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ROLE OF DEFINITIVE RADIOTHERAPY FOR LARYNX PRESERVATION IN PATIENTS WITH LARYNGEAL CANCER

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ABSTRACT

Background: Laryngeal squamous cell carcinoma (LSCC) is a common malignancy of the head and neck, strongly linked to tobacco and alcohol use. While total laryngectomy remains a curative option, it significantly affects quality of life. Definitive radiotherapy has become a preferred larynx-preserving alternative, particularly in early to moderately advanced stages of the disease. **Aim:** This study aimed to assess the effectiveness of definitive radiotherapy in managing non-metastatic LSCC, focusing on treatment outcomes, progression-free survival (PFS), and key prognostic factors influencing radiotherapy response. **Patients and Methods:** A retrospective observational study was conducted at Baghdad Teaching Hospital, including 20 patients diagnosed with stage I–III non-metastatic LSCC between 2017 and 2019. All patients received radical radiotherapy. Clinical data were collected, including demographics, tumor stage, radiotherapy regimen, and follow-up outcomes. Response and recurrence were evaluated using radiological and endoscopic assessments. Kaplan–Meier analysis was used to estimate PFS. **Results:** The study population had a mean age of 63 ± 9.3 years, with 75% being male. The majority (55%) presented with T3 stage tumors. The mean radiation dose was 66 ± 3.5 Gy over an average of 32 ± 3 sessions. After a mean follow-up of 36.3 months, 35% of patients remained progression-free, while 65% experienced recurrence. The median PFS was 28 months. Younger age and lower T stage were significantly associated with improved response ($p = 0.028$ and $p = 0.016$, respectively), whereas nodal involvement and radiation dose were not. **Conclusion:** Definitive radiotherapy provides a viable organ-preserving approach in LSCC, especially effective in younger patients with early-stage disease. However, recurrence in advanced cases highlights the need for tailored multimodal strategies.

KEYWORDS: radiotherapy, larynx, preservation, laryngeal, cancer.

INTRODUCTION

Laryngeal squamous cell carcinoma (LSCC) is among the most common malignancies of the head and neck region, accounting for a substantial proportion of morbidity and mortality worldwide. Its incidence is strongly linked to modifiable risk factors such as tobacco use and excessive alcohol consumption, both of which contribute synergistically to the pathogenesis of laryngeal cancer. Over recent decades, the management of locoregionally advanced LSCC has evolved significantly, driven by a growing emphasis on balancing oncologic control with the preservation of organ function and quality of life.[1] Historically, total laryngectomy was considered the gold standard for the treatment of advanced laryngeal cancer. While effective in disease control, this approach often led to significant impairment in voice, swallowing, and overall patient well-being. The paradigm began to shift with the introduction of organ-preserving strategies, particularly definitive radiotherapy (RT) and concurrent chemoradiotherapy (CCRT), which offered the possibility of curing the disease while maintaining laryngeal function.[2] A major turning point was the publication of the Radiation Therapy Oncology Group (RTOG) 91–11 phase III randomized controlled trial. This landmark study demonstrated that CCRT resulted in superior larynx preservation rates compared to induction chemotherapy followed by RT and RT alone, establishing CCRT as the standard of care for selected patients with locally advanced disease. However, while functional preservation was improved, overall survival (OS) did not significantly differ among the treatment groups. Notably, increased non-cancer-

related mortality in the CCRT group raised concerns, with emerging evidence suggesting a link to laryngo-esophageal dysfunction (LED), a complication that remains under-investigated in many studies.[3–5] In this context, definitive radiotherapy, either alone or as part of CCRT, continues to play a central role in the multidisciplinary management of laryngeal cancer. Its ability to preserve the anatomical and functional integrity of the larynx makes it an attractive option for both clinicians and patients. However, questions remain regarding its long-term efficacy, impact on survival, and associated toxicities.[4] This thesis aims to explore the role of definitive radiotherapy in the preservation of the larynx and its therapeutic efficacy in patients with laryngeal cancer.

