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Laryngeal Preservation Rates in Patients Treated with Definitive or Concurrent Chemo radiation: Study in A high Volume Cancer Center

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ABSTRACT

Introduction: The standard of care for patients with early-stage laryngeal cancer is radiotherapy and for locally progressed disease is concurrent chemo radiotherapy with cisplatin in all patients suitable for organ preservation. In patients not suitable for organ preservation surgery (Total laryngectomy) followed by radiotherapy is used. This organ saving treatment change from total laryngectomy to radiotherapy or concurrent chemoradiation has great impact on patients' quality of life. **Methods:** This prospective study comprised a total of 100 patients. The typical follow-up time was one year. Patients with early-stage and locally progressed laryngeal carcinoma were randomly allocated to receive either radiotherapy alone or concurrent chemoradiation with cisplatin. The main goal was to keep the larynx intact. **Results:** Out of 100, Patients made up roughly 97% men and 3% women. Early-stage groups made up 40% of the population, while locally advanced groups made up 59%. At one year, there had been no local relapse and in 89.6% of the patients larynx was preserved. It was shown that females had superior local control than males. **Conclusions:** These findings are significant, but it's important to keep in mind that irradiation is an effective method of treating these tumors, may have improved activity with modified fractionation or addition of simultaneous chemotherapy. Radiotherapy is a viable option to avoid total laryngectomy. On the other hand, new therapy options (biologic tools, imaging locations) and criteria for therapeutic success (quality of life, quality of maintained function, and cost-effectiveness) are emerging.

INTRODUCTION

Laryngeal cancer is the second most common site of respiratory cancer after lung [1]. The current rate, predominance and mortality of laryngeal cancer are estimated at 2.76 cases per year per 100,000 inhabitants, 14.33 cases/year per 100,000 inhabitants, and 1.66 deaths per year per 100,000 inhabitants respectively [2]. Laryngeal carcinoma is roughly 5-folds higher in males. Its incidence increases with ageing, peaking after 65 years of age [3]. Laryngeal cancers start in squamous cells that line the inside of the larynx. Anatomically, the larynx is divided into 3 regions including supra-glottis, glottis and sub-glottis. Majority of the laryngeal cancers have their origin from glottic region, followed by supraglottic and subglottic regions. Subglottic laryngeal cancers are less frequently occurring [4].

Most prevalent histology of laryngeal cancer is squamous cell carcinoma [5]. Common symptoms at time of presentation are persistent hoarseness and voice changes, difficulty or pain while swallowing, persistent cough associated with hemoptysis and difficulty in breathing with stridor [6].

In beginning of 18th century, the mainstay of locally advanced laryngeal cancers was total laryngectomy alone. In era of 19th century, radiotherapy was incorporated after surgery [7]. For a very long time, researchers aimed to explore the treatment options which could lead to organ preservation and could be of benefit to the patients [8]. An important milestone was achieved when studies were published introducing the role of concurrent chemo radiotherpy in patients with locally advanced laryngeal cancers that led to the success of preserving patients organs ensuring better quality of life [9].

Early detection and timely treatment play a crucial role in organ preservation and prognosis of the disease. Early-stage disease defined as Stage I-II are treated with radiation therapy alone, Stage III cancer are treated with concurrent chemoradiation and have resulted in good loco-regional control and improved overall survival [10]. Stage-IVa laryngeal cancers are treated with surgery

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followed by radiotherapy [11]. Stage IVb cancers are unresectable, organ is already damaged, usually tracheostomy is done and are treated with curative dose chemoradiation for longer term palliation [12].

This study was planned to review the organ preservation rate in our population suitable for radiation/ chemoradiation. This was assessed till one year of follow-up and stagewise organ preservation rate was documented.

The rationale of our study was to look for the larynx preservation rates in all suitable candidates, in our population. This will help in patient counselling for organ preservation and prove the mettle of organ preservation approach during the multi-disciplinary team meetings MDTs). This will add to the confidence of our oncologists on this approach.

Objective

To evaluate the rates of laryngeal preservation in patients with early-stage larynx cancers treated with radical radiotherapy/radical concurrent chemo radiotherapy at 12 months of follow up at multicenter institutes

METHODS AND MATERIALS

It is a multicenter institutional prospective study from Shaukat Khanum Cancer Hospital, CMH Lahore and INMOL Cancer Hospital Lahore during the period from January 2024 to April 2025. A sample size of 100 patients was calculated using WHO sample size calculator. Estimated laryngeal preservation rates were 80%. Power of the study was kept at 80%, and significant p-value was kept below 0.05.

