

## RESEARCH ARTICLE

# Radiotherapy and Concurrent Chemo-Radiotherapy in Locally Advanced Hypopharyngeal Cancers - A Hospital Registry Based Analysis

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### Abstract

**Background:** The survival of patients with hypopharyngeal cancer is low amongst head and neck cancer cases. The incidence rates of hypopharyngeal cancers in our population are amongst the highest in the world and there are limited data available on the literature on varied responses to first course of treatment with radiotherapy (RT) and concurrent chemo-radiotherapy (CRT) in our population. **Materials and Methods:** Clinical characteristics and initial responses to treatment in patients who had received radiotherapy and chemo-radiotherapy in a regional cancer center from January 2010 to December 2013 were evaluated. The data were obtained from the hospital cancer registry, and analysis was carried using descriptive statistics. Pearson's chi-square was used to test for differences in the variables and  $p < 0.05$  was considered statistically significant. **Results:** A total of 554 patients were included in the analysis, 411 (74.2%) receiving RT and 143 (25.8%) being given CRT. There was significantly lower number of patients above 70 years with a higher proportion of patients below 50 years who had received CRT ( $p < 0.05$ ). Some 79.3% and 84.6% of patients in the RT and CRT groups respectively presented with a favorable performance status, and in the RT group 240 (58.4%) showed complete response (CR), and in the CRT group 103 (72.0%) showed CR at the first follow-up ( $p < 0.05$ ). **Conclusions:** Concurrent chemo-radiotherapy gives better short term response to treatment in locally advanced hypopharyngeal cancers.

**Keywords:** Hypopharyngeal cancers - radiotherapy - chemo-radiotherapy - responses to treatment

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### Introduction

Head and neck cancers constitute around 30% of all cancers in our population and of which, major proportion arises from the hypopharynx. Squamous cell carcinoma is the common histological type in hypopharyngeal cancers. Hypopharynx is richly supplied by lymphatics, and hence, early lymphatic spread in hypopharyngeal cancers leading to stage III and stage IV is common. Stage III and stage IV disease without distant metastasis and T4b are locally advanced diseases. One of the goals in the treatment of hypopharyngeal cancers is organ preservation. Radiotherapy (RT) is the prime modality of treatment in hypopharyngeal cancers and chemotherapy is given as adjuvant to sensitise radiotherapy. Chemo-radiotherapy has been shown to be definitive in the treatment of head and neck cancers including hypopharyngeal squamous carcinoma (Lasrado et al., 2014). Concurrent chemo-

radiation (CRT) in the treatment of hypopharyngeal cancers has not only improved the outcome, but has also allowed organ preservation (Lefebvre et al., 1996). However, the use of chemotherapy as adjuvant to radiotherapy as first course of cancer directed treatment in stage III and stage IV hypopharyngeal cancers is limited by certain factors, such as, socio-economic condition of patient, willingness of patient for receiving chemotherapy, compliance due to tolerability, and general health of the patient. Majority of patients with hypopharyngeal cancers presents in locally advanced disease with a 5-year survival range of 15-45 % (Takes et al., 2012). Variations in the treatment outcome and survival can be also attributed to availability of resources and tumor biology of hypopharyngeal cancers in our population. In this retrospective analysis, authors have tried to ascertain the early tumor responses to first course of treatment with RT and concurrent CRT in patients with stage III/IV hypopharyngeal cancers.

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**Materials and Methods**

This retrospective study was done on the data of hypopharyngeal cancer patients registered at a hospital cancer registry in North-East India. Locally advanced (stage III and stage IV) hypopharyngeal cancer patients that received first course of cancer directed treatment with radiotherapy and chemo-radiotherapy during the period of January 2010 to December 2013 were considered for the present analysis. Hypopharyngeal cancers were identified from the data set by International Statistical Classification for Diseases, 10th revision coding (ICD10-C12). The data set included information on age, gender, clinical nodal status (N), performance status (WHO scale) and disease status at the first follow-up after completion of treatment or at 6 months follow-up, whichever was earlier (hospital cancer registry data according to the National Cancer Registry programme of India). The data of patients whose follow-up information was not available, patients with double primary tumors, patients who received prior first course of treatment before registration and patients with T4b disease were excluded from the present analysis. The final data set contained patient information on 554 (N) numbers of patient's.