METHOD

This retrospective observational study was conducted at the Radiotherapy Department of Baghdad Teaching Hospital, analyzing medical records of patients diagnosed with non-metastatic laryngeal squamous cell carcinoma (LSCC) who underwent definitive radiotherapy between January 2017 and December 2019. **Study Population:** The study included 20 patients aged 18 years or older with histologically confirmed stage I, II, or III non-metastatic LSCC. All patients received curative-intent external beam radiotherapy, with some cases involving concurrent chemotherapy. Patients were selected based on completion of the full prescribed course of treatment and availability of complete medical records. **Inclusion and Exclusion Criteria:** Inclusion criteria were as follows: confirmed diagnosis of stage I–III non-metastatic LSCC, completion of full prescribed radiotherapy, and treatment with or without concurrent chemotherapy. Patients were excluded if they had metastatic disease at presentation or if radiotherapy was incomplete. **Data Collection:** Patient data were retrieved from institutional medical records and included demographic details (age, sex), tumor characteristics (T and N staging), radiotherapy regimen, chemotherapy usage, and treatment response. Follow-up information was obtained through clinical notes and radiologic reports, primarily from contrast-enhanced CT scans and fiberoptic laryngoscopic examinations. **Radiotherapy Protocol:** All patients received radiotherapy via a linear accelerator, administered once daily, five days per week. Stage-specific dosing included 63 Gy in 28 fractions for stage I, 65 Gy in 29 fractions for stage II, and 70 Gy in 35 fractions for stage III, the latter combined with cisplatin-based chemotherapy. **Response Assessment:** Local control was assessed through regular clinical evaluations using fiberoptic laryngoscopy and radiologic imaging (contrast-enhanced CT). Patients were followed every three months in the first year and every 6–12 months thereafter. **Statistical Analysis:** Data were analyzed using SPSS version 23. Means and standard deviations described continuous variables; frequencies and percentages summarized categorical variables. Differences between groups were tested using independent-samples t-tests, Chi-square, or Fisher's exact tests. Kaplan–Meier analysis estimated progression-free survival (PFS), with significance set at $p < 0.05$. **Ethical Considerations:** Ethical approval was granted by the College of Medicine, University of Baghdad. Verbal informed consent was obtained from all patients after explaining the study's purpose and assuring voluntary participation.

RESULTS

There were 20 patients including in this study. Table 1 presents the demographic characteristics of the study population. The mean age of the participants was 63 ± 9.3 years, with a range of 39 to 76 years, indicating that the majority of patients were in the older adult age group. The cohort was predominantly male, comprising 75% of the sample (n=15), while females represented 25% (n=5).

Table 1: Demographic Data.

Variable	Frequency (Percentage)
Age **Mean ± SD Range**	63 ± 9.3 years 39 – 76 years
Sex Male **Female**	15 (75%) 5 (25%)

Table 2 presents the clinical characteristics of laryngeal cancer among the study participants. All cases (100%) involved primary tumors of the larynx, and histopathologically, all were confirmed as squamous cell carcinoma (SCC). Regarding tumor staging, the majority of patients presented with advanced disease: 55% were classified as T3, followed by T2 in 25% and T1 in 20% of cases. Nodal involvement was absent (N0) in 80% of patients, while 20% had regional lymph node metastasis (N2). Notably, no cases (0%) showed distant metastases at diagnosis (M0 = 100%).

Table 2: Laryngeal Cancer Characteristics.

Variable	Frequency (Percentage)
Type of Tumor **Larynx**	 20 (100%)
Sub-Type **Squamous cell carcinoma**	 20 (100%)
Staging T T1 **T2** **T3**	4 (20%) 5 (25%) 11 (55%)
Staging N N0 **N2**	16 (80%) 4 (20%)
Staging M **M0**	 20 (100%)

The mean total dose of radiotherapy administered to the patients was 66 ± 3.5 Gy, with a range between 60 and 70 Gy, delivered over a mean of 32 ± 3 sessions (range: 28 to 35 sessions). This treatment regimen aligns with standard definitive radiotherapy protocols for laryngeal squamous cell carcinoma. Assessment of treatment response revealed that 7 patients (35%) achieved a favorable response with no recurrence during the follow-up period, whereas 13 patients (65%) experienced tumor

recurrence following radiotherapy. Among the responders, the mean duration of response was 36.3 ± 19 months, with a range from 8 to 60 months. As in table 3.

Table 3: Radiotherapy Assessment and Efficacy Assessment.

Variable	Frequency (Percentage)
Dose of Radiotherapy Mean ± SD **Range**	66 ± 3.5 Gy 60 – 70 Gy
Number of Radiotherapy Sessions Mean ± SD **Range**	32 ± 3 sessions 28 – 35 sessions
Radiotherapy Response Assessment Responded **Recurrent**	7 (35%) 13 (65%)
Duration of Response Mean ± SD **Range**	36.3 ± 19 months 8 – 60 months

A total of 20 patients with laryngeal squamous cell carcinoma were included in the progression-free survival (PFS) analysis. During the follow-up period, 13 patients (65%) experienced disease progression, while 7 patients (35%) were remained progression-free at the time of analysis. The Kaplan–Meier estimate demonstrated a stepwise decline in progression-free survival over time. At 1 month, the cumulative PFS was 95%, decreasing to 90% at 12 months, 80% at 15 months, and 50% by 28 months. A continued decline was observed with the survival probability reaching 35% at 60 months, indicating that fewer than one- third of the patients remained progression-free five years after treatment. The median PFS time was 28.0 months (95% confidence interval [CI]: 20.33–35.67), while the mean PFS time was 36.3 ± 4.2 months (95% CI: 27.98–44.62). as in fig 1.

