

# Hypo-Fractionated Radiotherapy for Laryngeal Cancer; is Linac Based Treatment Better?

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## ABSTRACT

### BACKGROUND

Carcinoma larynx is the most common malignancy of the upper aero digestive tract. 75% of larynx cancers are attributable to cigarette smoking and alcohol use. Squamous cell carcinoma constitutes 95% of all malignant neoplasms of the larynx. Irradiation is the initial treatment for T1 and T2 lesions, and surgery is reserved for salvage after radiation therapy failure. Hypo fractionated radiotherapy (>2.0 Gy/fraction) has shown comparable local control to conventional radiation in carcinoma Larynx.

### METHODS

A total of 59 patients, newly diagnosed with stage I and II squamous cell carcinoma of glottic larynx who attended the OP clinic of Department of Radiation Oncology, of Kottayam Medical College, from November 2016 to November 2017 who were intended to receive radical treatment with a hypo fractionated regimen of radiotherapy were analysed for local control and toxicity.

### RESULTS

Loco regional control at 1 year of treatment is 93.2% and Overall survival is 96.61% and is comparable to published literature data. Majority of the patients in the study had grade 1 - 2 dysphagia, grade 2 - 3 dermatitis, grade 2 - 3 laryngeal mucositis. During 6<sup>th</sup> week, there was significantly higher incidence of grade 2 and 3 mucositis among patients treated in cobalt 60 machine in 28 out of 31 patients, (90.3%) as compared to linear accelerator-based treatment where 17 out of 28 patients (60.7%) had grade 2 and 3 mucositis.

### CONCLUSIONS

Hypo fractionated radiotherapy is a safe alternative for conventionally fractionated radiotherapy by reducing overall treatment time by 1 week without affecting locoregional control and survival. It also reduces the socio-economic burden. However linear accelerator-based treatment has better toxicity profile than Cobalt 60 treatment in hypo fractionated radiotherapy for Carcinoma Larynx.

### KEY WORDS

Laryngeal Cancer, Hypo-Fractionation, Radiotherapy, Linear Accelerator

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## BACKGROUND

Carcinoma larynx is the most common malignancy of the upper aero digestive tract, accounting for 1% of all malignancies and 25% of head and neck tumours.<sup>1</sup> 80% of larynx cancers occur in men, In India, laryngeal cancer accounts for approximately 3-6% of all cancers in men.<sup>2</sup>

### **Aetiology and Pathology**

75% of larynx cancers are attributable to cigarette smoking and alcohol use.<sup>3</sup> Voice abuse, occupational exposure to asbestos, diesel fumes, rubber, and wood dust contribute to the aetiology.<sup>4,5</sup> Deficiency of vitamins- Vitamin C, riboflavin, beta carotene can potentiate carcinogenesis.<sup>4,5</sup> Squamous cell carcinomas constitutes 95% of all malignant neoplasms of the larynx. Glottic carcinomas are usually well to moderately differentiated. Carcinomas of the supraglottis and subglottis are less differentiated.

### **Treatment of Carcinoma Larynx**

The treatment objective in early invasive carcinoma of the larynx is to obtain cure with laryngeal preservation and optimal voice quality with minimal morbidity, expense, and inconvenience. Early stage cancers are effectively treated with surgery or radiation. There are no randomized trials comparing surgery and radiation for the treatment of early stage larynx cancer. A Cochrane review compared the effectiveness of RT and surgery in early laryngeal cancer. It concluded that there was insufficient evidence to establish one modality as superior to the other.<sup>6</sup> Conclusions regarding management is based on a comparison of nonrandomized studies, and both modalities are currently accepted as standard treatment options.<sup>7</sup> In 2012 Yoo et al performed a systematic review regarding the treatment of T1 glottic tumours which incorporated one meta-analysis, 15 cohort studies, and two Cross sectional studies. They found no overall survival differences between surgery and radiation therapy.