The stage at the time of diagnosis of hypopharyngeal cancer was done according to the American Joint Committee on Cancer Classification (AJCC) (Edge et al., 2010). Responses following first course of treatment were one of the following complete remission (CR), partial remission/residual disease (PR), and progressive disease (PD). The criteria followed were based on response evaluation criteria for solid tumors as outlined by Eisenhauer et al (2009).

The data was exported onto an excel spread sheet program for the analysis. Descriptive statistics was used and Pearson's chi-square was used to test for differences in the variables. p<0.05 was considered statistically significant.

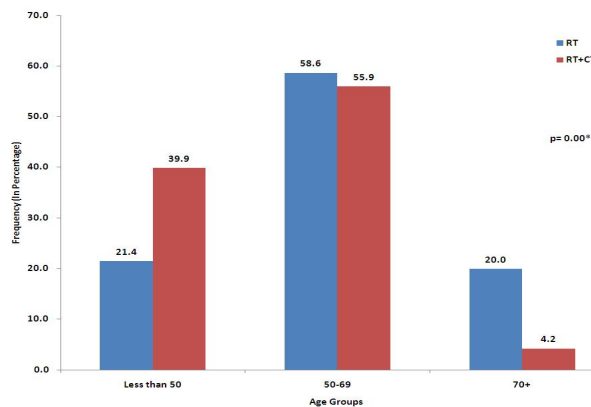
**Results**

Of 554 stage III and IV hypopharyngeal cancers, 411 (74.2%) patients received RT and 143 (25.8%) patients had received CRT. Majority of patients were males, 86.6% and 91.6% in the RT and concurrent chemo-radiotherapy groups respectively. The mean age of patients in the RT group was 58.4 years and 52.1 years in the CRT group. 4.2% and 20% of patients above 70 years received CRT and RT respectively, 39.9% and 21.4% of patients below 50 years had received CRT and RT respectively. Pearson's chi-square showed p=0.00 (Figure 1). The clinical regional nodal status were, in the RT group, majority were cN0 (35.8%) and majority in CRT were cN2 (35%) cervical lymphadenopathy (Table 1). 79.3% and 84.6% of patients in the RT and CRT group respectively presented with a favorable performance status prior to the start of first course of cancer directed treatment as shown on Table 1. The stage distribution in RT group showed stage III in 233 (56.7%) and stage IV in 178 (43.3%) patients. The stage distribution of patients in the CRT group was, stage

III in 76 (53.1%) and stage IV in 67 (46.9%) of patients (Table 2). The differences in the group was statistically insignificant (p=0.08).

*Responses to treatment*

Of 554 patients who received first course of treatment



**Figure 1. It Shows the Age Group Distribution in the Radiotherapy and Concurrent Chemo-Radiotherapy Groups**

**Table 1. Table Shows the Baseline Characteristics of the Two Groups of Patients with Hypopharyngeal Cancer**

| Characteristics        |        | RT              | RT+CT           |
|------------------------|--------|-----------------|-----------------|
|                        |        | (n=411)<br>#(%) | (n=143)<br>#(%) |
| Age                    | Mean   | 58.4            | 52.1            |
| Gender                 | Male   | 356(86.6)       | 131(91.6)       |
|                        | Female | 55(13.4)        | 12(8.4)         |
| Nodal Status           | cN0    | 147(35.8)       | 46(32.2)        |
|                        | cN1    | 132(32.1)       | 39(27.3)        |
|                        | cN2    | 103(25.1)       | 50(35.0)        |
|                        | cN3    | 29(7.1)         | 8(5.6)          |
| WHO Performance Status | 0      | 204(49.6)       | 90(62.9)        |
|                        | 1      | 122(29.7)       | 31(21.7)        |
|                        | 2      | 10(2.4)         | 2(1.4)          |
|                        | 3      | 1(0.2)          | 0(0.0)          |
|                        | NA     | 74(18.0)        | 20(14.0)        |

\*RT=Radiotherapy, CT=Chemotherapy

**Table 2. It shows the Stage Distribution of the Treatment Groups**

|       | Stage III<br>#(%) | Stage IV<br>#(%) | p value |
|-------|-------------------|------------------|---------|
| RT    | 233(56.7)         | 178(43.3)        | >0.05   |
| RT+CT | 76(53.1)          | 67(46.9)         |         |

RT=Radiotherapy, CT=Chemotherapy

**Table 3. The Table Shows the Various Responses at First Follow-up to the First Course of Treatment**

| FCT   | Disease Status |            |            | p value |
|-------|----------------|------------|------------|---------|
|       | CR<br>#(%)     | PR<br>#(%) | PD<br>#(%) |         |
| RT    | 240 (58.4)     | 159 (38.7) | 12 (2.9)   | 0.009*  |
| RT+CT | 103 (72.0)     | 35 (24.5)  | 5 (3.5)    |         |

