
AC	Involved	16	32
	Not involved	34	68
Histopathology			
Type/grade	Well-differentiated SCC	40	80
	Moderately differentiated SCC	5	10
	Poorly differentiated SCC	3	6
	Carcinoma in situ (Tis)	2	4
Comorbidities			
Comorbidity	None	23	46
	Hypertension (isolated)	11	22
	Type 2 diabetes	8	16
	Hypothyroidism	6	12
	Coronary artery disease	2	4
Treatment parameters			
RT technique	3DCRT	30	60
	IMRT	20	40
RT dose/fractionation	66 Gy in 33 fractions	40	80
	70 Gy in 35 fractions	10	20
Outcomes			
Response	Complete response	48	96
	Partial response	1	2
	Disease progression	1	2
Recurrence	No	47	94
	Yes	3	6

TABLE 1: Baseline patient and treatment characteristics (N = 50).

3DCRT: three-dimensional conformal radiation therapy; AC: anterior commissure; IMRT: intensity-modulated radiation therapy; RT: radiation therapy; SCC: squamous cell carcinoma; Tis: tumor in situ

Treatment adherence

Thirty patients were treated with 3DCRT, and 20 patients were treated with IMRT. The median radiation dose received was 66 Gy. All patients completed the prescribed radiation dose without any treatment breaks.

Outcomes

The median follow-up duration in these patients was 32 months (range, 1-66 months). Forty-eight patients (96%) had a complete response, one patient (2%) had a partial response, and one patient (2%) had disease progression in the form of brain metastasis. Locoregional recurrence was observed in two patients, and distant metastasis was observed in one patient. The median times to locoregional progression and distant metastasis were 30 and 45 months, respectively. Salvage surgery was performed for locoregional relapse. The five-year laryngeal preservation rate was 85% in patients with T2 disease. Distant failure occurred in the form of brain metastasis. One patient died due to a cardiac condition, and one patient was lost to follow-up.

OS was 34 months (Table 2).

Stage (n)	Local recurrence		Regional recurrence		Distant metastases		Total recurrence rate (%)	
	n	%	n	%	n	%	n	%
Tis (2)	0	0	0	0	0	0	0	0
T1 (total) (38)	0	0	0	0	0	0	0	0
T1aN0 (24)	0	0	0	0	0	0	0	0
T1bN0 (14)	0	0	0	0	0	0	0	0
T2N0 (10)	2	20	0	0	1	10	4	30
Total (50)	2	4	0	0	1	2	3	6

TABLE 2: Recurrence rates by clinical stage (N = 50).

Tis: tumor in situ

In the univariate analysis, clinical stage, AC involvement, and RT technique were evaluated. Clinical stage and AC involvement were found to be statistically significant for both DFS and OS. However, RT technique was not statistically significant. For LC, clinical stage and AC involvement were found to be statistically significant (Table 3).

Variable	Category	n	Recurrences, n	Recurrences, %	p-value	Significance
Clinical stage	Tis/T1	40	0	0	0.002*	Highly significant
	T2	7	3	42.9		
AC involvement	Not involved	34	1	2.9	0.003*	Highly significant
	Involved	16	2	12.5		
RT technique	IMRT	15	1	6.7	1.000	Not significant
	3DCRT	29	2	6.9		

TABLE 3: Univariate analysis for DFS (N = 50).

* Fisher's exact test/log-rank test; statistical significance at $p < 0.05$.

3DCRT: three-dimensional conformal radiation therapy; AC: anterior commissure; DFS: disease-free survival; IMRT: intensity-modulated radiation therapy; RT: radiation therapy; Tis: tumor in situ

In the multivariable analysis, AC involvement and clinical stage were found to be statistically significant for DFS and OS. Only AC involvement was statistically significant for LC (Table 4). None of the patients developed grade 2 or 3 radiation toxicity.