### **Early Vocal Cord Carcinoma (T1 and T2, Node Negative Disease)**

Irradiation is the initial treatment for T1 and T2 lesions, and surgery is reserved for salvage after radiation therapy failure.<sup>8</sup> For T<sub>1</sub> lesions, treated with primary RT the initial local control rates are in the range of 78% to 95%, and the ultimate local control rates after surgical salvage of failures are in the range of 94% to 99%.<sup>8,9</sup> For T<sub>2</sub> glottic tumours, RT is the preferred approach. Laser resection can be used for select tumours that are superficial and well localized. For T<sub>2</sub> carcinoma of the glottis treated with primary RT, the initial local control rates are in the range of 67% to 88%. After surgical salvage, the ultimate local control rates are in the range of 85% to 96%.<sup>8,9,10</sup>

### **Treatment of Early Supraglottic Cancer**

The prognosis for early stage supraglottic cancer is slightly worse than for early glottic cancer. All patients with early stage supraglottic larynx cancer should be treated with the intent to preserve the larynx. For early stage, favourable lesions, endoscopic laser resection, open-partial supraglottic laryngectomy, and radiation are all considered standard treatment options.<sup>11,12</sup> Orus and colleagues showed slightly

better initial local control with partial laryngectomy compared with radiation but, with salvage surgery, both resulted in ultimate local control of 90% for T<sub>1</sub>- and T<sub>2</sub>-No supraglottic tumors.<sup>12</sup>

### **Radiobiology of Altered Fractionation**

In principle, tumors should be treated for an overall treatment time that is as short as possible with acceptable acute morbidity, but with a dose per fraction that does not compromise late responding normal tissues, or total dose. The outcome of several large fractionation trials, mainly involving head and neck tumors, and particularly the CHART trial, have clearly demonstrated the importance of "acceleration" that is, shortening the overall treatment time, to improve local control. On the other hand, time taken for normal-tissue repair is about 6 hrs. This limits the strategy of using multiple treatments per day to maintain a large number of treatments in a short overall time. The alternative is a larger-dose per fractions. In hypofractionation there is increased tumour kill due to increased dose per fraction. Aside from tumor DNA damage, the extra effectiveness of hypofractionation may be due to its anti-angiogenic effect on micro-environment vasculature of tumour. But there are concerns about late tissue toxicity, cosmesis and local control rates. This is because the effective biologically equivalent dose (BED) used in this altered fractionation regime is actually less when compared to standard fractionation. For a well to moderately differentiated early glottis malignancy the BED will higher for the same dose and schedule compared to poorly differentiated tumours. This translates to higher local control for hypo fractionated regimens in better differentiated tumours. Approximately 90% early glottic carcinomas are of the well- or moderately-differentiated squamous type, implicating the clinical significance of hypofractionation in glottis malignancies.

### **Local Control with Altered Fractionation**

Between December 1993 and December 2001, 189 patients with invasive, previously untreated, T1 squamous cell carcinoma of the true vocal cords were enrolled in a prospective randomized trial in the Department of Radiation Oncology, Osaka Medical Center for Cancer and Cardiovascular Diseases, Japan. The trial compared 2 Gy per fraction versus 2.25 Gy per fraction in the treatment of stage 1 glottic cancer.<sup>[13]</sup> Patients were randomly allocated to treatment arm A (2 Gy/fraction) or B (2.25 Gy/fraction). Of the 180 patients (170 men and 10 women), 144 had Stage T1a and 36 had Stage T1b. For minimal tumors, 60 Gy in 30 fractions within 6 weeks (Arm A1) was adopted as the conventional schedule and 56.25 Gy in 25 fractions within 5 weeks (Arm B1) for the 2.25-Gy arm. For larger than minimal tumors, 66 Gy in 33 fractions within 6.6 weeks (Arm A2) was used for the 2-Gy/fraction arm and 63 Gy in 28 fractions within 5.6 weeks (Arm B) for the 2.25-Gy/fraction arm. The dose was prescribed at the isocenter, and all patients received the scheduled dose. The 5-year local control rate for the entire group was 86% (T1a, 83%; T1b, 91%; difference not significant), and the 5-year local control rates after radiotherapy were 76% for Arm A-1, 78% for Arm A-2, 91% for Arm B-1, and 92% for Arm B-2. A significant difference was found in local control between Arm A (77%) at 5 years Arm B (92%). The 5-year overall survival rate was 88%,

without any significant difference between the two arms. This study established hypofractionation with 2.25 Gy as a standard fractionation for T<sub>1</sub>-N<sub>0</sub> glottic cancer.<sup>13,14</sup>

