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CONCURRENT CHEMORADIATION IN UNFAVORABLE T2N0 GLOTTIC CANCER-A TERTIARY CENTER EXPERIENCE.

Oncology

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ABSTRACT

Background: To assess the result of local control (LC) and survival in patients with unfavorable T2N0 glottic cancer who were treated with radiotherapy with or without chemotherapy.
Methods: Forty seven patients with unfavorable T2N0 glottic cancer treated between 2005 and 2012 were analyzed retrospectively. Prognostic factors were evaluated by univariate analysis.
Result: The 5-year LC rate of all patients was 70%. In univariate analysis 5-year LC rate of all patients treated with chemo radiation was 93.1% and only radiation was 54.1% which was statistically significant. The 5 year OS rate of all patients was 75% of these treated with chemoradiation was 93.1% and only radiation was 62.5%.
Conclusion: The retrospective analysis shows that a high rate of local control in patients with unfavorable T2N0 glottic cancer treated with chemoradiation when compared to radiotherapy alone.

KEYWORDS:

Unfavorable, glottic cancer, chemoradiation, local control.

INTRODUCTION

Laryngeal cancer is the ninth and seventh most common cancer in male in Asia and India respectively. In 2012 as estimated 25,446 new cases were diagnosed and 17,560 Indians lost their lives due to laryngeal cancer [1]. In India, the incidence of laryngeal cancer has been reported to be 1.26-8.18 per 1, 00,000 population, in different regions of the country [2]. Most common site of laryngeal cancer is glottis. It is often treated with definitive radiotherapy as it is useful for preservation of laryngeal function. The 5 year local control rates with radiotherapy alone range from 67% to 87% in T2N0 glottic cancer [3-6]. To improve the local control rate, there is some evidence in patients of T2N0 glottic cancer treated with concurrent chemoradiation [7-10].

Unfavorable T2N0 glottic cancer is defined as deeply invasive tumor on radiographicimaging with (or) without subglottic extension, with impaired cord mobility (indicating deeper invasion)[11]. Local control rate with only RT for unfavorable glottis cancer that is with impaired vocal cord mobility and subglottic extension respectively 70% and 56 %[12].

The purpose of this study to review retrospectively our experience in unfavorable T2N0glottic cancer treated with radiotherapy with or without chemotherapy from 2005 to 2012.

METHODS

Patient characteristics

A retrospective review was performed of 47 patients who had undergone radical radiotherapy with or without chemotherapy to T2N0 unfavorable glottic cancer (Stage II) according to 2002 international union against cancer classification system. Patients were treated at Cancer institute, adyar between 2005 and 2012. Out of 47 patients, 28 patients present with impaired vocal cord mobility alone and 19 patients with subglottic extension with or without impaired vocal cord mobility

All patients received RT as first choice of treatment. Patient inclusion criteria were a histologic proven squamous cell carcinoma and no previous RT for head and neck neoplasm.

Forty four patients (94%) were male and three (6%) were female. The median age was 60 years (23 -83 Yrs.). The initial examinations before start of treatment include physical examination, blood count, biochemical examination; electrocardiograph and staging procedure include CT scan and DLDP. The presence of human papilloma virus was not examined. Table 1 contains a summary of the clinical characteristics of 47 patients who were included in the study. All patients followed for median period of 60 months (range 13-132 months).

Table 1 Patient clinical characteristics.

	N	Percentage
Total no of patients	47	100
Age median (range)	60 y (23-83)	
Male/Female	44/3	94/6
Histology Squamous cell carcinoma	47	100
Grade Low Intermediate High	16 19 12	34 40 26
Histology Squamous cell carcinoma	47	100
Smoking as definitive co factor	25	53

TREATMENTS IN DETAIL

Radiotherapy

Table 2 contains a summary of the treatment course of the 47 patients. Twenty seven patients were treated with RT alone, twenty received concurrent chemoradiation. Patient usually treated with 2 Gy per fraction, per day to total dose of 60-70 Gy over 6 -8 wks.

Tabel 2 Treatment.

	N	Percentage
RT	27	57
RT+CT	20	43

Chemotherapy

The various chemotherapy drugs and regimes used are listed in Table 3.The chemotherapeutic regime of seven patients treated with CDDP/5FU consist of bolus 5FU at a dose of 325mg/m2/day (cap at 500) on days 1-3, combined with a 2 hours infusion of CDDP at a dose of 70 mg/m2 /day on day 1.Same regime repeated once in three week.

Four patients treated with CDDP at dose of 70 mg/m2/day on day 1 for every 3 week. Nine patients treated with CDDP at a dose of 40 mg/m2 /day every week.

Table 3 Chemotherapy regime

	N	Percentage
Weekly CDDP	9	45
CDDP/5 FU	7	35
3 Weekly CDDP	4	20

Statistical analysis:
Local control was assessed from beginning of RT until evidence of recurrence. Statistical study done with help of Z score. The result were statistically significant at the level of P<0.05. In univariate analysis, the variable analyzed includeage (>63 vs. <63), chemotherapy and site of involvement.

Follow up
After RT alone or concurrent chemotherapy, the patient were evaluated at 1 month interval for first 6 months, at 2 months up to 1 year , at 3 months interval up to 3 year and at 6 months interval thereafter. The patient who presented with recurrence of disease in the follow up time submitted to treatment by total laryngectomy. The interval between these was recorded.