Variable	OS	DFS	DSS	LC
Stage (T2 vs T1/Tis)	NS	0.002	NS	0.005
AC involvement	NS	S (0.003)	NS	0.023
RT technique (3DCRT vs IMRT)	NS	NS	NS	NS

TABLE 4: Multivariable analysis for OS, DSS, DFS, and LC (N = 50).

NS = not significant (p > 0.05). Values in parentheses represent the univariate p-values for factors nearing clinical interest, which were evaluated for inclusion in the multivariable analysis.

3DCRT: three-dimensional conformal radiation therapy; AC: anterior commissure; DFS: disease-free survival; DSS: disease-specific survival; IMRT: intensity-modulated radiation therapy; LC: local control; OS: overall survival; RT: radiation therapy; Tis: tumor in situ

Discussion

Early glottic cancers can be cured with surgery and definitive RT [12]. This study was conducted to evaluate the outcomes of definitive RT using different RT techniques in patients with early-stage glottic cancer, with a focus on preserving laryngeal function without compromising oncological cure. In early-stage glottic cancer, excellent survival outcomes can be achieved; therefore, the emphasis of treatment extends beyond disease control to include laryngeal preservation and quality of life.

Our findings illustrate that definitive RT provides excellent tumor control and favorable survival outcomes, consistent with the existing literature. According to the literature, T1 early-stage glottic cancer is associated with high cure rates, with five-year LCRs of 85-95%, compared with 70-80% for T2 disease, and OS rates of 80-95% [13]. Our study also showed LCRs of 90% and 85% for T1 and T2 disease, respectively, and a five-year OS rate of 100%, reinforcing the role of RT as a standard definitive treatment for early-stage glottic cancer (Figures *1*-*5*).

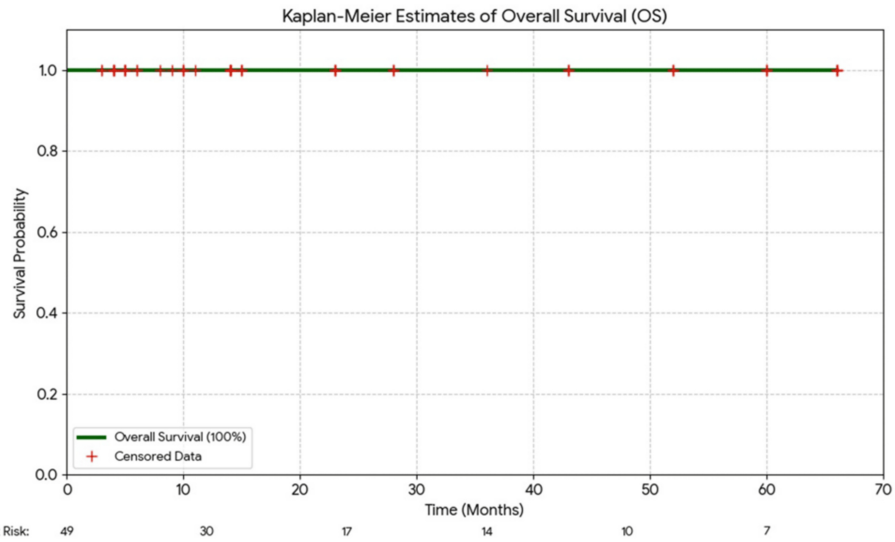


FIGURE 1: OS.