### T<sub>2</sub> Glottic Carcinoma

For T<sub>2</sub> carcinoma of the glottis treated with primary RT, the initial local control rates are in the range of 67% to 88%. After surgical salvage, the ultimate local control rates are in the range of 85% to 96%. The larynx is preserved in 71% to 88% of the patients irradiated. Many studies have shown that local control improves with hyper- or hypo fractionated radiation.<sup>[15,16]</sup> Garden and colleagues showed that more than 2 Gy per day improved local control whether it was delivered as more than 2 Gy per daily fraction or more than 2 Gy in smaller, twice-daily fractions<sup>[15,16]</sup>. In a retrospective study of T1N0 and T2N0 squamous cell carcinoma of glottic larynx treated with definitive RT by Bhishamjit S. Chera, et al in the Department of Radiation Oncology, University of Florida College of Medicine, Gainesville they analysed the effects of various parameters in local control-T stage (T1a vs. T1b vs. T2), anterior commissure invasion (yes vs. no), histologic differentiation (well, moderate, or not otherwise specified vs. poor), total dose (<63 Gy or >63 Gy), fractionation (2.25 Gy daily vs. 1.2 Gy twice daily vs. <2.25 Gy daily), overall treatment time and beam energy (60 Co vs. other). They observed a 5-year LC rate of more than 90% for T1a and T1b tumors, whereas LC rate is 70% and 80% for T2 tumors. Factors that adversely affected LC were T stage, overall treatment time exceeding 41 days, and poorly differentiated histology. There was a concern of increase toxicity to altered fractionation schedule when treated with Cobalt machines. But in this study, there was no statistical difference between machines<sup>17</sup>

### Effects of Treatment on Normal Tissues

Acute Effects of Radiation Therapy- Acute reactions during fractionated RT for carcinoma of the vocal cords are usually mild. It includes fatigue, hoarseness, sore throat, dysphagia, mucositis, and increased pigmentation of the skin in the radiation field<sup>18</sup>. They do not result in a treatment break. They are typically managed conservatively with topical anaesthetics, opioids, oral rinse solutions and anti-inflammatory agents. They usually subside completely within 6 to 8 weeks after completion of treatment<sup>18</sup>. In the majority of patients, the voice returns to normal within a few months after treatment. The use of 2.25 Gy per fraction, did not increase the risk of acute skin or mucosal toxicity compared with 2 Gy per fraction.

Late Effects- Laryngeal oedema may persist after RT. The incidence of mild to moderate laryngeal oedema persisting for more than 3 months after RT is about 10% to 25%.<sup>18,20</sup>. The incidence of severe laryngeal oedema is about 1.5% to 4.6%.<sup>20-23</sup> The incidence of laryngeal oedema increases with greater total dose, field size, dose per fraction, and T stage of the lesion. When using doses up to 66 Gy in 2 Gy fractions or 63 Gy in 2.25 Gy fractions, Yamazaki and colleagues observed no severe late complications.<sup>24</sup> Voice quality after radiation for larynx cancer is typically very good and superior to that achieved after larynx-preserving surgery. But up to 60% of patients experiences some decline in voice function.<sup>25</sup> In up to 80% of patients voice will return to normal quality after

radiation. But objective voice quality is almost always altered. Another common side effect of radiation to the head and neck region is hypothyroidism. 50% to 60% of patients who undergo thyroid-stimulating hormone (TSH) screening will have an elevated TSH level within 5 years of receiving 50 Gy to the low neck. When screening is not routinely used, the rate of hypothyroidism is around 30%.<sup>25</sup>

We wanted to assess the locoregional control rate of early stage (T1/T2) glottic carcinoma larynx and toxicity outcome of patients treated with hypo fractionated radical radiotherapy (63 Gy/28#). We also wanted to compare the toxicity profile and outcome between Cobalt and Linac Machines treatment.

