

## Evaluation of Response to Radiotherapy in Early Stage Laryngeal Carcinoma

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**Abstract:** Laryngeal carcinoma accounts for 15.88% cases of cancers in males and 3.57% in females in Bangladesh. Among the two main treatment modalities surgery is expensive, causes loss of voice and needs postoperative rehabilitation; radiotherapy is less costly, less mutilating and can preserve the voice in majority of cases. Thirty two diagnosed cases of carcinoma larynx with stages T1-T2, N0-N1, M0 were included in this study. All were treated with 6600 cGy gamma radiations in 33 fractions over 6.5 weeks by a cobalt-60 teletherapy machine. All patients were reviewed by indirect laryngoscopy every week during treatment and for every 6-weeks up to 6-months after the completion of treatment. The response was considered **complete** with total or near total regression of local tumour mass and involved lymph nodes, and **partial** with  $\leq 80\%$  regression of tumour mass and/or involved lymph nodes. Majority of the patients were tobacco smokers, belonged to lower socioeconomic group and were aged between 4th to 7th decades. Histologically all the cases were squamous cell carcinoma. Complete response to radiotherapy was highly significant in glottic variety ( $p < 0.001$ ) and significant ( $p < 0.01$ ) in supraglottic variety. Radiotherapy can be considered as the first choice for treating early stage laryngeal carcinoma in developing countries.

**Keywords** - Glottic, Larynx Cancer, Radiotherapy, Supraglottic, Tobacco Smoking.

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### I. Introduction

Head and neck cancer constitutes a large proportion of all malignancies; profound functional deficits and cosmetic deformities associated with the diseases heighten their relative importance. Head and neck region is the sole location of several sensory functions (vision, hearing, balance, taste and smell) as well as motor function (speech), the loss of which either by disease or by the treatment produces significant morbidity. From a cosmetic point of view it must be remembered that facial-oral-laryngeal structures are key mediators of social interaction and the diseases involving them and their treatment, both can be deforming and debilitating. A cured but mutilated and socially abandoned human being should not be the goal of any treatment. Eradication of the tumour by optimum radiation dose should allow reasonable preservation of normal tissue resulting in maintenance of function and aesthesis. The multifaceted problems presented by head and neck cancer dictate a multidisciplinary approach involving the physician, otolaryngologist, radiation oncologist, medical oncologist, plastic surgeon, pathologist, radiologist, dental surgeon, physiotherapist and other health care personnel. Co-operative joint consultations prior to treatment and post therapy follow up are essential for the optimal treatment of the disease.

### II. Subjects And Methods

This study was carried out in the department of radiotherapy, Dhaka Medical College Hospital and the department of radiation oncology, National Institute of Cancer Research and Hospital, Dhaka. This was a prospective study that had been done over a period of one year. A total number of 32 diagnosed cases of carcinoma larynx were included in this study consisting of 30 males and 2 females.

Prior to the study informed consent of the patients was taken. Patient's history including family history, history of present and past illness, occupation, socioeconomic status, diet, medicine intake, tobacco consumption and clinical findings were recorded at the beginning. Selection criteria included clinically diagnosed and histologically proven carcinoma larynx with clinical staging T1-T2, N0-N1 and M0 by indirect and direct laryngoscopy and CT scan (according to the 6<sup>th</sup> AJCC staging of laryngeal cancer)[1], any sex and age, patients without prior treatment, and with Karnofsky's performance status 80 or above[2].

All patients were treated by cobalt-60 teletherapy machine. The dose was 6600 cGy in 33 fractions over 6.5 weeks. Parallel opposed lateral pair of fields with appropriate wedges was used. All patients were reviewed weekly up to the completion of treatment by indirect laryngoscopy. After completion of treatment Indirect laryngoscopy was repeated at an interval of 6 weeks up to 6 months.

### III. Results and observations

Total 32 patients were included in this study. Out of 32 patients, 30 (93.75%) were male and only 2 (6.25%) were female (Table 1). Male- female ratio was 15:1. The incidence of supraglottic lesion was higher consisting of 21 cases (65.63%) and 11 cases (34.37%) were of glottic variety. Considering the occupation, highest incidence of laryngeal carcinoma was found in farmers (34.37%) (Table 2). Out of 32 patients, twenty-eight (28) were habitual smoker and four (4) were non-smoker. But all of the non-smokers were tobacco leaf chewer. The commonest symptom in both glottic and supraglottic carcinoma was hoarseness of voice found in twenty-nine (90.62%) patients (Table 3). Level II and III cervical lymphadenopathy was found in 9 (42.9 %) patients out of 21 cases of supraglottic carcinoma. None of the glottic carcinoma cases had cervical lymphadenopathy.

