



Retrospective Analysis of Rate of Larynx Preservation in Locally Advanced Laryngopharyngeal Squamous Cell Carcinoma Following Chemo RT – An Institution Based Study

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Abstract

Introduction: Chemo-radiation preceded by induction chemotherapy is reported valuable alternative to laryngectomy in laryngeal cancer for larynx preservation. This study was performed to assess the influence chemo radiation on preservation of larynx.

Materials and Methods: Sixty-three patients treated from January 2013 to December 2014 in our institute were reviewed and who were available for follow-up in this retrospective study. Total dose of 66-70 Gray was used at 2 gray per fraction daily for five days week were used. Larynx preservation rate at 1 year of median follow-up were analysed.

Results: Among 63 patients, larynx preservation was possible in 50 patients (78%). With chemo-radiation, excellent preservation of larynx was achieved in stage II (78%) disease, while in advanced stage III and stage IVA, larynx preservation was 67.06% and 64.35%, respectively.

Conclusion: Chemo-radiation (either neoadjuvant chemotherapy followed by chemoradiation or concurrent chemo-radiation) has better larynx preservation rate in early as well as advanced laryngeal cancer patients.

Introduction

Locally advanced laryngopharyngeal squamous cell carcinoma is very common among head and neck malignancies in developing countries. Current treatment modality is aimed at larynx preservation without compromising survival of the patients. Even though larynx preservation is achieved with both surgery and chemo RT, the latter is preferred by most of the patients.

Cancer larynx incidence in India is 3.2 per lakh male and female per year. The number of deaths is 1.1 per lakh male and female per year. These were age-adjusted and based on 2008-2012 cases and

deaths.¹ Total laryngectomy can provide disease control in locally advanced cancer larynx patients and thus having negative impact on patient quality of life. Organ preservation strategies started in the early 80's with initial trials demonstrating the potential of chemotherapy to cause tumour regression as well as predict response to radiotherapy.² since, then it is used in conjunction with radiotherapy as an approach to organ preservation in various combinations as sequential neoadjuvant and concurrent. The Veterans Affairs (VA) Study group was pivotal for establishing the role of larynx preservation in advanced laryngeal

cancers. In this study, patients were randomized to the experimental group of induction chemotherapy (ICT) followed by radiotherapy in those with partial response against the standard of care i.e. surgery followed by adjuvant radiation and they were able to achieve larynx preservation in 64% maintaining similar overall survival in both arms. This study set the stage for further larynx preservation studies and established induction chemotherapy as standard of care.³ In the 1990s, Forastiere et al. conducted a three armed study comparing induction chemotherapy, concurrent chemoradiotherapy (CCRT) and radiotherapy alone in patients with advanced laryngeal cancers.⁴ Overall survival was comparable in all the three arms, larynx preservation was best with concurrent CRT. Two-year larynx preservation rates of 88%, 75% and 70% in the CCRT, induction arm and radiation alone arm. This was further supported by the meta-analysis of chemotherapy in head neck cancer which demonstrated an absolute benefit of chemotherapy administered concomitantly.⁵ 10-year update of Radiation Therapy Oncology Group 91-11 studied into the long-term effect in these approaches.⁶ Radiotherapy alone was significantly inferior to both induction chemotherapy and concurrent chemo radiotherapy arms. With regards to toxicity, mortality not related to cancer or treatments were significantly higher in concurrent chemotherapy group (30.8% vs. 20.8% in the induction chemotherapy group versus 16.9% in radiotherapy alone group). It could be attributed to late toxicity related to swallowing dysfunction along with silent aspiration.⁷ Long-term interpretation of speech and swallowing showed acceptable results although available data was limited. Chemoradiation preceded by induction chemotherapy is reported valuable alternative to laryngectomy in laryngeal cancer for larynx preservation. This gave us the impetus to evaluate larynx preservation rate in our institute.

Aim of the Study

To analyse the rate of larynx preservation in patients with locally advanced laryngopharyngeal

squamous cell carcinoma who received chemo RT as the modality of treatment in the Department of Radiation Oncology, BIRO, RGGGH, Chennai.