## METHODS

A total of 59 patients, newly diagnosed with stage I and II squamous cell carcinoma of glottic larynx who attended the OP clinic of Radiation Oncology department of Kottayam Medical College from November 2016 to November 2017 who were intended to radically treat with a hypo fractionated regimen of radiotherapy were analysed for local control and toxicity.

### Statistical Analysis

Data analysis was be done with the help of Excel 2010 and SPSS 16 statistical software. Remission rates, toxicity grades and survival rates will be entered in Excel 2010 work sheet for each variable. The quantitative variables were analysed using chi square test. Local failure is defined by residual disease or recurrence at primary site alone (Glottis larynx). Loco regional failure is defined by residual disease or recurrence at all sub sites of larynx and regional lymph nodes. The highest toxicity during any cycle was considered as toxicity grade of that patient. The toxicities occurred in Linear accelerator and Cobalt 60 machines were compared with cross tabulation by Mann Whitney U test. Survivals in 59 patients were assessed by Kaplan Meir survival plot.

## RESULTS

A total of 59 patients, newly diagnosed with stage I and II squamous cell carcinoma of glottic larynx who attended the OP clinic of Radiation Oncology department of Kottayam Medical College from November 2016 to November 2017 who were intended to radically treat with a hypo fractionated regimen of radiotherapy were analysed. Patient related characteristics are listed in (Table 1.)

Males are more commonly affected by carcinoma larynx (994%) and smoking is the major etiological factor (93%). As the pack years increased the chance of laryngeal cancer also rises. (The trends are shown in the bar diagrams.) ENT evaluation showed a growth in one vocal cord in 42 (71.2%) patients and growth in both vocal cords in 17(28.8%) patients. In 22 (37.3%) patients there was anterior commissure involvement. In 9 (15.3%) patients there was impaired vocal cord mobility.100% of the patients are having squamous cell carcinoma. Most of the patients are from Dr.

Kuppuswamy Lower middle income (57%) and upper middle (30%) group.

Age	Frequency	
Mean	59.59	
SD	7.67	
Min	42	
max	75	
Gender	Frequency	%
Male	56	94.9
Female	3	5.1
Tobacco	Frequency	%
Yes	55	93.2
no	4	6.8
Pack years (Yrs.)	Frequency	%
0(0-10)	6	10.2
1(10-20)	4	6.8
2(20-30)	9	15.3
3(30-40)	15	25.4
4(40-50)	20	33.9
5(50-60)	5	8.5
Alcohol	Frequency	%
Yes	4	6.8
No	55	93.2
Laryngitis	Frequency	%
Yes	3	5.1
No	56	94.9
Hoarseness of voice Duration	Frequency	
Median	4	
IQR	1.5	
Min	1	
Max	48	
ECOG performance status	Frequency	%
0.1	58	98.3
2	1	1.7
Vocal cord Involvement	Frequency	%
T1 a	42	71.2
T1 b	17	28.8
Anterior commissure	Frequency	%
Present	22	37.3
Absent	37	62.7
Vocal cord mobility	Frequency	%
Present	50	84.7
Absent	9	15.3
Histopathology	Frequency	%
Well differentiated	36	61
Moderately differentiated	23	39
Pallor	Frequency	%
Yes	3	5.1
No	56	94.9
Clubbing	Frequency	%
Yes	26	44.1
No	33	55.9

Table 1. Patient Characteristics

Machine	Frequency	Percent		
Theratron	31	52.5		
Clinac	28	47.5		
Total	59	100%		
Local control	Frequency	Percentage		
Achieved	55	93.2		
Not Achieved	4	6.8		
Local Control and T Stage	LC yes	LC no	p-value	
T1	47	3	.574	
T2	8	1		
Machine and Local Control	LC yes	LC no	p-value	
COBALT -60	29	2	0.916	
LINAC	26	2		
Treatment Duration	Median	Iqr	Median-Diff	p-Value
Cobalt 60	4	1.5	.50	0.48
LINAC	4.50	2.25		
Mucositis Grade	Frequency	Percent		
Grade 1	14	23.7		
Grade 2	36	61.0		
Grade 3	9	15.3		
Total	59	100.0		
Duration of treatment	Weeks			
Min	5.5			
Max	7			
Mean	5.89			
SD	.299			

Table 2. Treatment Related Factors

**Treatment Related Factors**

All patients were treated with radical hypo fractionated radiotherapy of 63 Gy/28#. The treatment duration ranged from 5.5 to 6.4 weeks with a mean duration of 5.89 weeks. 31(52.5%) patients were treated in Theratron 780C cobalt machine and 28 (47.5%) patients in Varian CLINAC machine according to the availability of treatment slots. The mean field height was 7.3 cm and width was 7.5 cm. Details summarised in (Table 2).

