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Change in the quality of life in the patients of laryngeal and pharyngeal carcinoma after receiving radiation therapy: A prospective and observational study

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ABSTRACT

Background: The quality of life (QoL) of laryngeal and pharyngeal carcinoma patients is influenced by the side effects of treatment affecting functions such as swallowing, feeding, and speech, more so following conventional radiation using 2D technique. **Aims and Objectives:** This study was undertaken to determine the change in QoL of laryngeal and pharyngeal cancer patients after radiation using 2D technique in a Telecobalt unit in a resource constrained peripheral institution. **Materials and Methods:** In this prospective, observational, and single institutional study, fifty-one larynx and pharynx cancer patients were treated with radiation/chemoradiation in telecobalt unit using conventional 2D technique. QoL was evaluated using European Organisation for Research and Treatment of Cancer Quality of Life (EORTC QLQ) C30 and EORTC QLQ Head and Neck Module (HN43) pre-validated and locally adapted questionnaires at pre-treatment, immediately, 3 months and 6 months after radiation. The difference between the scores at different time points was verified using Friedman's non-parametric test. **Results:** Of the 46 evaluable patients, 71% were male with median age of 56.5 years, median follow-up of 8 months; 15 patients (32%) had Stage II disease and 78% of patients received concurrent chemotherapy. There was statistically significant deterioration of global health status and functional scales immediately after radiation. All the symptom scales of QLQ C30 and QLQ HN43 except neck swelling showed significant worsening at the end of radiation. After 6 months, the Global health status and all functional scales showed statistically significant improvement. Most symptom scales of QLQ C30 (except appetite loss and fatigue) were statistically significantly improved. At the end of 6 months, most of the symptoms showed significant improvement reaching pre-treatment values. There were however worsening of symptoms such as dry mouth, sticky saliva, and mouth opening. **Conclusion:** Laryngeal and pharyngeal carcinoma patients suffered from a deterioration of QoL after radiation. Six months later, most of the QoL scales showed a statistically significant improvement. These negative impacts on QoL can be reduced by use of newer techniques of radiation therapy such as 3D conformal radiotherapy, intensity-modulated radiation therapy, and image-guided radiation therapy.

Key words: Quality of life; Laryngeal cancer; Pharyngeal cancer; 2D technique; Telecobalt

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INTRODUCTION

Head-and-neck cancers are the sixth most prevalent type of cancer in the world. Overall 57.5% of global head-and-neck cancer occurs in Asia especially in India and it accounts for 30% of all cancers.[1] According to GLOBOCAN 2020, data visualization tools for exploring global cancer burden in 2020,[2] laryngeal cancer

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contributes to approximately 3–6% of all cancers in men.[3] Radiotherapy (RT) with concurrent chemotherapy is the most commonly used strategy because chemotherapeutic agents both radio sensitize cells and provide additive cytotoxicity.[4-6] This additive cytotoxicity increases both acute and late toxicity. Due to medical comorbidity and decreased creatinine clearance, some patients are treated by radical RT alone. Radiation therapy causes damage to the mucosa and soft tissue within the radiation treatment volume. Irradiation to the salivary glands causes dryness of mouth with sticky saliva production. Clinically, the patients develop mucositis, radiation dermatitis, and edema of the soft tissues. Pain, thickened, and more viscous mucous production, xerostomia, and tissue swelling contribute to acute dysphagia. By 3 months after the treatment, swallowing function begins to return for most patients. Late-effect lymphedema and radiation-induced damage to neural structures may also contribute to dysphagia.[7-10] Radiation-induced problems in opening mouth, loss of taste and smell, pain in the mouth, difficulty in speech, and skin discoloration are also significant. These complications and its severity depend on a number of factors including total dose of radiation delivered, dose per fraction, time, and the region where radiation therapy was received. With increased survival following chemoradiation, the health-related quality of life (QoL) has become very important. This study was undertaken to determine the change in QoL in patients of laryngeal and pharyngeal carcinoma, after radiation therapy using 2D technique in a telecobalt unit which is a common method of radiation therapy in resource constrained peripheral institutions.