Tissues were collected from the lesions of all the 32 patients by direct laryngoscopy under general anesthesia and routine histopathological examination was done. All the 32 (100%) lesions were diagnosed as squamous cell carcinoma of different grades.

After radiation treatment, complete response, seen as total (100%) or near total regression of the primary tumour mass and that of the involved lymph nodes was observed in 10 (90.91%) out of 11 cases of glottic carcinoma (Table 4); one patient had partial response. Among the 21 patients with supraglottic carcinoma, complete response was observed in 15 (71.43%) cases (Table 5); rest 6 cases had partial response. During radiation treatment some local and general effects were observed. Local effects included oedema, congestion, mucositis, pigmentation and dry desquamation of the skin. Loss of taste, dryness of mouth and throat, painful swallowing and spasm, impacted fish bone sensation and dysphagia for solid food was observed in almost all the patients. But these effects were not so severe and regressed spontaneously after completion of the treatment. Hoarseness of voice, which was a common complaint of nearly all patients in this study, improved a lot ranging from 10 to 80% after completion of the treatment and during the follow up period.

Table 1: Distribution of patients based on age and sex

Age Group	Sex				Total	
	Male		Female			
	n	%	n	%	n	%
21-30 yrs	1	03.33	-	-	1	03.12
31-40 yrs	5	16.67	-	-	5	15.63
41-50 yrs	8	26.67	-	-	8	25.00
51-60 yrs	9	30.00	2	100.00	11	34.38
61-70 yrs	6	20.00	-	-	6	18.75
71-80 yrs	1	03.33	-	-	1	03.12

Table 2: Distribution of patients based on occupation

Occupation	Number of cases	Percentage (%)
Farmer	11	34.37
Service holder	6	18.75
Businessman	4	12.51
School teacher	3	09.37
Rickshaw puller	2	06.26
Housewife	2	06.26
Night guard	1	03.12
Labour	1	03.12
Carpenter	1	03.12
Weaver	1	03.12

Table 3: Distribution of patients based on clinical presentation

Clinical Presentation	Number of cases	%
Hoarseness of voice	29	90.62
Sore throat	17	53.12
Referred otalgia	12	37.50
Dysphagia	15	46.87
Dyspnoea	4	12.50
Cervical lymphadenopathy	9	28.12

Table 4: Response to Radiotherapy in Supraglottic variety of Carcinoma larynx on weekly basis

Case No	Regression of tumour seen by Indirect Laryngoscopy							Lymph node Involvement	Lymph Node Regression	Dose Delivered
	1 <sup>st</sup> week	2 <sup>nd</sup> week	3 <sup>rd</sup> week	4 <sup>th</sup> week	5 <sup>th</sup> week	6 <sup>th</sup> week	7 <sup>th</sup> week			
1	0%	20%	40%	60%	90%	100%	-	-	-	6600 cGy # 33
2	10%	20%	30%	60%	80%	90%	100%	+	60%	6600 cGy # 33
3	0%	20%	30%	70%	80%	100%	-	-	-	6600 cGy # 33
4	20%	40%	60%	70%	90%	100%	-	-	-	6600 cGy # 33
5	30%	50%	70%	80%	90%	100%	-	-	-	6600 cGy # 33
6	10%	30%	50%	70%	100%	-	-	-	-	6600 cGy # 33
7	20%	40%	60%	70%	90%	100%	-	-	-	6600 cGy # 33
8	10%	30%	40%	60%	90%	100%	-	-	-	6600 cGy # 33
9	10%	20%	40%	70%	90%	100%	-	-	-	6600 cGy # 33
10	20%	30%	50%	60%	80%	90%	100%	-	-	6600 cGy # 33
11	10%	30%	40%	60%	70%	90%	100%	+	100%	6600 cGy # 33
12	0%	20%	40%	70%	80%	100%	-	+	100%	6600 cGy # 33
13	20%	30%	50%	60%	80%	100%	-	-	-	6600 cGy # 33
14	10%	20%	50%	60%	70%	90%	100%	+	100%	6600 cGy # 33
15	20%	40%	50%	70%	80%	100%	-	+	100%	6600 cGy # 33
16	20%	30%	50%	60%	70%	100%	-	-	-	6600 cGy # 33
17	0%	10%	40%	60%	70%	90%	100%	+	70%	6600 cGy # 33
18	10%	30%	40%	50%	70%	80%	100%	+	60%	6600 cGy # 33
19	10%	20%	40%	50%	60%	80%	80%	+	100%	6600 cGy # 33
20	20%	30%	60%	70%	80%	100%	-	+	80%	6600 cGy # 33
21	10%	20%	30%	40%	50%	60%	70%	-	-	6600 cGy # 33

Table 5: Response to Radiotherapy in Glottic Variety of Carcinoma larynx on weekly basis

