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Original Article

Experience of Radical Radiotherapy for Patients with Stages I-III Squamous Cell Carcinoma of the Glottic Larynx

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Abstract:

This study was carried out from May 2012 to April 2013, on short term effects of Radical Radiotherapy for patients with Stages I-III squamous cell carcinoma of the glottic larynx at National Institute of Cancer Research and hospital, Mohakhali, Dhaka. A total of 50 biopsy proved squamous cell carcinoma of the glottis larynx were treated with radical Radiotherapy, total dose of which was 66 Gy in 33 fractions over 7 weeks, conventionally fractionated with 200 cGy per fraction, one fraction per day and 5 fractions per week, using the machine 6 MV LINAC. The main outcome variables of the study were toxicities and clinical outcome of the patients. The peak age incidence was found in the age group of 51-60 years (56%). Among 50 patients, there were 82% males and 18% females and male to female ratio was 4.6:1. There were 86% found smokers and rests of the 14% patients were non smoker. Treatment related haematological and non-haematological acute and delayed toxicities were studied. Mucosities 28% (grade-II), skin reaction 78% (grade-II), anaemia 52% (grade-II), dysphagia 70% were the most common acute toxicities where as xerostomia 16% was the delayed side effect. With this treatment protocol, 86% patients responded completely.

Key words: Glottic larynx, Radical radiotherapy.

Introduction:

Laryngeal cancer makes up 1-2% of all malignancies worldwide. The incidence of the disease varies greatly from country to country[1]. Habibullah M et al: Cancer Registry, National Institute of Cancer Research and Hospital (NICRH), 2005-2007, laryngeal cancer occupied (3.5%), 7th in position out of top ten malignancies in both sexes[2]. Cancer of the larynx is closely related to cigarette smoking[3].

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The glottis represents the site where approximately 50% of laryngeal cancers arise, and 95% of laryngeal malignancies are squamous cell carcinoma[4]. Majority of lesions begins on the free margin and upper surface of the vocal cord and are easily visible. When diagnosed, about two-thirds are confined to one cord, usually the anterior two thirds of the cord. Extension to the anterior commissure is frequent[5]. Vocal cord cancer is usually a disease of the middle-aged chronic smoker, being more common among males (M: F = 3:1)[6]. Glottic cancer is more common than supraglottic cancer. Heavy smoking and adult age are the main known risk factors[7].

Squamous cell carcinomas confined to the glottic larynx can be treated with either surgery (often laser excision) or radiotherapy. Large retrospective series suggest equivalent cure rates as long as radiotherapy is followed by close surveillance to detect and treat recurrences[8]. The main treatments are surgery and radiotherapy. The best treatment of T1 and T2 tumours is radical radiotherapy, since the cure rates are comparable with surgery (cordectomy or hemilaryngectomy) but there is normally restoration of good quality of voice. Radical radiotherapy is advised, as initial treatment for T3 tumours since this will cure about 30% of such patients. Salvage laryngectomy will cure a further 30% of those with

persistent tumour[9]. Although radiotherapy techniques and doses may vary, a standard course of radiation for glottic cancer usually consists of a total of 60-70 Gy administered in single daily fractions over 6 weeks. Advantages of radiotherapy include the avoidance of surgery and the subsequent hospitalization and a superior voice outcome. A useful voice is preserved in 80-95% of patients who were treated with radiation for an early glottic tumor. Of these patients, 80-90% is reported to have good-to-excellent voice quality[10].

Materials and Methods:

A total of 50 patients of glottic cancer of the larynx were selected randomly from the radiotherapy outpatient department of NICRH and convenient sampling was done. The main outcome variables of the study were toxicities and clinical outcome of the patients. Inclusion criteria includes histopathologically confirmed squamous cell carcinoma of glottic larynx with stages I-III. Patient's Karnofsky performance status > 60 and Age > 20 years. Minimum laboratory criteria required to includes Hemoglobin more than 10 gm/dl (≥ 60%), Absolute WBC count ≥ 4000 cell/ml, Platelets count ≥100,000 cells/ml, S. Bilirubin level ≤ 1 mg/dl, AST level not more than four times the normal upper limit and S. Creatinine level ≤1.5 mg/dl. Exclusion criteria includes previous history of radiotherapy in head and neck region, double malignancies, patients with uncontrolled infection, serious concomitant medical illness including severe heart disease, uncontrolled diabetes mellitus or hypertension, pregnancy or lactation and prisoners. Operational definitions includes radiotherapy planning was done under a simulator with appropriate patient's position and fixation. Parallel opposed lateral pair of fields were used. For T1 lesions The whole larynx were treated and For T2 tumors the field were extended depending on anatomic distribution of the tumour.