Materials and Methods

Type of study: Retrospective study

Total number of patients: 63

Study Period: January 2013 –December 2014

Follow up period: 1 year

Inclusion Criteria

1. Patients with biopsy proven squamous cell carcinoma were included in the study
2. Locally advanced carcinomas in the sites supraglottis, glottis and hypopharynx were taken
3. T3/T4 disease with N1/N2/N3 nodal status were included in the study

Exclusion Criteria

1. Patients with histopathological reports suggestive of malignancy other than squamous cell carcinoma
2. Patients who underwent any form of surgery
3. Malignancy arising from oropharynx, nasopharynx and subglottis
4. T1/T2 disease or N0 nodal status

Thermoplastic mask or cast was used for immobilization in all the patients. Initially, the radiation portals encompassed primary disease, involved lymph nodes and microscopic disease around primary and in clinically uninvolved lymph nodes. Superior border of the lateral portal was placed at lower margin of the ala nasi to lower edge of tragus, inferior border at lower margin of the clavicle. Anterior border is along the vertical line joining the anterior end of the zygoma to the junction of the first and second molar and posterior border at the spinous process. After delivering 40 Gy in 20 fractions, the posterior neck field was reduced to spare spinal cord. Last 6 Gy boost was given to involved primary sites with primary echelon and involved lymph nodes (only gross disease). The primary goal of this study was to assess the influence of curative chemoradiotherapy on laryngeal preservation at 1 years of median follow up. It was

an objective analysis, and disease-free larynx with grade 0 or grade I hoarseness and satisfactory swallowing function have been considered as functional preservation of larynx. Absence of CR (complete response) or more than grade I hoarseness (unsatisfactory speech) is considered as failure of laryngeal preservation. For statistical analysis, data was arranged in excel format and was converted to SPSS format version 16 for computing 1-year laryngeal preservation.

Treatment Protocol

Total number of patients: 63

- 1) 58 patients received Concurrent chemo RT 66-70 Gy with weekly/ 3 weekly CDDP (weekly 40 mg/m² & 3weekly 100mg/m²)
- 2) 5 patients received Induction PFT (Paclitaxel 175mg/m², 5FU 1000mg/m², CDDP 100mg/m²) three cycles followed by chemo RT (66-70 Gy with weekly CDDP 40mg/m²)

Follow up Period: 1 year

First follow up at 6 weeks and monthly follow up thereafter.

Results

Patient Characteristics

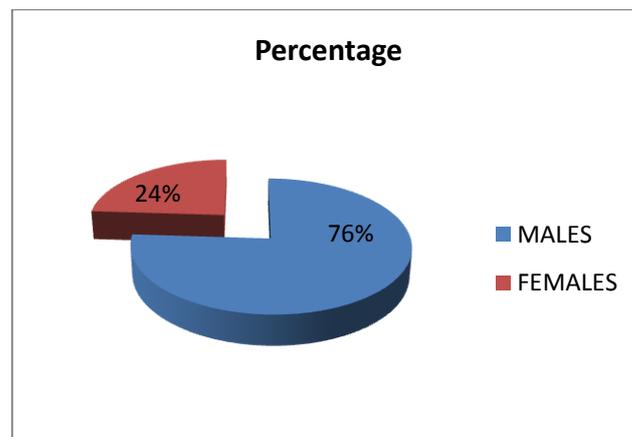
In this retrospective analysis, age of the patients ranged between 32 and 74 years with median age of presentation being 58 years. There were 48 males and 15 females. All patients were of cancer supraglottis, glottis and hypopharynx out of which 5(8%) were of stage II, 47(75%) were stage III and 11(17%) were stage IV. 5 (8%) patients received induction chemotherapy and rest of other patient received concurrent chemo-radiation or radical radiotherapy alone.