OS: overall survival

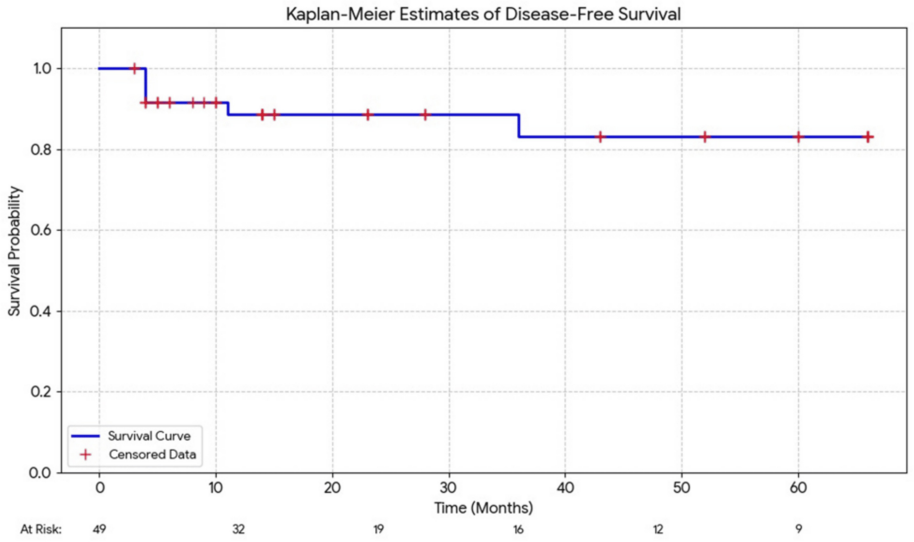


FIGURE 2: DFS.

DFS: disease-free survival

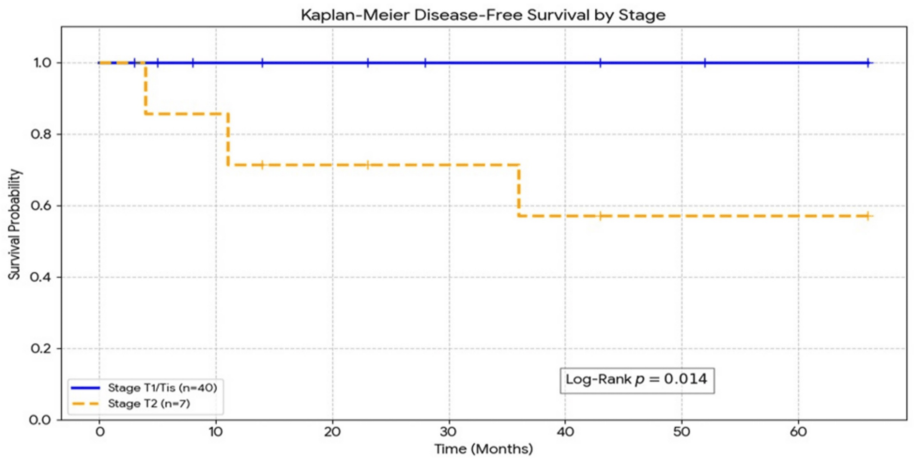


FIGURE 3: DFS by stage.

DFS: disease-free survival

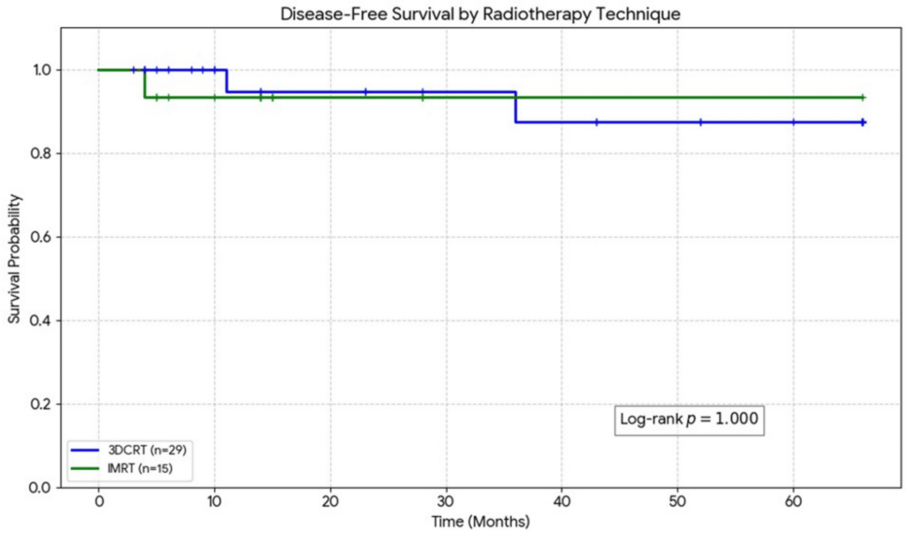


FIGURE 4: DFS by RT technique.