FCT= First course of treatment, RT=Radiotherapy, CT=Chemotherapy, CR=Complete remission, PR=partial remission, PD=progressive disease

with RT and CRT, the responses were complete remission (CR) in 62% (343) patients, 35% (194) showed partial remission (PR) and progressive disease (PD) was seen in 3% (17) of patients. In the RT group 240(58.4%) showed CR, and in the CRT group 103 (72.0%) showed CR at the first follow-up after the completion of treatment (univariate analysis,  $p=0.009$ ) as shown on Table 3. Partial response was seen in 38.7% of patients who received RT and in 24.5% of patients who had received CRT had PR. Progressive disease was seen in 3.5% and 2.9% of patients who received CRT and RT respectively (Table 3).

## Discussion

Of laryngo-pharyngeal cancers, laryngeal cancers are relatively less common in our population. The age adjusted incidence rates of hypopharyngeal cancers in males and females of our registry is amongst the highest in the world (National Cancer Registry Programme, 2013). However, there are limited studies that have focused on the varied treatment outcomes following the first course of treatment in hypopharyngeal cancers in our population. This study is a step forward towards determining the outcome of treatment in hypopharyngeal cancers of North East India. Locally advanced hypopharyngeal cancers are in the spectrum between early and very advanced disease groups with treatment options ranges from RT alone, CRT and surgery followed by RT. Moreover, in developing countries the outcome of treatment to head and neck squamous carcinoma is lagging behind developed nations and a relatively poor survival in hypoharyngeal cancers with a five year overall survival of 10% (Wong et al., 2015). This also highlights the importance of the present study.

Our study has shown that the mean age of patients who received CRT was lower than that of those who had received RT alone. Furthermore, the age-group distribution showed patients who were above 70 years received significantly less CRT ( $p<0.05$ ). However, concurrent CRT may be less effective in elderly patients (VanderWalde et al., 2014). Previous study has shown that majority of patients with head and neck cancers that includes hypopharyngeal cancer presents with a favorable pre treatment performance status (Krishnatreya et al., 2014). This retrospective review of data has shown that 80-85% of patients who received RT and CRT presents with favorable performance status. A recent study has shown high risk Human Papilloma Virus (HPV) infection in squamous carcinoma of the hypopharynx (Joo et al., 2013). And, HPV associated hypopharyngeal cancers may be well responsive to CRT and amenable for organ preservation (Shaughnessy et al., 2014). So, it will be of interest to determine the varied responses to RT and CRT in HPV positive hypopharyngeal cancers in our population. In the present analysis, clinically N0 nodal status was most seen in the RT group, with a decreasing trend from N1 to N3, however, there was no such trend in patients who had received CRT. Patients with T4 were excluded from the present analysis, as these patients were subjected to upfront surgery followed by radiotherapy in our setting. A Hypopharyngeal cancer occurs as synchronous tumor in

head and neck cancers (Krishnatreya et al., 2013). But, for the present study, synchronous or index hypopharyngeal tumor was excluded from the data set for the analysis.

In the present analysis, stage distribution in the RT and CRT group was statistically insignificant ( $p>0.05$ ). So, stage IV cases in either group could not have influenced upon the outcome or response to treatment at the first follow-up. A recent study has shown that CRT provides treatment outcome comparable to surgery followed by RT in locally advanced hypopharyngeal cancers (Kim et al., 2015). This retrospective study has shown statistically significant ( $p<0.05$ ) better complete remission and lower rates of partial remission with CRT compared to RT in locally advanced hypopharyngeal cancers. However, there was no better outcome for progressive disease in the CRT group. This could be probably due to the fact, in cases of progressive diseases were biologically aggressive and in such cases, addition of chemotherapy was not beneficial for prevention progression. In this study the patient's characteristics was well balanced in each group including stage distribution.

There are several limitations of this study, the foremost being the differences in the numbers of patients in the two groups, which would make the comparison difficult. It was a retrospective study, and hence the effect of randomization to assess the outcome was absent. This study can only comment on the initial responses to RT and CRT, and the long term outcome and survival of patients who received RT and CRT cannot be derived from this type of study.

In conclusion, in our setting, increase in the age of patients was a factor for not receiving CRT and, CRT gives better short term response to treatment in locally advanced hypopharyngeal cancers.

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