**Toxicities Assessment**

Treatment related toxicities are assessed with CTCAE version 4. Grade 3 dermatitis was noted in 2 (3.4%) patients during 5<sup>th</sup> week and in 11 patients (18.6%) during 6<sup>th</sup> week The 1 year local control rate was 93. 2%. The mean time for local control was 11.6 months (with 95% confidence interval). Pain was present for 55 patients (93.2%) and is gradually increased with accumulatoin of radiation dose and fractions and by 6<sup>th</sup> week,45(76.3%) patients had grade 1 pain and 10 patients developed grade 2 pain. Anorexia is present for 32 patients (54.2%) and is grade 1 only.32 patients (54.2%) had ryles tube feeding at some point during radiotherapy and there was no significant weight loss associated with radiation. 6 patients had grade 1 vomiting (10.2%) and is relieved with supportive care and is statistically not significant. Mucositis was the major toxicity limiting radiation treatment and was associated with pain.100% patients has mucositis by 2<sup>nd</sup> week. 55 had grade 1 and 4 had grade 2 mucositis by 2<sup>nd</sup> week. Mucositis was evaluated in detail with respect to the machine used for radiation treatment and the impact was assessed. The results are given below.

**Association between Treatment Machine Used and Grade 2 and 3 Mucositis**

Mucositis is the major treatment limits toxicity associated with pain and anorexia and resultant weight loss. This can lead to radiation treatment breaks which can be detrimental on disease outcome. Grade 1 mucositis can be supported without any treatment interruption. But grade 2/ grade 3 mucositis can affect locoregional control and survival by producing treatment breaks. Hence it was assessed in detail as given below.

Cross Tabulation Week 3				
Mucositis				
Machine	Grade 1	Grade 2	Total	p-value
Cobalt-60 Linac	16	15	31	0.002
Linac	25	3	28	
<b>Total</b>	<b>41</b>	<b>18</b>	<b>59</b>	

Table 3. Mucositis Week 3

Cross Tabulation week 6						
Mucositis						
Machine		Grade 1	Grade 2	Grade 3	Total	p-value
		Cobalt-60	3	22	6	
Linac	11	14	3	28		
<b>Total</b>		<b>14</b>	<b>36</b>	<b>9</b>	<b>59</b>	

Table 3a. Mucositis Week 6

This cross tabulation shows a statistically significant (p=0.027) association between the machine used and the grade 2/3 mucositis developed at week 6.22 patients developed grade 2 mucositis with Cobalt 60 machine but only 14 patients in Linear accelerator. The grade 3 toxicity is reduced by 50% with radiation treatment taken in linear

accelerator. The mucositis is progressively increased from week 2 of radiation for patients treated with Cobalt 60 Machine. This is associated with significant increase in pain and anorexia but can be managed by supportive care.

**Association between Machine Used and Grade 2 & 3 Dermatitis**

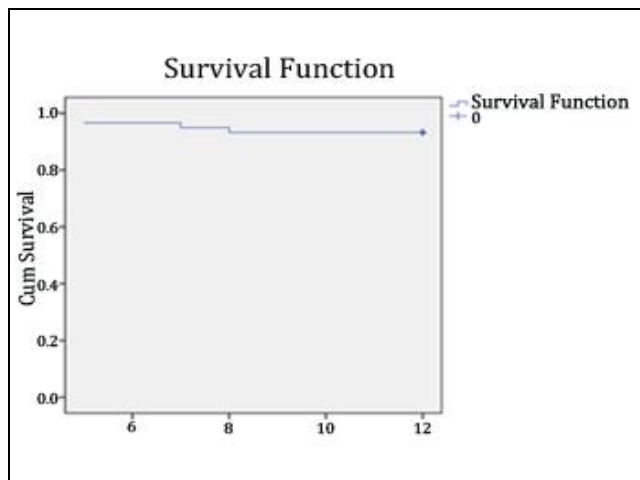
A weekly assessment of dermatitis between the machine is being done, but it was not statistically significant till week 3. In week 4, the assessment revealed a trend towards improved incidence of dermatitis in patients treated with linear accelerator (p=0.511) than Cobalt 60 machine but it was not statistically significant. This effect persisted in week 5 and 6.