DFS: disease-free survival; RT: radiation therapy

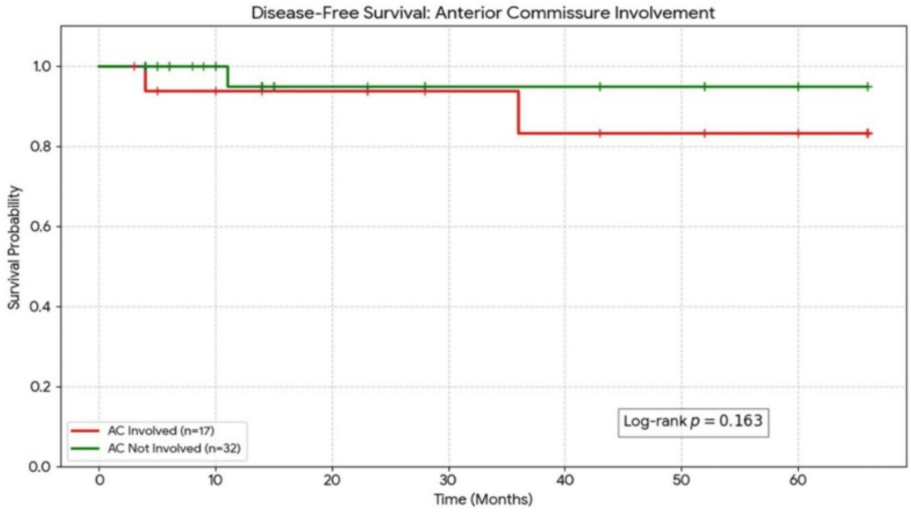


FIGURE 5: DFS by AC involvement.

AC: anterior commissure; DFS: disease-free survival

The main strength of RT in early glottic cancer lies in organ preservation. Surgical approaches, on the other hand, may compromise voice quality depending on the extent of resection. Published data have shown that the oncological outcomes of RT and TLS are similar, but voice quality tends to be superior in patients treated with RT [14,15]. Our study demonstrated encouraging laryngeal preservation outcomes, with clinically favorable voice-related observations during follow-up; however, these were not assessed using standardized voice-quality instruments.

In our study, patients were treated with RT using two techniques: 3DCRT and advanced IMRT. Two-dimensional lateral opposing fields were the standard technique in the past because of their effective target coverage and simplicity. However, exposure of adjacent OARs with these techniques can lead to long-term toxicities.

With advances in technology, IMRT has emerged as a promising alternative, enabling OAR sparing and improved dose conformality. Recently published data have demonstrated that IMRT provides comparable oncological outcomes while reducing the dose to critical structures [16]. Dosimetric studies further highlight the advantages of carotid-sparing IMRT in significantly reducing radiation doses to critical vascular

structures without compromising target dose coverage [17].

In our study, we observed comparable disease control with 3DCRT and IMRT, indicating that technological advancements may primarily improve the therapeutic ratio rather than dramatically alter survival outcomes. This suggests that, although tumor control remains consistently high with both modalities, the choice of technique should be guided by the goal of minimizing toxicity and preserving long-term function.

In early glottic cancer, voice outcomes remain a critical endpoint. RT has been associated with improved voice quality over time, with minimal long-term deterioration. Long-term functional studies have shown that most patients maintain voice-related quality of life for years after treatment completion [15]. We also observed preservation of voice-related quality of life in our study. Arytenoid-sparing IMRT has recently been explored to further preserve voice function [16].

Clinical outcomes are also influenced by several prognostic factors, which were evaluated in our study. In accordance with previous research, clinical stage and AC involvement emerged as significant factors associated with clinical outcomes [13]. Compared with T1 lesions, T2 glottic lesions tend to have relatively poorer outcomes because of increased tumor volume and impaired vocal cord mobility. Moreover, treatment-related factors, such as radiation dose and overall treatment time, also influence LC, emphasizing the importance of adherence to the scheduled treatment plan.