Aims and objectives

1. To determine the change in Quality of life in patients of Laryngeal and Pharyngeal carcinoma, before and after radiation therapy.
2. To assess the toxicities following radiation therapy in patients of laryngeal and pharyngeal carcinoma in different time interval.

MATERIALS AND METHODS

This prospective and observational study was carried out with 51 patients in the Department of RT in a peripheral Medical College from May 2021 to July 2022 after due consent and ethics committee approval. The functional scales and symptom scales with multiple and single item scales of the prevalidated and locally adapted European Organisation for Research and Treatment of Cancer Quality of Life (EORTC QLQ)-C30 and QLQ-Head and Neck Module (H&N43) questionnaires were obtained through the Interviews at different time intervals – at the baseline, before starting, just after completion (within 3 weeks of completion), 3 months and 6 months after completion of radiation therapy using 2D technique in a Telecobalt unit.

The raw score for each scale is calculated by obtaining the average of the items that contribute to the scale. A linear transformation is used to standardize the raw score, so that scores range from 0 to 100. A high score for a functional scale represents a high/healthy level of function, a high score for the global health status represents a high QOL/high score for a symptom scale/item represents a high level of symptomatology. The QoL scores (median and range) were calculated at various time points, and compared to baseline values using the Friedmann test. It is used to test for differences between groups when the dependent variable being measured is ordinal. All statistical analyses were carried out for two-tailed significance at 5% level of significance with $P<0.05$ being considered as significant. To aid in the interpretation of the results, the clinical significance of the change of scales was also presented. According to the advice from King and Osoba et al., a 10-point difference on a scale of 0 to 100 was regarded as clinically significant. From the study of Osoba et al., >20 points change in the score was considered a large effect, and <10 points change was considered a small effect in the QoL. A change in the score between10 and 20 points was called a moderate impact on the QoL.[11] All data transferred from case report forms to a data mining software Microsoft Excel (Microsoft Inc, USA) and analyzed using appropriate statistical software (SPSS v 26, IBM Inc, USA).

Inclusion criteria

All histologically proved cases of primary carcinoma of Larynx and Pharynx planned for RT (with or without Chemotherapy) at Burdwan Medical College and Hospital, age between 18 and 70 years and performance Status ECOG 0-2.

Exclusion criteria

Patients underwent surgical treatment for laryngeal or pharyngeal carcinoma, previous history of RT or chemotherapy, hemoglobin count <10 g %, total leukocyte count <4000 and >12000/mm^3, ANC <1500/mm^3, platelet count <1 Lakh, serum urea >45 mg/dL, serum creatinine >1.1 mg/dL, any distant metastasis, and patients who had impaired liver function, bone marrow suppression or renal dysfunction.

RESULTS

Out of 51 patients recruited, two patients died in course of treatment and three patients did not follow-up. Of the 46 evaluable patients, 33 (71%) were males (Table 1) with median age 56.5 years. The literacy rate using schooling

Table 1: Patient characteristics (n=46)

Characteristics	No of patients	% of patients
Gender		
Male	33	71
Female	13	29
Literacy		
Literate	30	65
Illiterate	16	35
Tumour site		
Supraglottic Larynx	21	46
Oropharynx	15	33
Hypopharynx	5	11
Nasopharynx	3	6
Glottic Larynx	2	4
Tumor stage		
I	10	22
II	15	33
III	14	30
IVA	7	15
Treatment with concurrent chemotherapy		
Yes	36	78
No	10	22
ECOG-PS status		
0	9	19
1	22	48
2	15	33