Machine * Dermatitis at Wks. 6 Cross Tabulation						
Count	Dermwk6			Total	p-value	
	1	2	3			
Machine	Co 60	3	23	5	31	0.511
	Linac	5	17	6	28	
<b>Total</b>		<b>8</b>	<b>40</b>	<b>11</b>	<b>59</b>	

*Table 4. Cross Tabulation Dermatitis; Week 4, 5 and 6*

**Locoregional Control and Survival**

Local control was achieved in 93.2% patients at the end of study period by Hypo fractionated radiotherapy protocol. 4 patients developed loco regional failure and 2 patients died of the disease. The overall survival was 96.61 at the assessment period of the study.



*Figure 1. Overall Survival for Hypo Fractionated Radiotherapy Patients at 1 Year of Treatment is 96.61% and is Comparable to Published Literature Data*

**DISCUSSION**

Cancer of the larynx is the most common malignancy of upper aerodigestive tract. While in early stage glottic malignancy surgery and radiotherapy has equal results in terms of cure rates, radiotherapy has the advantage of preserving voice quality.<sup>26-30</sup> A useful voice is preserved in 80 to 95% of patients who are treated with radiation and 80 to 90% are reported to have good to excellent voice quality. A standard course of radiation for early glottic cancer consists of 2 gray

per fraction, once a day, 5 days a week, to a total dose of 70 gray in 35 fractions during 7 weeks. In this study a hypo fractionated schedule of radiation therapy was used- dose of 2.25 gray per fraction, once a day, 5 days a week to a total dose of 63 gray in 28 fractions during 6 weeks. 59 patients with biopsy proven early squamous cell carcinoma of glottic larynx who attended the outpatient clinic of Department of Radiation Oncology, Medical College Kottayam were included in the study.

**Patient Related Factors**

The mean age of patients included in the study was 60 years with ages ranging from 42 to 75 years. 94.9% were males and 5.1% females. This higher incidence in males is in accordance with the data from national cancer registry and also the international data of incidence.<sup>2,3</sup> The higher incidence in males and the strongest etiological factor of smoking has a positive association. Majority of the patients (93.2%) were smokers with pack years of 30 to 40 years. 93.2% gave a history of chronic alcohol intake. Studies have proven that 75% of laryngeal carcinomas are attributable to cigarette smoking and alcoholism. The excess risk declines when smoking is ceased and becomes negligible after 20 years. In our study the patients were current smokers or had recently stopped smoking after the onset of symptoms. There was no significant association between the smoking status of the patient and local or locoregional control in our study. Similar results were observed in the study conducted by Lee et al.<sup>30</sup> Hoarseness is the most common symptom in early vocal cord cancer and is the main reason why glottic malignancies are usually diagnosed at an early stage.<sup>8</sup> ENT evaluation showed a growth in one vocal cord (T1a) in 42 (71.2%) patients and growth in both vocal cords (T1b) in 17 (28.8%) patients. In 22 (37.3%) patients there was anterior commissure involvement. In 9 (15.3%) patients there was impaired vocal cord mobility. (T2). In the study conducted by Lee et al, anterior commissure involvement was associated with decreased local control for T1 lesions. For T2 lesions local control decreased with impaired vocal cord mobility and subglottic extension. In this study no significant association could be made between the tumour extend and locoregional failure. This is probably due to the small sample size and less number of events of locoregional failure.<sup>30</sup>

**Treatment Related Factors**

In our study patients were treated in Theratron 780C cobalt 60 machine or Varian Clinac machine according to the availability of treatment slots. 31(52.5%) patients were treated in Theratron 780C cobalt machine and 28 (47.5%) patients in Varian CLINAC machine. There was no significant association between the local failure rate and machine/energy used in treatment. The findings of the prospective trial by Le et al<sup>[30]</sup> gave a similar result. In the study beam energy (cobalt 60 vs 6 MV vs 4 MV) was not significantly associated with the local control following radiotherapy. The treatment duration ranged from 5.5 to 6.4 weeks with a mean duration of 5.89 weeks. This range was owing to delays due to personal reasons and machine delays in 4 cases. In this study no significant association was established between locoregional control and treatment duration.

