

Management of Newly Diagnosed T1, T2 Glottic Cancer Using External Beam Radiotherapy (Cobalt 60) as Sole Modality for Curative Treatment at Radiation Oncology Center with Limited Resources

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Abstract

Background: Treatment outcome using either radiotherapy or surgery for early-stage squamous cell carcinoma of vocal cord remains equally same yet with a significant chance of getting a local recurrence.

Aim: To assess local control, disease-free survival, larynx preservation, quality of voice, acute and chronic toxicity using cobalt 60 for the external beam radiotherapy treatment of early stage (T1, T2) squamous cell carcinoma vocal cord.

Materials and Methods: This prospective study included 32 newly diagnosed patients with T1/T2 N0 M0 Glottic Cancer (biopsy proved squamous cell carcinoma) treated from June 2010 till September 2014 at the Department of Radiation Oncology and Head and Neck Surgery, SMHS Hospital Government Medical College, Srinagar. All patients received radiotherapy delivered as 60-Gy to 70-Gy (conventional fractionation 2.2 Gy/fraction, 5factions/week) by two parallel opposed portals, on a cobalt 60 teletherapy unit.

Results: A total of 32 newly diagnosed cases of T1, T2 glottic cancer were registered during the study period, comprising 28 males and 4 females, with M:F ratio of 7:1. Age ranged from 43 years to 66 years, with median age 53 years. Histopathologically, well-differentiated squamous cell carcinoma was the most common histological type 87.50% ($n = 28$), whereas poorly differentiated squamous cell carcinoma constituted 12.50% ($n = 4$).

Conclusion: This study demonstrated excellent outcome in terms of 93.75% complete response with manageable acute and chronic toxicity.

Key words: Early stage, Local control, Quality of voice, Radiotherapy, Vocal cord

INTRODUCTION

Although there is insufficient evidence to demonstrate clear difference in the results between radiotherapy and

surgery in regard to local control or overall survival in early stage cancer of vocal cord (T1, T2), yet retrospective data suggest that in comparison with surgery, radiation therapy might cause less perturbation of voice quality without a significant difference in patient perception.⁹ Keeping in view the importance of preserving voice, evaluation of treatment outcome needs to be reported in various ways: Locoregional control, disease-free survival, with preservation of voice as an important parameter to evaluate. Radiation is the non-surgical treatment for early-stage glottic tumors without laryngeal fixation or lymph node involvement. Advantages of radiotherapy include the

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avoidance of surgery and the subsequent hospitalization. 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. Radiation failures can be salvaged successfully with surgery; however, complication rates may be higher than with primary surgical procedures.

Disadvantages to the use of radiation include long treatment course, early and late.

Adverse effects associated with radiation and difficulty in diagnosing recurrent or second primary tumors in the irradiated larynx. Early adverse effects of radiation include mucositis, dermatitis, xerostomia, dysphagia/odynophagia, and weight loss. Late complications include xerostomia, hypothyroidism, carotid artery stenosis, pharyngeal strictures, and osteoradionecrosis of the mandible.¹⁻⁶ So, as to prevent most of the complications, use of linear accelerators has become a routine in managing head and neck cancers. With advancement in radiotherapy techniques such as use of intensity modulated radiotherapy (IMRT), many radiation oncologists and patients feel compromised with the use of cobalt unit for delivering external beam radiation treatment in laryngeal cancer. We share our experience of successfully managing early stage vocal cord cancer (T1, T2) using external beam radiotherapy (cobalt 60) as sole modality for curative treatment, eyeing the limited resources such as non-availability of laser surgery and linear accelerator at our center. Although main stress was on local control, disease-free survival, larynx preservation, yet due consideration was given to quality of voice preservation and acute and chronic toxicity profile.

MATERIALS AND METHODS

This prospective study included 32 newly diagnosed patients with T1/T2 N0 M0 Glottic cancer (biopsy proved squamous cell carcinoma) treated from June 2010 till September 2014 at the Department of Radiation Oncology and Head and Neck Surgery, SMHS Hospital Government Medical College, Srinagar. Approval from ethical committee was sought before initiation of the radiotherapy protocol. Advantages and disadvantages of radiotherapy versus surgery were explained in detail to every patient and after that a formal consent was received. Although the use of radiotherapy in T1 and T2a lesions remains our primary treatment, yet 2 patients with T2b lesion were included after their wish to avoid surgery for voice preservation. Patients were taken up for counseling on permanent cessation of smoking with main stress on active smokers and those who had left smoking.