RESULTS

Local control and pattern of failure
For all 47 patients five year local control was 70% of these only impaired vocal cord mobility T2No glottis cancer 5 year local control was 75% and with subglottic extension T2 N0 glottic cancer was 62.5%.

Of the 47 patients 27 patients treated with only RT .This group 10 patients had loco regional failure. Of these 4 had residue, 3 had local recurrence and 3 had nodal recurrence. Here 5 year follow up eligible patient is 24.

Of these 47 patients 20 patients treated with concurrent chemoradiation. This group one had residue and underwent total laryngectomy. One patient defaulted for follow up. Here 5 year follow up eligible patient is 16.

Overall survival
The 5 year OS rate for all patients was 75%. The 5 year OS rate for patient treated with chemoradiation was 93.1% and only radiation was 62.5%.

Univariate analysis
The variable analyzed in 47 patients include age, chemotherapy and site of involvement.

5 year local control described in Table 4. The 5 year local control rates for patient treated with chemo radiation was 93.1% and only radiation was 54.1% which was statically significant. The 5 year local control rate for patient with impaired vocal mobility only T2No glottis treated with chemo radiation was 100 %and only radiation was 57.1% which was statically significant. Rest of the variable statistically not significant.

Table 4 Univarate analysis (in 40 patient)

Parameter	5 year local control rates (%)	Z Score	P-Value
1.Age >63 yrs. (n-15) <63 yrs. (n-25)	 66.6 72	-35	0.71
2.Chemotherapy All sites Combined (n-16) None (n-24)	 93.1 54.1	 2.67	 0.007 (Sig)
2a.Chemotherapy (Site) Only Impaired Vocal cord mobility Combined(n-10) None (n-14)	 100 57.1	 2.39	 0.01 (Sig)
2b.Chemotherapy (site) Subglottic extension with or without impaired vocal cord mobility Combined(n-6) None(n-10)	 83.3 50	 1.33	 0.18

Complication
There were no severe acute complications. No late complication was not seen such as chondronecrosis.

DISCUSSION
The goal of treatment for early unfavorable T2N0 glottis cancer includes cure and laryngeal preservation. In this study 5 year local control rate for patient treated with only radiotherapy was 54.1%. To improve the local control rate, clinicians have performed CCRT for T2N0 glotticcancer and CCRT has been reported to be effective. Itoh et al. reported that administration of low dose cisplatin and 5 –flurouracil resulted in an initial local control rate of 91.0% and ultimate laryngeal preservation by cordectomy all cases [7]. Akimoto et al. documented that administration of cisplatin (CDDP) alone, CDDP plus docetaxel or docetaxel alone resulted in a 5 –year disease free survival rate of 91.8 %[8]. Niibe et al. reported that administration of UFT resulted 3 year local control rate of 91 %[9]. Nishimura et al .documented that administration of carboplatin and UFT resulted in 5 year larynx preservation survival rate of 93.3%.[10].Several other report [13-14] have indicated that chemo radiation for T2GC is promising and local control rate higher than RT alone in Japan.

In this study also shows 5 year local control for T2 No unfavorable glottis cancer treated with chemo radiation was 93.7%. It shows adding chemotherapy with RT in deeply infiltrative T2 No glottis cancer shows promising result.

In this study vocal cord mobility found to influence local control. Other authors have demonstrated vocal cord mobility to be significantly related to local control with radiation therapy [15].Some authors recommended high dose radiation therapy or hyper fractionated radiation therapy to improve local control for glottis cancer s with impaired cord mobility [16-17].

In the present analysis, patient with subglottic extension with or without impaired vocal mobility had lower local control with only RT (83.3 vs. 50%) when compare to chemo radiation. Other investigator has also demonstrated subglottic extension to be related to lower local control with radiation therapy[15,18].Therefore, more effective treatment modalities such as hyper fractionated radiation therapy or concurrent chemoradiation need to be developed in T2N0 glottic cancer with subglottic extension.Garden et al reported that hyperfractionated radiation therapy for T2N0 glottis cancer had an improvement in local control compared with conventional radiation therapy by increasing dose to 77Gy[19].

In this study there were approximately 11% nodal failure with only radiation. No nodal failure in chemoradiation group. Overall rate is 6%.Specter et al recommended elective neck treatment especially for advanced T2N0 lesion to achieve high cure rate [20].

Mendenhall et al., however reported that elective neck treatment was not indicated for T2N0 glottic cancer (21). Frata et al. also reported that the complete formal inclusion in the treated volume of the first echelon of the lymphatic drainage was not worthwhile [22].

Our study had limitations. First we were unable to determine the best combination of therapies using anticancer drugs because this study was not prospective and various chemotherapy regimens were used at different times. Because many regimens of chemotherapy were used in the cases presented in this study,a prospective trail must be conducted in which chemotherapy regime is used on optimal dosing schedule for unfavorable T2 N0 glottis cancer with radiotherapy. In future we are planning to do a phase II study using S-1(per oral anticancer drug) for unfavorable T2 N0 glottis cancer.

Conclusion
In unfavorable T2No glottic cancer we concluded that concurrent chemo radiation is effective, well tolerated and able to achieve high cure rate when compared to radiotherapy alone.

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