### Acute Adverse Events

An objective of the study was to assess the treatment related toxicities and their grading according to CTCAE v 4. Pain, mucositis, anorexia, vomiting and dermatitis were evaluated.

During the 4<sup>th</sup> week of treatment 50 (84.7%) of patients had grade 2 skin toxicity. By 5<sup>th</sup> week 38 (64.4%) patients had grade 2 and 2 (3.4%) patients had grade 3 dermatitis. This progressed to grade 2 toxicity in 40 (67.8%) patients and grade 3 toxicity in 11 (18.6%) patients during the 6<sup>th</sup> week. 10 (16.9%) patients experienced grade 2 pain during the 6<sup>th</sup> week of treatment. There was no documented grade 2 or higher anorexia during the radiation course. 4 (6.8%) patients experienced grade 2 mucositis during the 2<sup>nd</sup> week of treatment. By 6<sup>th</sup> week 36 patients (61%) had grade 2 mucositis and 9 (15.3%) patients had grade 3 mucositis. There was no grade 4 mucositis recorded in the study. There was no grade 2 or higher vomiting in any of the patients.

Majority of the patients in the study had grade 1 -2 dysphagia, grade 2- 3 dermatitis, grade 2-3 laryngeal mucositis. None of the patients in the study had any grade 4 toxicities. The mean time of recovery from dermatitis was 2.5 weeks with no statistically significant difference in recovery time between the patients treated in the two machines. The recovery from hoarseness due to laryngeal mucositis and oedema began by a mean duration of 4 months. There was no persistent laryngeal oedema requiring tracheostomy in any of the patients.

In this study there was statistically significant difference between the machine in which patient received treatment and the incidence of grade 2 or higher dermatitis and laryngeal mucositis. During week 2, 3 and 6 of treatment there was higher grade 2 and 3 laryngeal mucositis among patients treated in cobalt 60. During week 4 there was significantly higher incidence of grade 2 and 3 dermatitis among patients treated in cobalt 60 machine. This finding suggests that there is a trend towards better toxicity profile in terms of dermatitis and laryngeal mucositis in patients treated in Linac though there is no difference in local control between the two beam energies used in treatment. This result is contradictory to the published data that cobalt 60 is non inferior to linear accelerator in terms of acute skin toxicity. This finding needs further validation in larger trials.

The primary objective of our study to find out the local and loco regional control at a period of one year. In our study local control was achieved in 55 (93.2%) patients at 1 year. There was loco regional failure in 4 (6.8%) patients. These results were similar to the study conducted by Yamasaki et al [29] where the 5 year loco regional control following primary treatment was 92% in the hypo fractionated RT arm and 77% in the conventional RT arm. The results of our hypo fractionated regimen is thus comparable to the historical data of similar studies using a hypo fractionated dose of radiation and superior to the conventional fractionation in terms of local control.

From the point of view of health economics, the hypo fractionated schedule is advantageous compared to conventional schedule, because the shorter overall treatment time reduces the socioeconomic burden, both for patients and institutions especially in less privileged countries. Patients benefit from the reduced costs, treatment time and early resolution of acute toxicities of radiation. The institutions can

maintain the machine and human resources required to meet the increasing demand for radiotherapy.

### CONCLUSIONS

Hypo fractionated external beam radiotherapy of 63 Gy/28# for early stage glottic carcinoma has comparable outcome to conventionally fractionated regimens and is convenient due to shorter overall treatment time which reduces the socioeconomic burden, both for patients and institutions. However, this study suggests an improved toxicity outcome in hypo fractionated radiotherapy for patients treated with linear accelerator compared to cobalt 60 Machine.

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