The pre-treatment assessment was done in every patient by physical and detailed ENT examination. Baseline

investigations, such as complete blood counts, liver and renal function tests, thyroid function test, chest X-ray and contrast enhanced computed tomography scan and/or MRI, were done in every patient before administration of treatment, at 8 weeks after completion of treatment and at follow-up. A detailed video-assisted laryngoscopy was done in every patient. Patients were staged using American Joint Committee (AJC) staging system:

T1 - Tumor limited to the vocal cord (may involve anterior or posterior commissure) with normal mobility, stage T1 subdivided into:

1. T1a - Tumor is limited to 1 vocal cord and
2. T1b - Tumor involves both vocal cords

T2 - Tumor extension to the supraglottis and/or subglottis and/or impaired vocal cord mobility, stage T2 subdivided into:

1. T2a - Tumor is growing into the supraglottis and/or subglottis
2. T2b - Vocal cords do not move normally.

Radiotherapy Treatment Plan

All patients received radiotherapy delivered as 60-Gy to 70-Gy (conventional fractionation 2.2-Gy/fraction, 5 fractions/week) by two parallel opposed portals, on a cobalt 60 teletherapy unit. (At the time of study our center lacked facility of linear accelerator). As a routine practice, T1 lesions were planned for 60-Gy and T2 lesions for 70-Gy. Corticosteroids and other supportive care drugs were administered whenever indicated. Response was defined as per the World Health Organization definitions as:

Complete response (CR): Disappearance of all measurable disease and the absence of new lesions for at least 2 weeks. Partial response (PR): Reduction of >50% of sum of products of cross-sectional diameters of all measurable lesions, together with absence of new lesions for at least 2 weeks. Stable disease: Reduction of <50% or an increase of <25% in the sum of products of cross-sectional diameters of all measurable lesions and no clear pattern of either regression or progression of disease (PD) for at least 8 weeks. PD: Increase of >25% in the sum of products of the cross-sectional diameters of measured lesions, along with an increase in assessable disease or the appearance of new lesions.

Toxicity of radiotherapy was assessed using radiation therapy oncology group toxicity criteria. All patients were assessed daily for acute toxicities. Acute toxicity was defined as that which occurs within 90 days of treatment, and chronic toxicities were defined as occurring after 90 days. Patients were followed monthly for 1st year, 3 monthly for 2nd year, and 6 monthly thereafter for local control

assessment and chronic toxicity till closure of the study in September 2014.

RESULTS

A total of 32 newly diagnosed cases of T1, T2 glottic cancer were registered during the study period, comprising 28 males and 4 females, with M:F ratio of 7:1. Age ranged from 43 years to 66 years, with median age 53 years.

Histopathologically, well-differentiated squamous cell carcinoma was the most common histological type 87.50% ($n = 28$), whereas poorly differentiated squamous cell carcinoma constituted 12.50% ($n = 4$).

About 13 patients had T1 lesion; of these, 10 patients had T1a (77%) and 3 patients T1b (23%). 19 patients had T2 lesion; of them, 17 patients had T2a (89.47%) and 2 patients T2b lesion (10.52%). In aggregate, T1 and T2a comprised 93.75% ($n = 30$).

About 22 cases (68.75%) were current smokers at the time of diagnosis, whereas 31.25% ($n = 10$) were non-smokers. The majority of male glottis cancer patients were smokers, i.e., 75% (21/28). Of the smoker's 50% ($n = 14$) smoked cigarettes, 25% ($n = 7$) used only filtered cigarettes, whereas the rest smoked Hookah, bidi, and Hookah (water-pipe), interchangeably. Two patients were using chewable tobacco, and both were males.

About 30 patients (93.75%) had complete response. At a mean follow-up of 26.87 months, 96.87% ($n = 31$) were disease free. Our longest follow-up was 47 months, and the shortest follow-up was 3 months. Two patients (both T2b lesions) had partial response. One patient responded to supplement dose of 20-Gy/7fractions (patient had initially received only 55-Gy at 2.2-Gy/fractions). The patient showed good response and is disease free at 41 months follow-up with xerostomia and persistent mucositis. The second patient with T2b lesion got severe mucositis with odynophagia. The patient defaulted treatment for 4 months, and came with progression of disease, presently being planned for radical laryngectomy.