Case No	Regression of tumour seen by Indirect Laryngoscopy							Dose Delivered
	1 <sup>st</sup> week	2 <sup>nd</sup> week	3 <sup>rd</sup> week	4 <sup>th</sup> week	5 <sup>th</sup> week	6 <sup>th</sup> week	7 <sup>th</sup> week	
1	20%	40%	60%	90%	100%	-	-	6600 cGy # 33
2	20%	30%	40%	80%	90%	100%	-	6600 cGy # 33
3	10%	20%	40%	70%	90%	100%	-	6600 cGy # 33
4	10%	40%	70%	80%	90%	100%	-	6600 cGy # 33
5	20%	60%	70%	90%	100%	-	-	6600 cGy # 33
6	0%	30%	40%	80%	90%	100%	-	6600 cGy # 33
7	0%	10%	20%	40%	60%	70%	70%	6600 cGy # 33
8	0%	20%	50%	60%	70%	80%	100%	6600 cGy # 33
9	0%	20%	60%	70%	80%	100%	-	6600 cGy # 33
10	20%	40%	60%	90%	100%	-	-	6600 cGy # 33
11	10%	40%	60%	70%	80%	100%	-	6600 cGy # 33

#### IV. Discussion

Carcinoma of the larynx is common in Bangladesh. It accounts for 15.88% cases of cancer incidence in male and 3.57% in female [3]. A high incidence of laryngeal carcinoma is also seen in India, Hong Kong, Brazil, Poland and France [4]. It is primarily a disease of middle aged man and the peak incidence is in sixth decade. Eighty per cent of laryngeal carcinoma occurs in the 5<sup>th</sup>, 6<sup>th</sup> and 7<sup>th</sup> decades of life. The average age is 59 years [5]. In this study the major number of patients was in the ages between 4<sup>th</sup> to 7<sup>th</sup> decades and the average age was 54.2 years (Table 1). Obviously the male sufferers were more than the females as there were 30 (93.75%) males and 2 (6.25%) females with male-female ratio 15:1. Predominance of carcinoma larynx in man is also common in other populations with male-female ratios 6:1 in Canada and 32:1 in Italy [4]. In the current study, the incidence of laryngeal carcinoma was higher in the lower socioeconomic group (19 cases belonged to this group of which 11 were farmers) that is comparable to findings of previous study [6].

Laryngeal carcinoma is extremely rare in non-smokers, rather smoking is the most significant risk factor for laryngeal cancer [7,8]. US Surgeon General report in 1964 stated that there was a correlation between

heavy smoking and laryngeal cancer [9]. In this study 28 patients were smokers (consumed  $\geq 20$  sticks of non-filtered cigarettes per day for more than 10 years) and 4 were non-smokers, but all of the non-smokers were tobacco leaf chewers.

The most common presenting symptom of carcinoma larynx was hoarseness of voice, which was present in 29 (90.62%) patients (Table 3). The next significant symptom was sore throat experienced by 17 (53.13%) supraglottic cases. Twelve patients had referred otalgia. The symptoms mentioned above were in accordance with Rubin [10] and Ackerman and Regato [11].

The incidence of supraglottic carcinoma was found higher than the glottic variety in studies carried out in Spain, Finland and China [4,8]. The current study depicted the same picture with 21 supraglottic and 11 glottic cases. No subglottic cancer was found among the observed 32 patients, a finding similar to other western studies that revealed subglottic lesions in less than 1% of all cases [5,12].

In a previous study, lymph node involvement was observed in 0.04-2% cases of glottic variety of laryngeal carcinoma [5]. No lymph node involvement was seen in any of the 11 cases of glottic carcinoma in the current study. In the present study the incidence of lymph node involvement in supraglottic laryngeal carcinoma was 9 (42.9%) of 21 cases whereas other studies revealed nodal involvement in 21-32% [5], 25-35% [7] and 45-55% cases [10].

Histologically squamous cell carcinoma is by far the commonest type of laryngeal carcinoma accounting for more than 90% cases [13]. In this study all the 32 cases (100%) were squamous cell carcinoma of different grades.

Each of the patients was weekly reviewed clinically along with indirect laryngoscopy till the completion of the treatment. Indirect laryngoscopy findings were compared weekly with that of the previous findings. After completion of the treatment patients were advised to come for follow up examination every six weeks up to 6 months. Among 21 Supraglottic cases irradiated with 6600 cGy # 33, 15 (71.43%) showed complete response which can be considered significant ( $p < 0.01$ ) that is similar to the findings of Spirano *et al* [14]. The remaining 6 patients showed partial response (Table-4) as featured by either partial ( $\leq 80\%$ ) regression of the tumour mass or incomplete regression of the involved lymph nodes. Complete response to radiotherapy was found in 10 (90.91%) cases of glottic cancer which can be considered highly significant ( $p < 0.001$ ) that was in accordance with the study done by Brunin [15]. The remaining one revealed partial response (Table-5).