Results:

Among 50 patients, the mean age for male was 57 years, for female 52 years and for both sexes it was 55 years. The peak age incidence was found in the age group of 51-60 years (56%). There were 41 (82%) males and 09 (18%) females and male to female ratio was 4.6:1. Regarding religion of patients 80% were Muslims, 14% were Hindus, 4% were Christian and 2% were Buddhist. Among the patient of treatment group 92% were Married, 8% were unmarried of whom 20% were illiterate, 28% below primary, 32% above primary up to SSC, 12% HSC and rest of the 8% passed graduate and above. The ratio of literate and illiterate is 4:1. In this study patients 28% were farmer, 38% were businessman, 10% were officials, 18% were daily laborer, 4% were industrial worked and 2% were others. Among them 40% were poor class, 48% were middle class and 12% were upper class. According to the place of residence, most of the patients (76%) reside mainly in rural areas and minority (24%) resides in urban areas. Among patients 86% were found smokers and rests of the patients were non smoker (14%). Out of 50 patients, stage-I were found 32%, stage-II were found 60% and stage-III were found only 8% (Figure, I-IV, Table-I)

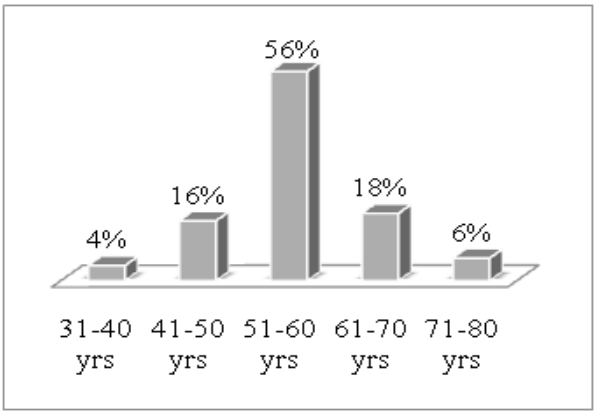

Figure-I: Distribution of patients by age (n=50)