beyond eighth standard was 65%. The maximum number of patients, 46% (21 patients) were diagnosed cases of carcinoma of supraglottic larynx, 33% (15 patients) were of oropharyngeal carcinoma. A few cases were of nasopharyngeal and glottic laryngeal carcinoma, 3 (6%) and 2 (4%) respectively. All the patients were staged using American Joint Committee on Cancer NCCN latest (8^{th}) guidelines. There were 15 (33%) and 14 (30%) patients of Stage II and III disease respectively. Only 7 (15%) patients are of stage IVA. The recruited patients were of ECOG PS 0-2. There were 22 (48%) and 15 (33%) patients of ECOG PS 1 and 2, respectively. Total 78% (36 patients) received concurrent chemotherapy (eligibility criteria, creatinine clearance ≥50 mL/min, and ECOG PS ≤2) with Inj. Cisplatin 100 mg/m^2 3 weekly (with minimum 2 cycles of concurrent chemotherapy) with proper hydration, pre-medication and post-medication.

Using QLQ C30,[11] all functional scales (physical function, role function, emotional function, cognitive function, and social function) and symptom scales (fatigue, nausea, and vomiting, pain, dyspnea, appetite loss, and financial difficulties) along with global health status showed clinical and statistical significant deterioration in QoL in immediate post-treatment with respect to the pre-treatment baseline ($P<0.05$ and the difference in median score values is more than 10, Table 2).

In QLQ H&N43, the score of neck swelling was reaching or just near to the baseline value, that is, this change is not statistically and clinically significant ($P>0.05$ all other symptom scales of QLQ H&N43 (pain in the mouth, swallowing, problems with teeth, dry mouth, and sticky saliva, problems with senses, speech, body image, social eating, skin problems, fear of progression, problems opening mouth, coughing, social contact, weight loss, and wound healing problems) showed clinical and statistical significant deterioration of QoL in immediate post-treatment (Table 3).

In QLQ C30, all item scales except fatigue and appetite loss showed statistically significant improvement ($P<0.05$). Fatigue and appetite loss were not clinically and statistically improved ($P>0.05$), scores reaching their baseline value, though they have improved significantly from their immediate post-treatment values. Functional scales such as cognitive functioning, social functioning and symptom scales like pain showed clinically significant improvement. Other item-scales are either improved or reaching around their baseline values, but not clinically significant. All item scales except fatigue and appetite loss showed significant improvement at 6 months after the treatment completion.

In QLQ H&N43, among all symptom scales, statistically significant improvement was seen in swallowing, social contact, social eating, cough, fear of progression, and neck swelling ($P<0.05$). Statistically significant deterioration was seen in dry mouth and sticky saliva, skin problems, and problems in opening mouth ($P<0.05$). Statistically non-significant improvement was seen in pain, speech problems, teeth problems, problems with senses, body image, and weight loss were not statistically significantly improved ($P>0.05$). The scores had decreased from their immediate pre-treatment values, reached nearing their baseline, but not statistically significant with respect to baseline. Symptom scales such as fear of progression, cough, and social contact showed clinically significant improvement. Some symptoms such as dry mouth and sticky saliva, skin problems, and problems in opening mouth were clinically significantly deteriorated with respect to their baseline scores. The median scores of symptom scales such as pain, swallowing, teeth problems, problems with senses, speech problems, body image, social eating, neck swelling, weight loss, and wound healing are reaching their baseline value (not showing difference of more than 10) hence not clinically significant.

DISCUSSION

All functional scales (physical function, role function, emotional function, cognitive function, and social function) and symptom scales (fatigue, nausea and vomiting, pain, dyspnea, appetite loss, and financial difficulties) along with global health status of QLQ C30 showed clinical and statistical significant deterioration in QoL with respect to the pre-treatment baseline. All symptom scales of QLQ H&N43 (pain

Table 2: QoL scores in the general Questionnaire and Changes in QoL from pre-treatment to 6 months after the treatment in EORTC QLQC30