Laryngeal Preservation Rate

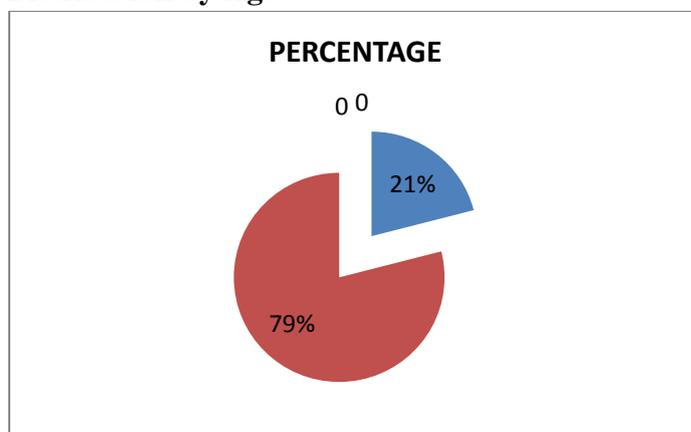
At a median follow up of 1 year for 63 patients who were available for follow-up, overall laryngeal preservation was observed in patients (68%). Larynx preservation of up to 78% was observed in stage II and in stages III, IV it was 67.06% and 64.35%, respectively. Among 48 males, larynx was preserved in 36 patients, while

in females out of 15 patients, larynx preservation was possible in 12 patients.