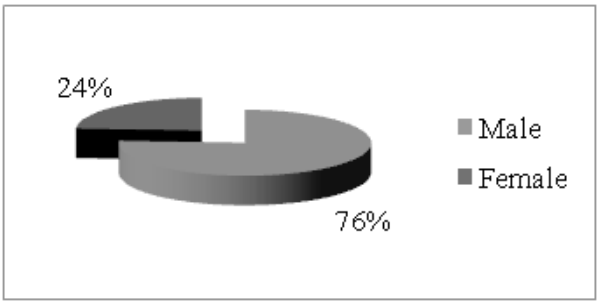

Figure II: Distribution of patient by sex

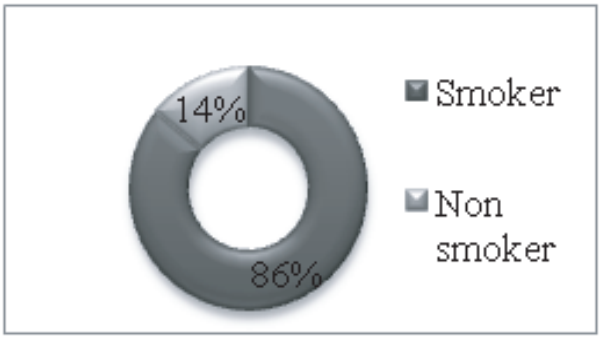

Figure-III: Distribution of patients by smoking status

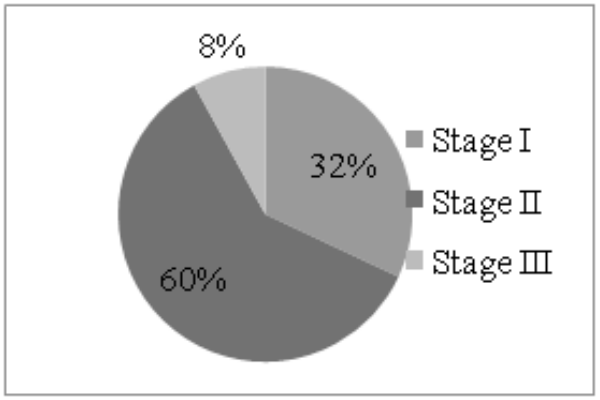

Figure-IV: Distribution of the patients by stage of the disease

Table-I: Distribution of the patients by socio-demographic characteristics

Characteristics	Number	Percentage (%)
Religion		
Muslims	40	80
Hindus	7	14
Christian	2	4
Buddhist	1	2
Marital status		
Married	46	92
Unmarried	4	8
Level of education		
Illiterate	10	20
Below primary	14	28
Above primary up to SSC	16	32
HSC	6	12
Graduate and above	4	8
Occupation		
Farmer	14	28
Businessman	19	38
Officials	5	10
Daily laborer	9	18
Industrial worker	2	4
Others	1	2
Socio-economic status		
Poor class	20	40
Middle class	24	48
Upper class	6	12
Place of residence		
Rural	38	76
Urban	12	24

Table-II: Distribution of the patients by toxicities

Toxicities	No. of patients	Percentage (%)
Nausea G-II & III	31	62%
Vomiting	24	48%
Mucosities G-II&III	14	28%
Dysphagia	38	76%
Loss of taste	43	86%
Loss of weight	19	38%
Skin reaction	36	72%
Anaemia	23	46%
Leucopenia	11	22%
Xerostomia	8	16%

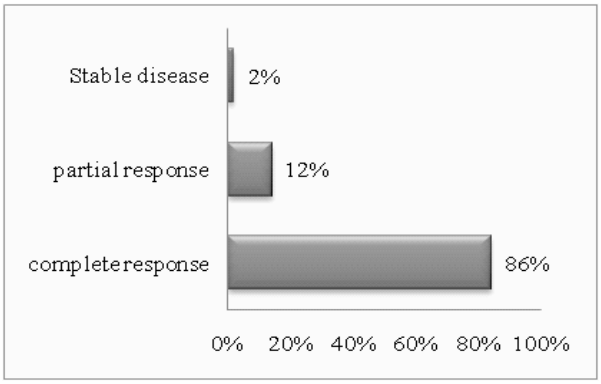

Figure-V: Distribution of the patients by final responses

Table-III: Distribution of the patients by recurrence

Characteristics	No. of patients (n = 50)	Percentage (%)
No Recurrence	41	82
Recurrence	2	4

Treatment related haematological and non-haematological toxicities of the patients were studied. Mucosities (grade-II), skin reaction (grade-II), Anaemia (grade-II) dysphagia were the most common toxicities. (Table-II)

By overall treatment response 06 weeks after completion of treatment, 43 (86%) were found complete responses, 6 (12%) were found partial responses and only 1 (2%) were found stable disease. Among the patients who achieved complete response, only 02 (04%) patient developed recurrence within 06 months. (Figure-V, Table-III)

Discussion:

The treatment of laryngeal cancer must always associate oncologic treatment efficiency with function preservation. Traditionally, initial glottic carcinomas can be effectively treated through surgery or radical radiotherapy, with high local control and survival rates[4,5]. Despite radiotherapy complications such as disorders are usually less impacting that the surgical procedures[11].