## **V. Conclusion**

Surgery and radiation therapy are the main modalities of treatment of T1-T2, N0-N1, and M0 laryngeal carcinoma. Surgery causes loss of voice and post-operative care is difficult to ensure due to lack of facilities in Bangladesh. It is also expensive and needs speech therapy for voice rehabilitation. Chemotherapy is recommended in advanced disease. Radiation therapy is relatively less mutilating and in majority of cases it preserves the voice. In the present study where sequences of radiation effect were observed in the treatment of laryngeal carcinoma, a complete response considered as total (100%) or near total regression of the primary tumour mass and that of the involved lymph nodes was observed in 90.91% of glottic and 71.43% of supraglottic cases. The remainder revealed a partial response with appreciable regression of the primary tumour and unsatisfactory regression of the secondary lymph nodes. The encouraging aspects of radiation therapy apart from the very high rate of complete response were, its low cost and a very good tolerance of the patients to the required radiation doses especially in the malnourished population coming from the lower socio-economic group. Since larynx is not a deep structure, radiation energy from Co-60 teletherapy machine is sufficient to treat cancer larynx. This is of paramount importance for developing countries as higher energy radiation yielding Linear Accelerators are quite expensive to install and maintain.

However full effectiveness of radiation therapy that is complete remission can only be assessed after a long follow up, which was beyond the scope of this study. A five year long post-treatment follow up is advocated in this type of patients.

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Conflict of interest – None.

### References

- [1]. F. L. Greene, D. L. Page, I. D. Fleming, et al., eds. *AJCC Cancer Staging Manual*. 6th ed. New York, NY: Springer; 2002.
- [2]. V. Mor, L. Laliberte, J. N. Morris and M. Wiemann, The Karnofsky performance status scale: An examination of its reliability and validity in a research setting. *Cancer* 53(9), 1984, 2002–2007.
- [3]. S. F. Huq, Cancer incidence in Bangladesh. *Journal of Bangladesh College of Physicians and Surgeons*, 5(1):1987 August, 1-7.
- [4]. J. Hibbert. *Scott-Brown's Otolaryngology, Laryngology and Head and Neck Surgery*. 6th edition. Butterworth- Heinemann; 1997. Volume 5, p. 5/11/10-5/11/42.
- [5]. M. M. Paparell and D. A. Shumrick, *Otolaryngology Volume III Head and Neck*; 2nd edition W.B. Saunders Company, 1980; 2510-2525.
- [6]. H. S. Raitiola and J. S. Pukander. Etiological factors of laryngeal cancer. *Acta-Otolaryngol-Suppl-Stockh* 1997; 529:215-7.
- [7]. C. W. Cummings and J. M. Fredrickson. *Otolaryngology-Head and neck surgery*. 2<sup>nd</sup> edition. Mosby Year book; 1993. vol 3, pp. 1793-1798, 1925 -1950,2122-2145.
- [8]. X. Guo, M. Cheng and S. Fei, A case control study of the etiology of laryngeal cancer in Liaoning province. *Chn-Med-J-Engl*. 1995; 108 (5): 347-350.
- [9]. T. Luther et al. *Smoking and Health: Report of the Advisory Committee to the Surgeon General of the United States*. U-23 Department of Health, Education and Welfare. Public Health Service Publication No. 1103. 1964.
- [10]. P. Rubin. *Clinical oncology A multidisciplinary approach for physicians and students*; 7<sup>th</sup> edition. WB Saunders Company, Philadelphia 1993; 341-345.
- [11]. L. V. Ackerman and J. A. Del Regato. *Cancer, diagnosis, treatment and prognosis*. 5<sup>th</sup> edition. St louis: The CV Mosby Company; 1985. p. 308-325.
- [12]. A. L. Turner and A. G. D. Maran. *Logan Turner's disease of the nose, throat and ear*; 10<sup>th</sup> edition. PG publishing Pte Ltd, 1989; 145-178.
- [13]. S. S. Sternberg, D. A. Antonioli, D. Carter, S. E. Mills, H. A. Oberman, eds. *Diagnostic Surgical pathology Vol 1*; Raven press New York 1989; 697-713.
- [14]. G. Spirano, P. Antognoni, R. Piantanida, D. Varinello, R. Luraghi, L. Cerizza, M. Tordiglione. Conservative management of T1-T2N0 supraglottic cancer: a retrospective study. *Am J of Otolaryngol* 1997 Sep-Oct; 18(5):299-305.
- [15]. F. Brunin, J. Rodriguez, S. Cougniot-Lescure, D. Point, C. Jaulerry, J. Brugère. Management of laryngeal cancers. *Rev Prat* 1995 Apr1; 45(7):848-54.