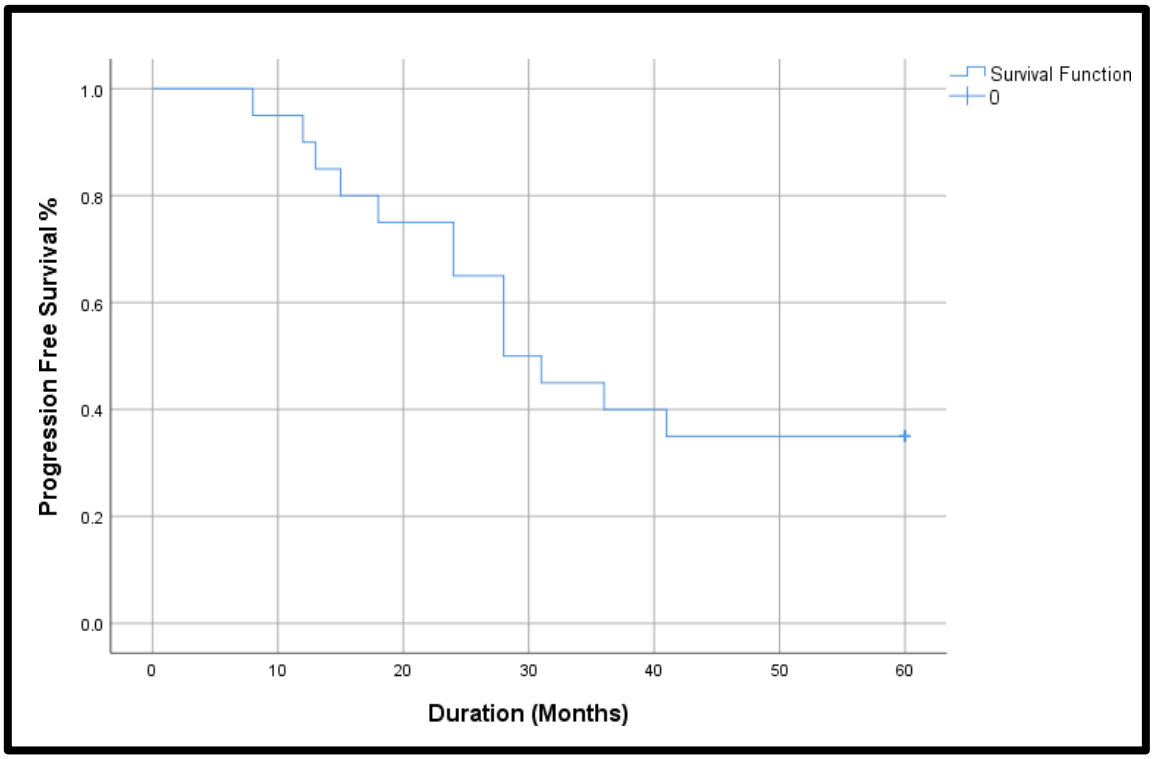

Figure 1: Progression-Free Survival Among Laryngeal Cancer Patients Factors Associated with Radiotherapy Response.

An analysis was conducted to identify clinical and treatment-related factors associated with response to radiotherapy among the 20 patients. Of these, 7 patients (35%) responded to radiotherapy with no evidence of recurrence, while 13 patients (65%) were classified as non-responders due to documented recurrence. Age was found to be significantly associated with radiotherapy response, with responders having a lower mean age of

59.8 ± 10.3 years compared to 64.7 ± 8.6 years in non-responders (p = 0.028). No significant association was observed between sex and treatment response (p = 0.4), although males constituted the majority in both groups. Tumor T-stage was also significantly associated with response outcomes. Among responders, T1 and T3 tumors were equally represented (each 42.9%), while in non-responders, the majority had T3 tumors (61.5%) with fewer early- stage (T1: 7.7%, T2: 30.8%) cases (p = 0.016). This suggests that early-stage tumors may have a more favorable response to radiotherapy. No significant difference was found in nodal staging (N0 vs. N2) between the two groups (p = 0.48), indicating that nodal status alone did not predict radiotherapy efficacy in this cohort. Likewise, radiotherapy dose and number of treatment sessions were similar between responders and non-responders (p = 0.44 and p = 0.39, respectively), suggesting that variations within standard therapeutic ranges did not impact outcomes. As in table 4.