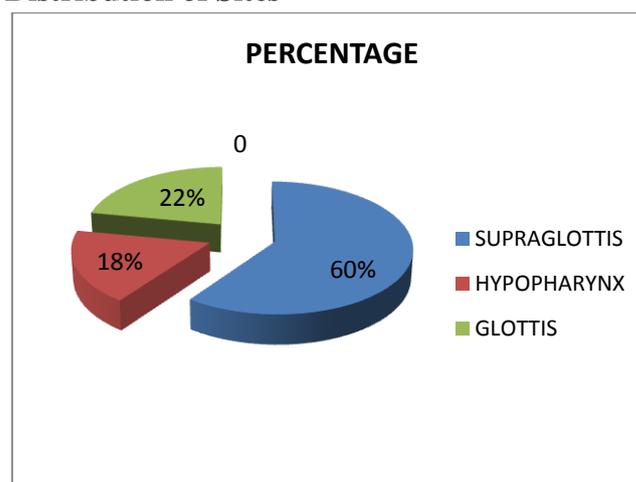
Sex Distribution



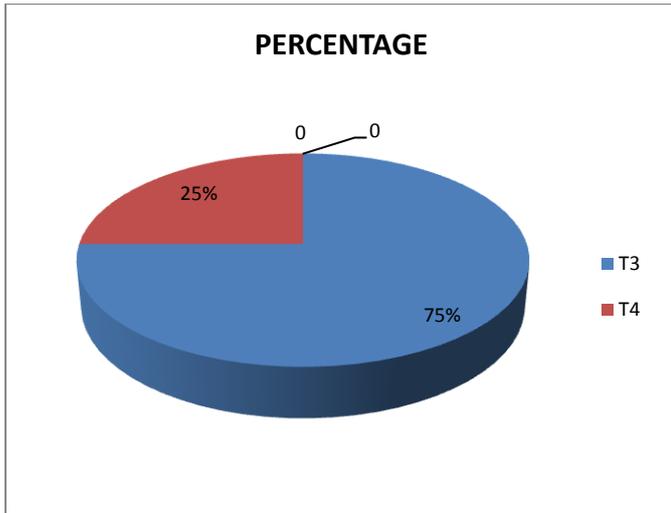
Distribution by Age



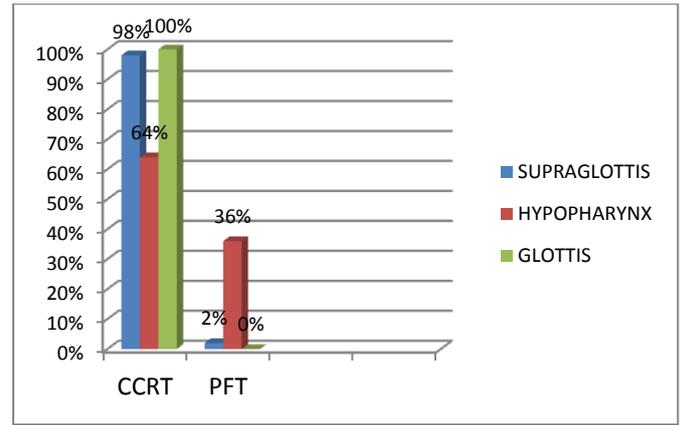
Distribution of Sites



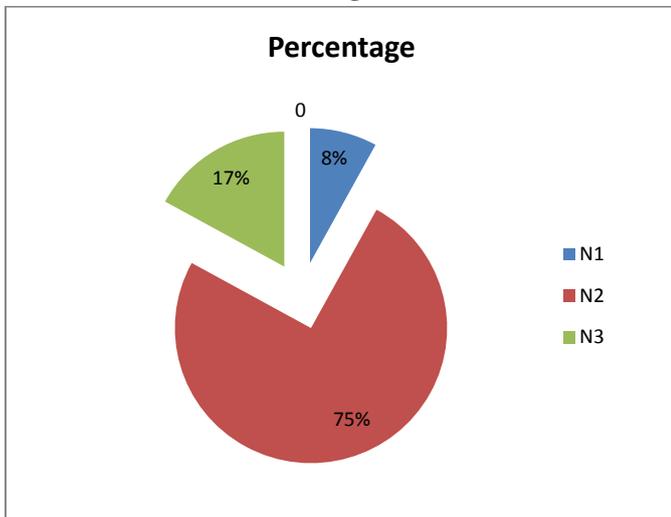
Distribution by Tumor Size



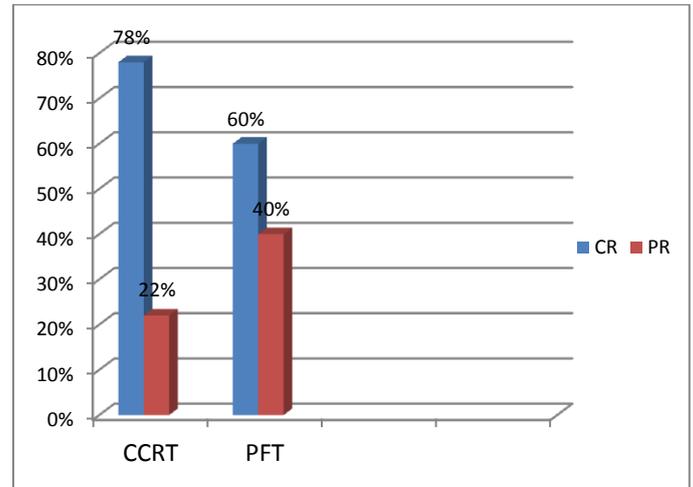
Site of the Disease vs Treatment Given



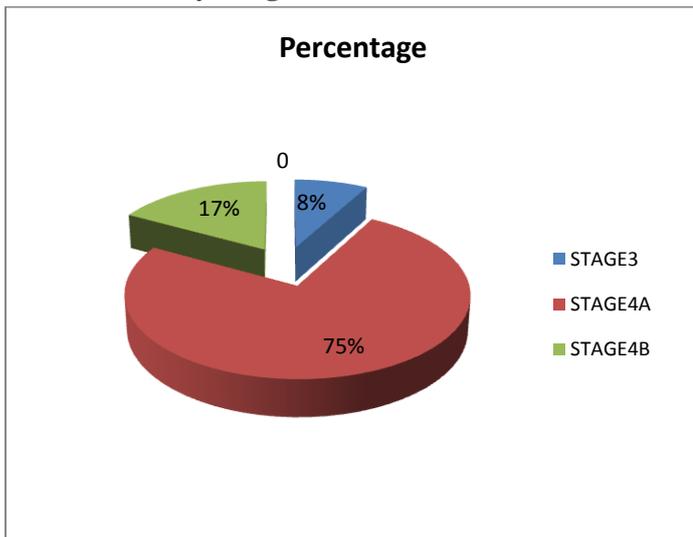
Distribution of Nodal Stage



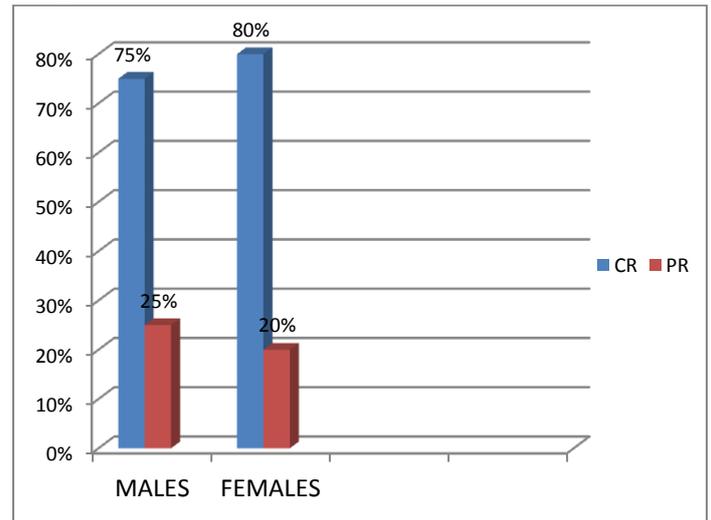
Response by Recist Criteria



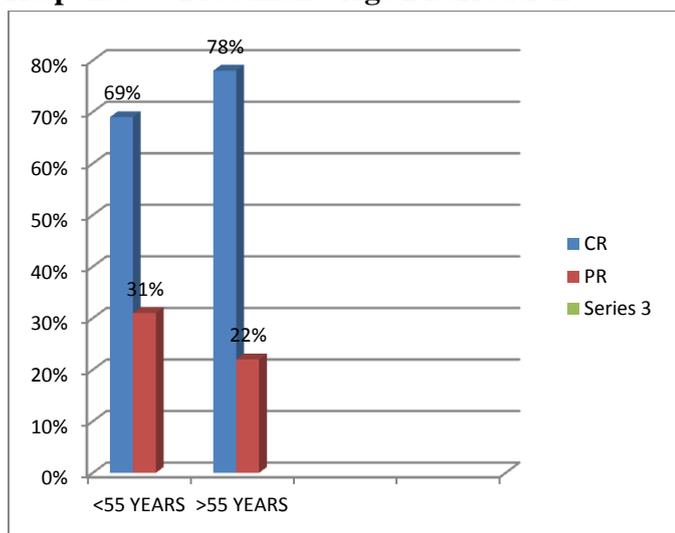
Distribution by Stage



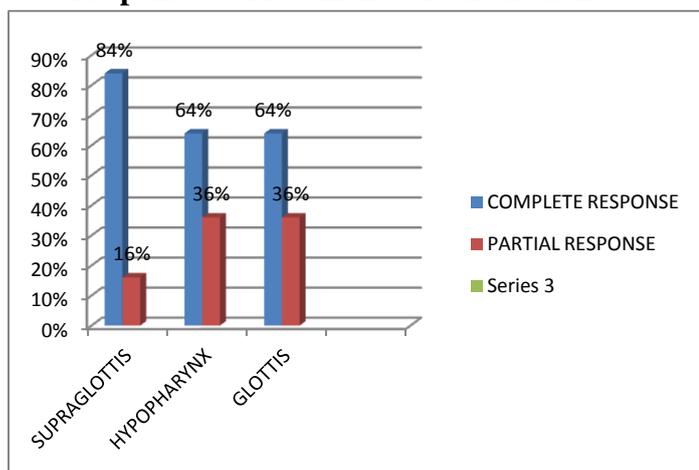
Response to Treatment: Sex Distribution



Response to Treatment: Age Distribution



Response to Treatment: Site Duration



Discussion

Larynx cancers account for nearly 1% of all malignancies and approximately 25% of head and neck tumors. Glottic cancers are approximately 3 times more common than supraglottic tumors; tumors of the subglottic larynx are rare, accounting for approximately 1% to 2% of carcinoma larynx. we decided to analyze cancers of supraglottis, glottis and hypo pharynx in this retrospective analysis. Usually the laryngeal cancer patients median age of presentation is 65 years and less than 4% of our patients are younger than 45 years old and it is seen predominantly in male population.⁹ Approximately two thirds of patients with laryngeal cancer have their disease limited to the laryngeal structures and less than 10% present with distant metastases at presentation.⁹ In our study, median age of

presentation is 58 years and 76% of patients were males. Majority of laryngeal cancer patients are now treated with organ preservation protocols. The treatment objective for early laryngeal cancer that can be treated with surgery or radiation, is to obtain cure with functional larynx with least morbidity. Treatment emphasizes avoiding combination of surgery and radiation because preservation of larynx may be compromised. There is no one treatment that has proven to be superior with regard to all treatment goals.