In our study, we also observed that disease stage and AC involvement were associated with clinical outcomes. The five-year DFS rate was 72% in patients with T2 disease and 100% in those with Tis/T1 disease, whereas the five-year OS rate was 100% in both T1 and T2 disease, which was noteworthy. Patients with AC involvement had a five-year DFS rate of 83%, whereas those without such involvement had a five-year DFS rate of 97%; this difference was statistically significant ($p < 0.05$). The five-year LCR for this laryngeal cancer cohort (N = 50) was 92.6% (Figure *6*).

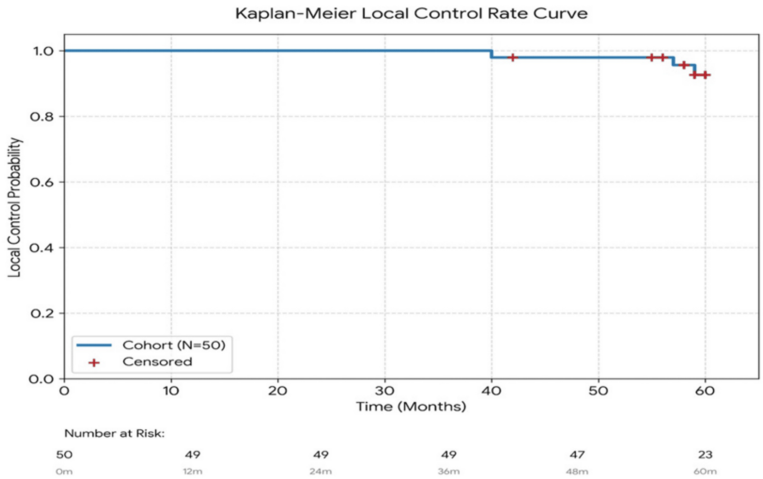


FIGURE 6: Kaplan-Meier estimate of LCR.

LCR: local control rate

Regarding treatment compliance, compliance in our study was satisfactory, reflecting the feasibility of delivering definitive RT in a real-world tertiary care setting. Tumor control is adversely affected by treatment interruptions; therefore, compliance rates are critical to achieving optimal outcomes. Treatment was also well tolerated, with manageable acute toxicities, consistent with recent literature demonstrating the safety of modern RT techniques [5,6].

This study has certain limitations. As a retrospective study, it may be subject to inherent biases, including selection bias and variability in treatment techniques over time. Moreover, the small sample size and heterogeneity in treatment approaches may affect the generalizability of the results. However, the real-world nature of our data provides relevant insights into clinical practice in a tertiary care setting in North India.

From a broader perspective, our study highlights the continued importance of RT as a cornerstone of the management of early glottic cancer. With advances in RT techniques, treatment planning is rapidly moving toward a personalized approach that balances oncological efficacy with functional preservation. Future

research should focus on prospective comparative studies evaluating different fractionation schedules and advanced technologies, as well as incorporating patient-reported outcomes to better assess quality of life.

Conclusions

Definitive RT represents an effective organ-preserving treatment approach for early-stage glottic cancer, with encouraging disease control and laryngeal preservation outcomes in our cohort. Both 3DCRT and IMRT were associated with satisfactory oncological outcomes; however, the present study does not establish the superiority of either technique in terms of disease control or treatment-related toxicity. Although IMRT offers potential dosimetric advantages, its clinical toxicity benefit could not be conclusively demonstrated in our study. Furthermore, in the absence of formal voice-quality assessment, conclusions regarding functional voice preservation remain limited. Longer follow-up and prospective studies incorporating standardized oncological, toxicity, and voice-related assessments are warranted to better define long-term outcomes. Preservation of the larynx while maintaining disease control remains the fundamental therapeutic objective in early-stage glottic cancer.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Institutional Ethics Committee, Sher-i-Kashmir Institute of Medical Sciences issued approval RP 18/2021. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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