Current study was conducted at the Department of Radiation Oncology of National Institute of Cancer Research and Hospital (NICRH), Mohakhali, Dhaka. This study was carried out from May 2012 to April 2013, on short term effect of Radical Radiotherapy for patients with Stages I-III squamous cell carcinoma of the glottic larynx. A total of 50 biopsy proved squamous cell carcinoma of glottic larynx were selected randomly. The patients were treated with Radiotherapy, total dose was 66 - 70 Gy in 33 - 35 fractions over 7 weeks, conventionally fractionated with 200 cGy per fraction, one fraction per day and 5 fractions per week, using the machine 6 MV LINAC. The main outcome variables of the study were toxicities and clinical outcome of the patients. Radiation effects on skin, mucous membrane, salivary glands, pharynx & oesophagus, larynx, WBC, neutrophils, platelets and Hb were observed at the end of every week during radiotherapy and thereafter every six weeks interval up to 90 days. It was describe according to the toxicity criteria of Radiation Therapy Oncology Group (RTOG). Tumour regression was evaluated by Fibre Optic Laryngoscopy(FOL) at 1½ month & three month of completion of treatment and also by CT scan of the neck at 4½ month of completion of treatment. It was describe in light of Response Evaluation Criteria in Solid Tumours (RECIST).

Among the studied group, ages of the patients were between 35-70 years. The mean ages for both sexes were 55 years. The peak age incidence was found in the age group of 51-60 years (56%). A study was done by Ridge JA et al on Head and neck tumours and state that the incidence of head and neck cancer increases with age, especially after 50 years of age[12]. There was a study on locally advanced head and neck cancer, done by Arup MMH et al in Year 2010. In this study it have been shown that majority of the patients belong to age group 51 - 60 years (58%)[13]. Regarding sex distribution of the studied patients, maximum number of the patients were males (82%) and male to female ratio was 4.6:1. A study was done by Greenlee RT et al on Cancer statistics in the year 2000 and shown that in carcinoma of the glottic (larynx) the male to female ratio was approximately 4.5 to 1[14]. Regarding the personal habit, smoking is strikingly in head and neck cancer patients and is implicated as etiologic factors[7]. In this study most of the patients were found to be smoker (86%). Out of smoker patients most of the patients were smoked more than 20 sticks per day (58.1%). Study of Petrakos I et al on Glottic and supraglottic laryngeal cancer: epidemiology, treatment patterns and survival in 164 patients; shown that of the patient cohort 84.1% were smokers [15].

Treatment related haematological and non-haematological toxicities were studied. Out of all patients, 62% developed nausea (grade-II & III), 86% occurred loss of taste, 72% occurred skin reactions (grade-II), 76% occurred dysphagia; these were the most common toxicities where as only 16% patient's developed xerostomia. A study was done by Arup MMH et al on locally advanced head and neck cancer and shown that treatment related toxicities were skin reaction 78%, nausea 66%, loss of taste 82%, dysphasia 70% and xerostomis 36% occurred[13].

In consideration of treatment response, among studied patients 86% were found complete responses, 12% were found partial responses and only 2% were found stable disease. By pattern of recurrence following treatment among the patients who achieved complete response, only 04% patient developed recurrence within 06 months of completion of treatment. Jin J et al analyzed the prognostic factors for early-stage glottic cancer (T1N0M0) treated with radiotherapy alone. The median follow-up time was 127 months (range: 4-410 months). Five year over all survival rates were 84.0% and 5-year loco-regional control rate was 82.2%[16]. Study on T1-T2N0 Squamous Cell Carcinoma of the Glottic Larynx Treated with Radiation Therapy, done by William M. Mendenhall et al. In this study five hundred nineteen patients were treated with radiation therapy and had follow-up for > 2 years. Local control rates at 5 years after radiation therapy were as T1A, 94%; T1B, 93%; T2A, 80%; and T2B, 72%. Rates of local control with laryngeal preservation at 5 years were as follows: T1A and T1B, 95%; T2A, 82%; and T2B, 76%. This study concluded that Radiation therapy cures a high percentage of patients with T1-T2N0 glottic carcinomas[17].

Conclusion:

The prospective analysis showed a high rate of Local Control and larynx preservation in patients with stages I-III squamous cell carcinoma of the glottis larynx by means of Radical Radiotherapy. But such study requires more time and logistic support and another constrain was that the extrapolation of the study findings would be difficult to general population as sampling was done with accidental method in hospital. This is a hospital based study within short period of time (01 year). So, further comprehensive studies with large sample size of radical radiotherapy should be justified for Bangladesh perspective in the treatment of carcinoma of the glottic larynx.