^{10,11,12} Radical radiation is as effective as radical surgery in early stage with added advantage of larynx preservation. Inmost centers, upfront radiation is preferred for T1 and T2tumors, with surgery being reserved for salvageal though hemilaryngectomy produces similar cure rates for selected T1 and T2 laryngeal cancers; irradiation is usually associated with better quality of voice.^{13,14} In 1974, Bataini and colleagues published an overall loco regional control rate of 76% for relatively large series patients with T1, T2, N0-2 supraglottic carcinomas treated by radiotherapy alone.⁹ In our study, 1 year larynx preservation rate in stage II is 78%. Locally advanced laryngeal cancers (stages III and IV) require radical surgery followed by external radiotherapy. Chemo-radiation is an active alternative for surgery when organ preservation is desired. The landmark trial conducted by VA group established ICT followed by radiotherapy as an alternative to radical surgery for advanced carcinoma larynx. RTOG 91-11 study showed organ preservation was finest achieved with CCRT.^{3,4} In our study, we have found that overall larynx preservation of 68% could be achieved with chemo-radiotherapy (neoadjuvant chemotherapy followed by chemo-radiotherapy, concurrent chemoradiotherapy and radiotherapy alone which formed a veryfew number of patients)as the sole treatment modality inpatients of stage II-IVA laryngeal cancer. In our study 1 year larynx preservation rate in stage III and stage IV were67.06% and 64.35 % respectively. When compared with RTOG 91-11, our study does not show inferior results. Study conducted by Grouped' Etude des Tumeurs de la