Table 4: Factors Associated with Radiotherapy Response.

Variable	Responders (N=7)	Non-Responders (N=13)	P value
Age, years Mean ± SD	59.8 ± 10.3	64.7 ± 8.6	**0.028**
Sex Male Female	6 (85.7%) 1 (14.3%)	9 (69.2%) 4 (30.8%)	0.4
Staging T T1 T2 T3	3 (42.9%) 1 (14%) 3 (42.9%)	1 (7.7%) 4 (308%) 8 (61.5%)	**0.016**
Staging N N0 N2	5 (71.4%) 2 (28.6%)	11 (84.6%) 2 (15.4%)	0.48
Dose of Radiotherapy Mean ± SD	65 ± 3.3 Gy	66 ± 3.4 Gy	0.44
Number of sessions Mean ± SD	31.2 ± 3.2	32.5 ± 2.9	0.39

DISCUSSION

The demographic and clinical characteristics of our study cohort align closely with established global and regional epidemiological patterns of laryngeal squamous cell carcinoma (LSCC). With a mean age of 63 years and a male predominance (75%), our findings echo trends documented in both Western and Iraqi populations. Mousavi et al. reported a median diagnosis age of approximately 65 years in the U.S., primarily affecting individuals over 60.[6] Similarly, Mjali et al. observed a median age of 65 years in Karbala, Iraq, with 97.67% of cases occurring in those above 40, reinforcing the age-associated risk for LSCC in Iraq.[7] The male-to-female ratio in our cohort (3:1) is also consistent with the literature, as Mjali et al. reported a ratio of 4.37:1.[7] This male predominance is typically attributed to higher tobacco and alcohol exposure among men—recognized risk factors for LSCC.[8] As Chaturvedi et al. noted, while HPV-related oropharyngeal cancers are increasing, LSCC remains primarily linked to traditional carcinogens, particularly in older men.[9] Kong LN et al. further underscored the global correlation between smoking prevalence and LSCC incidence.[10] All patients in our study had squamous cell histology, in accordance with global data indicating SCC as the predominant subtype.[11] A notable 55% of our cohort presented with T3 tumors, mirroring Mjali et al.'s findings of a substantial portion of Iraqi patients presenting with advanced-stage disease.[11] The high percentage of advanced T-stage tumors likely reflects delayed diagnosis and limited early detection. Furthermore, nodal involvement (N2) was present in 20% of patients, with all being M0 at presentation, consistent with the typically localized nature of LSCC at diagnosis.[11,12] Our analysis of treatment outcomes revealed a 35% progression-free survival (PFS) rate at 60 months, with a median PFS of 28 months following definitive radiotherapy. This is consistent with findings by Gharib et al., who reported similar PFS outcomes in patients receiving single-modality radiotherapy, especially in early-stage disease.[13] Akbaba et al. emphasized poor outcomes in cases of locoregional recurrence post-radiotherapy, a trend we also observed, particularly among T3-stage and older patients.[14] Conversely, Yuan et al.'s 2024 meta-analysis suggested better outcomes with systemic therapy, challenging the sufficiency of radiotherapy alone in advanced or aggressive tumors.[15] De Virgilio et al. similarly advocated for combined modality treatments, citing improved locoregional control and laryngeal preservation.[16] Age and tumor stage emerged as significant predictors of radiotherapy response in our cohort. Younger patients (<60 years) and those with early-stage tumors (T1/T2) demonstrated better outcomes, consistent with Sato et al.'s findings on hypopharyngeal SCC.[17] Although nodal status and radiotherapy dose/session count were not statistically significant, larger studies may clarify their impact. Collectively, our findings reinforce the importance of

individualized treatment strategies and highlight the potential benefits of integrated multimodal approaches in high-risk LSCC patients. This study is limited by its small sample size and retrospective design, which may introduce selection and information bias. The follow-up period may not capture long-term outcomes or late toxicities. Additionally, molecular markers, comorbidities, and performance status were not assessed.

CONCLUSION

In this study, the 5-year progression-free survival (PFS) rate was 35%, highlighting that fewer than one-third of patients remained disease-free five years post-treatment. Younger age and lower T-stage were significantly associated with better response to radiotherapy, reinforcing the importance of individualized treatment planning based on clinical characteristics. The study emphasizes the need for stratified treatment strategies based on clinical predictors to enhance radiotherapy efficacy.

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