Inclusion Criteria

Set of the patients included the patients diagnosed with laryngeal cancers from stage I to III and willing to undergo radiotherapy. For stage III, the patients should have estimated glomerular filteration rate (GFR) of more than 60 ml/min to be eligible for concurrent cisplatin 100 $mg/m^2$for 3 doses.

Exclusion Criteria

Patients with T4a and T4b disease or T3 with eGFR < 60 ml/min or patients who had laryngectomy.

A sample comprising total of 100 consecutive patients fulfilling the inclusion criteria was taken. The patients were treated and followed from January 2024 to April 2025. All the patients of stage I or II were treated with radical radiotherapy to a dose of 55 gray (Gy) in 20 fractions (Fx). All patients with stage III disease were treated with 70 Gy in 35 Fx to high risk volume, 63 Gy in 35 Fx to intermediate risk volume and 56 Gy in 35 Fx to low risk areas with a simultaneous integrated boost (SIB) technique intensity modulated radiotherapy (IMRT). concurrent cisplatin 100 mg/m2 on Day 1, 22 and 43 of start of radiotherapy (for 3 doses). The dose of radiation and radiation schedule remained same for all the patients.

After completion of CCRT all the patients had response evaluation by fiberoptic direct laryngoscopy at 6 weeks and PET scan at 3 months for node positive cases Purpose of the study was to determine organ preservation rates in patients diagnosed with early-stage cancers that were treated with radiotherapy alone or with concurrent chemo radiation. Weekly regular follow ups were made to assess and manage the chemo radiation induced side effects. Response assessment was made 6-8 weeks post completion of chemo radiation including detailed head and neck examination, CT imaging and direct laryngoscope showing vocal cord mobility.

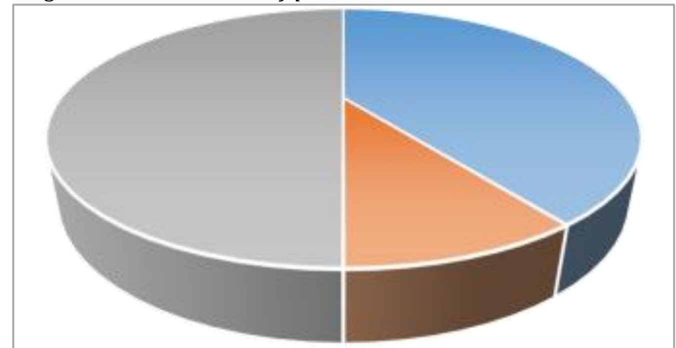
Statistical analysis was performed using Statistical Package for Social Sciences software 22.0. Frequencies were calculated for categorical variables like gender, stage, treatment done (RT group vs CCRT Group) and response of the disease Data was plotted on pie chart and presented in tabular form.

RESULTS

Median age of presentation was 57 years. Stage wise distribution of patients with Stage I, II, III were as under:

Figure 1

Stage wise distribution of patients

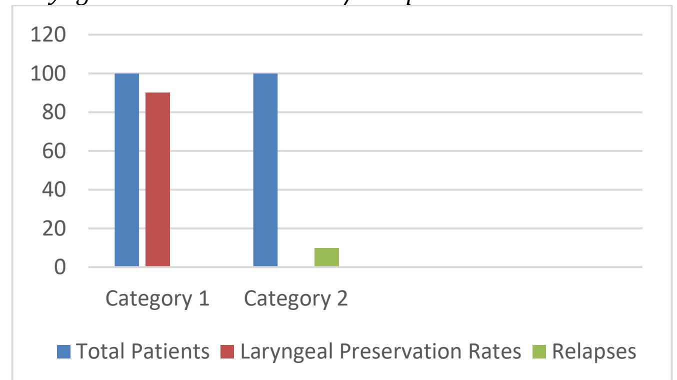


Of the total number of patients, largest group of patients was of stage III disease (50%) followed by stage I disease (40%) followed by Stage II disease (10%).