TeTte et duCou (GETTEC), Head and Neck Tumour Study Group had to be prematurely abandoned due to a strong patient preference for organ preservation over surgical resection difference between radiotherapy alone and ICT followed by radiation group.⁴ In our study, local control rate in stage III is around 67.06% and in stage IV, it is found to be 64.35%, which is quite impressive when compared to western literature. It is important to remember that, in addition to showing the advantage of using chemotherapy with radiation, RTOG91-11 trial also demonstrated that radiotherapy alone is a reasonable treatment option for patients who cannot tolerate chemotherapy. In addition, it is critical to remember that the benefits of adding chemotherapy must be waived by the higher rates of treatment related sequelae, some of which can be life-threatening. chemotherapy in these patients needs to be further investigated. Intensity modulated radiotherapy (IMRT), a new RT technique, has the advantages of precise delivery, target conformity and normal tissue sparing. It is able to achieve a very high rate of locoregional control with less morbidity under optimal target delineation, appropriate physical quality control and accurate patient setup.¹⁶

Conclusion

Our study concluded that chemo-radiation (either neoadjuvant chemotherapy followed by chemo-radiation or concurrent chemo-radiation or radiation alone) has better larynx preservation rate in early as well as advanced laryngeal cancer patients. Quality of life is much improved in patients treated by nonsurgical approach and hence our study's preliminary results were very motivating and gave us the motivation to continue the same protocol for future.

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