In all 15 patients got manageable acute toxicity, of them 10 were smokers. 21.87% ($n = 7$) patients had a combination of mucositis and odynophagia, whereas 4 patients each got mucositis and odynophagia separately. None of our patients needed Ryles tube feeding. Long-term toxicity was present in 6 patients. Of them, 4 patients had dissatisfied quality of voice, 2 patients had xerostomia, and 1 patient had persistent mucositis. Of the 6 patients with long-term toxicity, 5 were smokers. In this study, 87.5% ($n = 28$) had

satisfied quality of life. Pre-treatment hypothyroidism was found in 1 patient, 3 patients developed hypothyroidism at mean follow-up of 39 months (Table 1).

DISCUSSION

Treatment outcome using either radiotherapy or surgery for T1, T2 squamous cell carcinoma of vocal cord remains equally same yet with a significant chance of getting a local recurrence. Radiotherapy has an advantage of sparing vocal cord a means of voice preservation and delaying/preventing laryngectomy in a sizable percentage of patients

Radiation is the primary non-surgical treatment for early-stage glottic tumors (i.e., T1, T2) without laryngeal fixation or lymph node involvement. Advantages of radiotherapy include the avoidance of surgery and the subsequent hospitalization.¹⁵ 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. Radiation failures can be salvaged successfully with surgery; however, complication rates may be higher than with primary surgical procedures.¹⁻⁶ In this study, complete local control rate was excellent with 93.75% ($n = 30$) and disease-free survival was even better with 96.87% at a mean follow-up of 26.87 months. High percentage of CR in this study could be attributed to the fact that majority of our patients had T1 and T2a stage ($n = 30$). Only 4 patients (12.5%) experienced the dissatisfied quality of voice including 2 patients with T2b lesions who had PR to treatment.

Disadvantages to the use of radiation include long treatment course, early and late adverse effects associated with radiation and difficulty in diagnosing recurrent or second primary tumors in the irradiated larynx. Early adverse effects of radiation include mucositis, dermatitis, xerostomia, dysphagia/odynophagia, radiation exposure, and weight loss. Late complications can include xerostomia, hypothyroidism, carotid artery stenosis, pharyngeal strictures, and osteoradionecrosis of the mandible.

In this study, 15 patients got manageable acute toxicity, of them 10 were smokers. 21.87% ($n = 7$) patients had a combination of mucositis and odynophagia, whereas 4 patients each got mucositis and odynophagia separately. None of our patients needed Ryles tube feeding. Long-term toxicity was present in 6 patients. Of them, 4 patients had dissatisfied quality of voice, 2 patients had xerostomia, and 1 patient had persistent mucositis. Of the 6 patients with long-term toxicity, 5 were smokers