40% patients were treated with radical radiotherapy whilst 60% of the patients received concurrent chemo radiotherapy. The results for this group of patients are as under:

Figure 2

Laryngeal Preservation Rates /Relapses



As the above graph shows that at 1 year of follow up, among the patients treated with radical radiotherapy or radical concurrent chemo radiotherapy, only 10% of the patients had local recurrence requiring total laryngectomy and neck dissection. 90% of the patients did not show any recurrence on follow up.

Hence laryngeal preservation rate in our study population was 90%, at 1 year of median follow up

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DISCUSSION

This prospective study was conducted at a high-volume cancer center in Pakistan, demonstrated a laryngeal preservation rate of 90% and a local relapse rate of 10% at a median follow-up of one year among 100 patients with stage I–III laryngeal cancer treated with radical radiotherapy (RT) or concurrent chemoradiotherapy (CCRT). These outcomes compare favorably with the long-term findings of the Radiation Therapy Oncology Group (RTOG) 91-11 trial by Forastiere et al., which reported laryngeal preservation rates of 84% for CCRT, 72% for induction chemotherapy followed by RT, and 67% for RT alone at two years [13].

While RTOG 91-11 set a new standard for non-surgical management of laryngeal cancer, several factors may account for the superior preservation rate observed in our cohort. Firstly, our treatment protocol exclusively employed cisplatin as the concurrent chemotherapy agent, specifically 75 mg/m^2 administered on days 1, 22, and 43 of radiotherapy. The radiosensitizing effect of cisplatin is well established, and adherence to this standardized regimen likely reduced treatment variability, improving oncological outcomes [14,15].

Secondly, our radiotherapy technique differed from both RTOG 91-11 and several subsequent studies. While IMRT and IGRT were not utilized, all patients were treated using volumetric modulated arc therapy (VMAT). VMAT allows for superior target volume conformity and more efficient sparing of critical adjacent structures compared to conventional IMRT, without extending treatment times significantly [16,17]. Prior studies, including Nutting et al.'s PARSPORT trial, demonstrated the clinical benefits of IMRT; however, VMAT has since emerged as a preferred technique for its dosimetric and logistical advantages [18,19].

Our findings are also consistent with other modern series reporting laryngeal preservation rates exceeding 80%. Lefebvre et al. reported a preservation rate of 81–85% using sequential chemoradiotherapy [20]. Similarly, Beitler et al. observed preservation rates above 80% in patients receiving contemporary CCRT regimens with improved radiotherapy techniques [21]. However, the exclusive use of VMAT and cisplatin in our study provides a distinct treatment homogeneity, which may contribute to our relatively higher preservation rates.

Further improvements in laryngeal preservation may be achieved through several strategies. Incorporation of functional imaging modalities such as PET-CT for response assessment and adaptive radiotherapy could help tailor treatment more precisely [22]. Additionally, biomarker-driven patient selection and molecular profiling may allow for more individualized treatment approaches, reducing overtreatment while maintaining disease control [23,24].

Despite its strengths, our study is not without limitations. Although anatomical preservation was the primary endpoint, functional outcomes including voice quality, swallowing function, and quality of life measures were not systematically evaluated, which limits the comprehensive assessment of laryngeal preservation in a broader clinical context. A further limitation is the relatively short follow-up duration of one year, whereas late relapses and functional deterioration may become apparent beyond this period.

Nevertheless, the strengths of this study include its focus on a homogenous patient population, consistent use of cisplatin-based CCRT, and VMAT as the sole radiotherapy technique. These factors contribute to a clear interpretation of treatment efficacy, offering valuable real-world evidence from a high-volume cancer center in a low-to-middle-income country setting.

In conclusion, the observed laryngeal preservation rate of 90% and local relapse rate of 10% at one year suggest that concurrent cisplatin-based chemoradiotherapy delivered using VMAT is an effective strategy for non-surgical management of stage I–III laryngeal cancer. These results compare favorably with historical data, including RTOG 91-11 and other contemporary studies, reinforcing the importance of continued advances in radiotherapy technology and treatment protocol standardization. Prospective multicenter studies incorporating functional outcomes and longer follow-up are warranted to validate these findings.

CONCLUSION

For a very long time, treatment of locally advanced laryngeal carcinoma was considered to be total laryngectomy. By the virtue of evolvement of concurrent chemo radiation, organ preservation was achieved. As above results show that the laryngeal preservation rates in our population was estimated to be 90% with 10% local recurrence, these results.

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