References :

1. Rubin P, Bakemeier RF, Basil J, Benton JB, Brady LW, Bragg DG et al: Clinical Oncology: A Multidisciplinary Approach for Physicians and students. 8th edn. W.B. Saunders Company, Philladelphia 2001.p.435

2. World Health Organization (WHO): Cancer Registry Report. National Institute of Cancer Research and Hospital. 2005-2007. p.09-10.

3. Halperin EC, Wazer DE, Freeman C, Prosnitz LR, Ahamad A, Allison RR et al : Perez and Brady's Principles and Practice of Radiation Oncology. 5Th edn. Lippincott Williams & Wilkins. Philadelphia 2008. p.975-984.

4. DeVita VT, Lawrence TS, Rosenberg SA (Eds): Devita, Hellman & Rosenberg's Cancer: Principles & Practice of Oncology. 8th edn. Lippincott Williams & Wilkins. Philadelphia 2008. p.845-47.

5. Barrett A, Dobbs J, Morris S, Roques T, Harrowven J. Practical Radiotherapy Planning. 4th edn. Hodder Arnold, UK 2009. p164-175.

6. Pejavar S, Hansen EK,Yom SS, Schechter NR. Larynx and Hypopharynx Cacer. Inn: Roach M, Hansen EK. Handbook of Evidence-Based Radiation Oncology. 2nd edn. Springer, London 2010. p.152

7. Mondal D, Kundu S, Chattopadhyay S, De S, Dastidar AG, Roy A. Carcinoma in situ of true vocal cord in a nonsmoker adolescent female. Indian J Med Paediatr Oncol. 2009; 30(1):43-45.

8. William MM, Robert JA, Christopher GM, Russell WH: Journal of Clinical Oncology 2001; 19(20):4029-36.

9. Bomford CK, Kunkler HI, Hancock BW. Walter and Miller's Textbook of Radiotherapy. 6th edn. Edinberg, London. Churchill Livingstone. 2003. p.382

10. Cortan RS, Kumar V, Robbins SL. Robbins Basic Pathology; 7th edition, Saunders; Philadelphia, Pensylvania, 19106. p.849-50.

11. Pontes P, Brasil ODOCD, Filho FDSA, Moraes BTD, Pontes A, Neto JC. Radiotherapy for early glottic cancer and salvage surgery after recurrence: Braz J Otorhinolaryngol 2011; 77(3):299-302.

12. Ridge JA, Glisson BS. Head and neck tumours. In: Pazdur R, Wangman LD, Camphausen KA et al (Eds). Cancer Management: A Multidisciplinary Approach. 13th ed. UBM Medica LLC; 2010. p.1-50.

13. Arup MMH, Moklesuddin M, Rahman AKMH. Induction Chemotherapy followed by Concurrent Chemo-radiotherapy in Locally Advanced Head and Neck Cancer. Ban Can Reports2010; 35(1&2):9-16.

14. Greenlee RT, Murray T, Bolden S. Cancer Statistics, 2000, CA Cancer J Clin 2000; 50:7-33

15. Petrakos I, Kontzoglou K, Nikolopoulos TP, Papadopoulos O, Kostakis A. Glottic and supraglottic laryngeal cancer: epidemiology, treatment patterns and survival in 164 patients. Journal of BUON 2012; 17:700-5. Jinj, LIaoZ, Gool, Hcigang X, Cci G.

16. JIN J, LIAO Z, GAO L, HUANG X, XU G. Analysis Of Prognostic Factors For T1n0m0 Glottic Cancer Treated With Definitive Radiotherapy Alone: Experience Of The Cancer Hospital Of Peking Union Medical College And The Chinese Academy Of Medical Sciences : Int. J. Radiation Oncology Biol. Phys. 2002; 54(2):471-78.

17. Mendenhall WM, Amdur RJ, Morris CG, Hinerman RW. T1-T2N0 Squamous Cell Carcinoma of the Glottic Larynx Treated With Radiation Therapy: J Clin Oncol. 2001; 19:4029-36.