Parameters	Pre-treatment (baseline) (T0) Median (Range)	At the end of treatment (T1) Median (Range)	Post-treatment (after 3 months) (T2) Median (Range)	Post-treatment (after 6 months) (T3) Median (Range)	Baseline versus end of treatment (T1-T0) P-value	Baseline versus 6 months post-treatment (T3-T0) P-value
Physical	80 (60–94)	53 (33–73)	73 (53 – 87)	87 (67-100)	<0.001	<0.001
Role	83 (50-100)	50 (34-83)	75 (50-83)	91 (67-100)	<0.001	<0.001
Emotional	67 (42-83)	50 (17-67)	58 (33-83)	75 (58-92)	<0.001	<0.001
Cognitive	83 (67-100)	67 (50-83)	83 (67-100)	100 (83-100)	<0.001	<0.001
Social	67 (34-83)	34 (17-50)	50 (34-67)	83 (50-83)	<0.001	<0.001
Fatigue	11 (0-55)	55 (33-100)	33 (11-78)	11 (0-55)	<0.001	>0.132
Nausea and vomiting	0 (0-17)	34 (0-50)	17 (0-34)	0 (0-17)	<0.001	<0.05
Pain C30	34 (17-50)	67 (50-100)	50 (34-67)	17 (0-34)	<0.001	<0.001
Dyspnea	0 (0-67)	0 (0-33)	0 (0-33)	0 (0)	<0.05	<0.001
Appetite Loss	33 (0-33)	67 (33-100)	33 (0-67)	33 (0-33)	<0.001	>0.05
Financial	33 (0-67)	67 (0-100)	33 (0-67)	33 (0-33)	<0.001	**<0.05**
Global	67 (33-75)	37.5 (17-58)	58 (33-67)	75 (50-83)	<0.001	<0.001

QoL: Quality of life

Table 3: QoL scores in the general Questionnaire and Changes in QoL from pre-treatment to 6 months after the treatment in EORTC QLQ H&N43

Parameters	Pre-treatment (baseline) Median (Range)	At the end of treatment Median (Range)	Post-treatment (after 3 months) Median (Range)	Post-treatment (after 6 months) Median (Range)	Baseline versus end of treatment P-value	Baseline versus 6 months post-treatment P-value
Pain	17 (8–58)	67 (50–100)	42 (33–75)	25 (8–50)	<0.001	**>0.144**
Swallowing	33 (8–50)	67 (50–100)	50 (33–75)	25 (8–67)	<0.001	<0.001
Teeth problems	0 (0–22)	16.5 (0–44)	11 (0–22)	0 (0–22)	<0.001	**>0.05**
Dry mouth and sticky saliva	0	67 (0–100)	50 (0–67)	17 (0–33)	<0.001	<0.001
Problems with senses	0 (0–33)	33 (0–67)	17 (0–50)	0 (0–33)	<0.001	**>0.05**
Speech problems	20 (6–60)	60 (40–94)	40 (26–73)	20 (13–60)	<0.001	**>0.05**
Body image	11 (0–33)	44 (11–66)	22 (11–44)	11 (0–22)	<0.001	**>0.05**
Social eating	25 (0–33)	67 (33–83)	42 (17–58)	17 (8–33)	<0.001	<0.001
Skin	0 (0–11)	44 (0–55)	22 (0–33)	11 (0–22)	<0.001	<0.001
Fear of progression	67 (33–100)	75 (50–100)	33 (33–83)	25 (17–50)	<0.001	<0.001
Problem opening mouth	0 (0–33)	67 (0–100)	33 (0–67)	33 (0–33)	<0.001	<0.001
Cough	33 (0–67)	33 (33–67)	33 (0–33)	0 (0–33)	<0.001	<0.001
Social contact	33 (0–33)	100 (67–100)	33 (33–67)	0 (0–33)	<0.001	<0.001
Neck swelling	0 (0–67)	0 (0–67)	0 (0–33)	0 (0–33)	**>0.05**	<0.05
Weight loss	33 (0–33)	67 (33–100)	33 (0–67)	33 (0–33)	<0.001	**>0.05**
Wound healing	0	33 (0–33)	0 (0–33)	0	<0.001	_

in the mouth, swallowing, problems with teeth, dry mouth, sticky saliva, problems with senses, social eating, weight loss etc except neck swelling) showed clinical and statistical significant deterioration of QoL with respect to the baseline.