Table 1: Management of T1, T2 Glottic Cancer

Age/ sex M, F	T1/T2	S, NS	AT, MS, OP	Date of completion of treatment	Total follow-up till 09/2014	CR/PR/PD/LR	Late toxicity X, PMS, DVQ
46 F	T1a	NS	...	11/2010	47	CR/DF	
54 M	T2a	S	MS+OP	12/2010	46	CR/DF	X+DVQ
49 M	T2a	S	MS+OP	01/2011	44	CR/DF	
55 M	T2a	S		02/2011	43	CR/DF	
59 F	T1a	NS		02/2011	43	CR/DF	
63 M	T1a	NS	MS+OP	03/2011	42	CR/DF	
49 M	T2a	S		03/2011	42	CR/DF	
66 M	T2b	S	MS	04/2011	41	PR/DF	PMS+X+DVQ ... PR after 55-gy/25 fr treated with suppl. RT ... 20-Gy/7 fr ... DF at present
43 F	T1a	NS		05/2011	40	CR/DF	
48 M	T1b	NS	OP	06/2011	39	CR/DF	
52 M	T2a	S		08/2011	37	CR/DF	
48 M	T2a	S	MS	08/2011	37	CR/DF	X+DVQ
50 M	T2a	S	10/2011	35	CR/DF	
53 M	T1a	S		01/2012	33	CR/DF	X
49 M	T2a	S	MS+OP	01/2012	33	CR/DF	
48 F	T1a	S	MS	03/2012	31	CR/DF	
51 M	T1a	NS		04/2012	30	CR/DF	
49 M	T2a	NS	OP	06/2012	28	CR/DF	
45 M	T2a	NS		08/2012	26	CR/DF	
64 M	T2b	NS	MS+OP	11/2012	23	PD	DVQ+PMS severe ... after 50-Gy/25 fr pt defaulted treatment for 4 months progression of disease planned for total laryngectomy
49 M	T2a	S	...	03/2013	19	CR/DF	
54 M	T1a	S	...	06/2013	16	CR/DF	
55 M	T2a	S	MS	08/2013	14	CR/DF	
58 M	T2a	S	MS+OP	08/2013	14	CR/DF	
57 M	T1a	S	MS+OP	09/2013	13	CR/DF	
49 M	T1a	S	...	12/2013	10	CR/DF	X
57 M	T2a	S		12/2013	10	CR/DF	
49 M	T1b	S		02/2014	07	CR/DF	
58 M	T1b	S	OP	03/2014	06	CR/DF	
61 M	T2a	S		04/2014	05	CR/DF	
59 M	T2a	S	...	06/2014	03	CR/DF	
58 M	T2a	NS	OP	06/2014	03	CR/DF	
F=4, M=28, 43-66 years, Median=53	T1=13 T1a=10 T1b=3 T2=19 T2a=17 T2b=2	S=22 Fs=1 Ms=21 NS=10	AT=15 MS=11 OP=11 MS+OP=7		Longest=47 Shortes=3 Mean=26.87 month	CR=30 LR=2 DF=31	DVQ=4 X=2 PMS=1 PMS+X+DVQ=6

M: Male, F: Female, S: Smoker, NS: Non-smoker, AT: Acute toxicity, MS: Mucositis, OP: Odynophagia, PMS: Persistent mucositis, DVQ: Dissatisfied voice quality, X: Xerostomia, CR: Complete response, PR: Partial response, PD: Progression of disease

An overview of the published data on results of radical radiation therapy for head and neck cancer suggests a significant loss of local control when the administration of radiation therapy was prolonged; suggesting, lengthening of standard treatment schedules should be avoided whenever possible.^{7,8} We kept fraction size at 2.2-Gy/fraction with conventional fractionation. Only in case of one patient with T2b lesion having PR a supplement of 20-Gy at 3-Gy/fraction was delivered.

The risk of lymph node metastases in patients with Stage I glottic cancer ranges from 0% to 2%, and for more

advanced disease, such as Stage II and Stage III glottic cancers the incidence is only 10% and 15%, respectively. Thus, there is no need to treat glottic cancer cervical lymph nodes electively in patients with Stage I tumors and small Stage II tumors. Consideration should be given to using elective neck radiation for larger or supraglottic tumors.^{10,11}

Patients who smoke during radiation therapy appear to have lower response rates and shorter survival durations than those who do not;¹² therefore, patients must be counseled to stop smoking before beginning radiation therapy. We

had 22 smokers and none of them continued smoking following initial counseling before planning of treatment.

Depression complicates head and neck cancer treatment in 20-40% of patients. Recently, a randomized, placebo-controlled, double-blinded study comparing prophylactic antidepressant therapy with placebo for patients undergoing surgery or radiation therapy for advanced head and neck cancer was performed by Lydiatt *et al.*¹⁵ This study showed that if escitalopram was started before treatment and continued for 16 weeks, patients in the experimental arm had a significantly lower depression rate (10% vs. 24.6%), and their quality of life was better than the placebo group up to 3 months after cessation of therapy. On subgroup analysis, this was especially true for those undergoing radiotherapy; however, the surgery subgroup also trended toward lower rates of depression. Treatment of depression can improve the quality of life and likely also improves survival. Therefore, prophylactic antidepressants should be strongly considered as an adjuvant to standard therapy. We experienced depression in one lady patient.

Accumulating evidence has demonstrated a high incidence (i.e., >30-40%) of hypothyroidism in patients who have received external beam radiation to the entire thyroid gland or the pituitary gland. Thyroid function testing of patients should be considered before therapy and as part of post-treatment follow-up.^{13,14} Three of our patients developed hypothyroidism on an average follow-up of 39 months.

CONCLUSION

Use of cobalt unit for treating early (T1 and T2a) stage cancer of vocal cord demonstrated excellent outcome in terms of 93.75% complete response. Preservation of voice quality was very good with manageable acute and late toxicity.

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