Among all the functional and symptom scales of QLQ C30, fatigue and appetite loss are not statistically and clinically improved, that is, patients having complains of fatigue and appetite loss even after 6 months after completion of radiation. All other item scales (physical function, role function, emotional function, cognitive function, social function, nausea and vomiting, pain, dyspnea, and financial difficulties) showed significant improvement with respect to pre-treatment. Cough, social contact, and fear of progression showed both clinically and statistically significant improvement. Symptoms such as dry mouth and sticky saliva, skin problems, and problems in opening mouth showed both statistically and clinically significant deterioration. Some symptoms were statistically significant in improvement but did not show clinically significant relevance. These symptoms were swallowing, social eating, and neck swelling. The rest of the symptoms were not statistically improved from baseline, but improved with respect to their immediate post-treatment conditions. These were pain, teeth problems, problem with senses, speech problems, body image, and weight loss.

Some symptoms such as dry mouth and sticky saliva, skin problems, problems in opening mouth, and swallowing problems along with functional items such as fatigue and

appetite loss were significantly present at 6 months after radiation, though they had improved from their immediate post-treatment conditions. Overall, the QoL of these patients had improved in almost all item-scales except a few from the baseline at 6 months after the treatment.

Lima et al., in a study on head-and-neck cancer patients found that HRQOL became worse in short-term after the treatment. These effects appeared within the 1st month after starting treatment and remained until the end of therapy. Several physical symptoms also worsened over time, such as: Fatigue, nausea and vomiting, dry mouth and sticky saliva, swallowing and skin symptoms, senses, and teeth problems.[12]

Wan Leung et al., in a study on HRQOL in head-and-neck cancer survivors after RT using EORTC QLQ-C30 and QLQ-HN35 questionnaires stated that technological advance of RT substantially improves the head-and-neck-related symptoms and broad aspects of HRQOL for HNC survivors. Compared with 2DRT, intensity-modulated radiation therapy (IMRT) had significant better outcome in the scales of global QOL, physical functioning, swallowing, senses (taste/smell), speech, social eating, social contact, teeth, opening mouth, dry mouth, sticky saliva, and feeling ill.[13]

Volkenstein et al., in his study on health-related QoL after Oropharyngeal Cancer treatment showed significantly better results and thus a better QoL. In this study, the overall QOL had also improved at 6 months after completion of treatment except for fatigue, appetite loss, and a few symptoms such as dry mouth, sticky saliva, pain in opening mouth, and skin problems.[14]

Fang et al., on a study on changes in QoL of head-and-neck cancer patients following post-operative RT stated that the differences in all the QLQ-C30 scales between the two time points (before and 2 years after RT) were not statistically or clinically significant. Of all the scales in the QLQ-H&N35, only problems in social eating, teeth, dry mouth, and sticky saliva became worse with both statistical and clinical significance.[15]

Nordgren et al., in his study on HRQOL in patients of pharyngeal carcinoma – A 5-year follow-up stated that treatment of pharyngeal carcinoma often results in long-term side effects such as dry mouth problem with teeth and thick secretions. In this study, these adverse effects were present even after 6 months after completion of radiation affecting the QoL of the patients; hence, similar outcome is noted.[16]

Cengiz et al., in his assessment of QOL of 187 nasopharyngeal carcinoma patients with EORTC QLQ-C30 and HN-35 modules showed that QoL is adversely affected in our nasopharyngeal carcinoma patients treated with combined therapies.[17]

Al-Mamgani et al., in a prospective evaluation of QOL in patients after chemoradiation for oropharyngeal cancer found that the scores of QLQ-H&N35 swallowing returned to baseline level while the scores on dry mouth, sticky saliva, opening mouth, and teeth were significantly deteriorated compared to baseline. The most significant QoL deterioration was seen in patient related with xerostomia.[18]

Jellema et al., in a study of head-and-neck cancer patients with Stage I-IV disease without metastasis on impact of radiation-induced xerostomia on QoL after primary RT on 2007 found that there is a significant association was found between RTOG-xerostomia and overall QoL outcome. A significant relationship with global QoL, all functioning scales, and fatigue and insomnia were observed.[19]

Shepherd and Fisher in his study of QoL in patients with oral and oropharyngeal cancer from diagnosis up to 3-month post-treatment stated that functioning was reduced immediately post-treatment, with most functions improving to near baseline levels by 3-month post-treatment. Many symptoms significantly increasing post-treatment. Functioning was found to reduce immediately post-treatment, with most functions improving to near baseline levels by 3-month post-treatment. Many symptoms significantly increased post-treatment, with many still scoring greater than at baseline levels at the end of the study.[20]

Maingon et al., on his article on QoL for patients treated for head-and-neck carcinoma showed that xerostomia is the most frequent complication reported after head-andneck radiation therapy. Odynophagia is considered one of the detrimental component of QoL.[21]

Williamson et al., in an article, QoL after the treatment of laryngeal carcinoma: A single center and cross-sectional study showed that those undergoing chemoradiotherapy or combined surgical treatment and chemoradiotherapy reported the worst QOL, particularly in terms of social eating, taste, and saliva production.[22]

Liao et al., in his article on health-related QoL and utility in head-and-neck cancer survivors showed that disease and treatment of head-and-neck cancer lead to disability and poor health-related QOL and utility.[23]

Elumalai et al., in his study on "The patient-reported outcome measures in oropharyngeal, laryngeal, and

hypopharyngeal cancer patients treated with Volumetric Modulated Arc-based simultaneous integrated boost RT" concluded that there was a statistically significant (P<0.001) reduction in global QoL scores at the end of treatment when compared to baseline scores, but by 3 months, there was the return in the QOL scores in most scales similar to the baseline value.[24]

An assessment of pre- and post-RT QoL of 60 head-and-neck cancer patients was done by Sadhya et al.,[25] using the European Organization for Research and treatment of cancer QoL questionnaire head-and-neck cancer module (EORTC QLQ H&N 35). Statistically significant differences were observed compared to baseline (P<0.001) at the completion of RT in pain, swallowing, speech, cough, dry mouth, mouth opening, and senses scale and at 3.6 months of follow-up, while the HNSS (sticky saliva) scale showed statistically insignificant result at Zero (0) months (at the time of completion of radiation). The authors concluded that the QoL in head-and-neck carcinoma patients is affected in various functional and symptoms-related domains and their overall health and QoL perceived were not very satisfactory.

Hence, like our study, studies carried out elsewhere also showed deterioration of QOL after radiation which improved mostly later on with time. With the improvement in overall survival in the patients of pharyngeal and laryngeal malignancy, the heath-related QoL has become very important. Patients expect a good QoL without any compromise in treatment outcomes. Being a resource constraint peripheral institution, we had to use 2D technique in a telecobalt unit which have more negative impact on QoL post-radiation therapy. Modern radiation treatment delivery systems such as 3D conformal RT, IMRT, and image-guided radiation therapy (IGRT) reduce the deterioration of QoL in these cancers and are preferred.

Limitation of the study

1. The covid pandemic limited our sample size.
2. The post operative follow up period of six months was inadequate to note all the adverse outcomes especially late toxicities.

CONCLUSION

Laryngeal and pharyngeal carcinoma patients suffered from a deterioration of QoL after receiving radiation therapy using 2D Technique in Telecobalt unit (which we had to use in a resource constraint peripheral institution) due to radiation-induced side effects most of which gradually improved thereafter. By 6 months after radiation therapy, most of the QoL scales showed a statistically significant improvement, while some of the specific head and neck symptoms (Dry mouth, sticky saliva, and trismus) persisted. These negative impacts on QoL post radiation therapy can be minimized using newer techniques such as 3D conformal radiation, IMRT, and IGRT.

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