

# Quality of life in patients with squamous cell carcinoma of hypopharynx after radiotherapy in a tertiary care centre

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## Abstract

EORTC is a well-accepted and peer reviewed tool of assessment. EORTC QLQ 30 measures the general clinical features of any cancer and specific EORTC. **Objectives-** To determine the quality of life in patients who have undergone Radiotherapy following various modalities of treatment for different subsites of Hypopharyngeal Squamous cell carcinoma. **Methods-** Two Hundred and two patients seen in ENT, Head and Neck surgery department after postoperative Radiotherapy for Hypopharyngeal Squamous Cell cancers were served with both EORTC quality of life questionnaire 30 and specific Head and Neck 35. Patients above the age of 20 years, 6 weeks after Radiotherapy with Pyriform Fossa, Posterior Pharyngeal wall and Post cricoid region squamous cell carcinoma were assessed. The study aimed at determining the quality of life and associated comorbidities. **Analysis-** Data was entered into Microsoft Excel (Windows 7; Version 2007) and analyses were done using the Statistical Package for Social Sciences (SPSS) for Windows software (version 22.0; SPSS Inc, Chicago). Descriptive statistics such as mean and standard deviation (SD) for continuous variables, frequencies and percentages were calculated for categorical Variables were determined. Association between Variables was analyzed by using Chi-Square test for categorical variables. **Results-** Dyspnoea and Odynophagia were the most important symptoms which crippled the patients irrespective of the subsite in which cancer presented (PFS 3.35, PPW 3.35, PCR 3.31 ;<0.001) Psychological ,Cognitive, Social functions though were affected there was not much difference amongst the individual subsites (PFS 3.66, PPW 3.18, PCR 3.01; 0.001). Almost all the patients had significant financial problems (PFS 3.36, PPW 2.91, PCR 3.59;0.001). **Conclusion-** Quality of life questionnaires provide an insight into the life of patients who suffer from morbidity of the disease as well as its treatment. Thorough assessment of the condition of the patient in the post treatment status helps in timely rehabilitation.

**Keywords:** EORTC, Quality of Life, Hypopharyngeal SCC

## Introduction

Squamous Cell Carcinomas of the Hypopharynx form one of the major tumours of the Head and Neck. They constitute nearly 35% of the total tumours of the region. Hypopharynx is oncologically is divided into three different subsites based on the anatomy of the region and spread of the malignancies. These three subsites are Pyriform Fossa (PFS), Posterior Pharyngeal Wall (PPW), Post Cricoid Region (PCR).

Pyriform fossa SCC is a commonly occurring malignancy of the Head and Neck which is second only to Laryngeal SCC. Management of these tumours involves extensive surgery like Laryngopharyngectomy

which can be partial or total with primary or Flap based reconstruction of the tumour site. This will be followed by Selective or Modified Radical Neck dissection depending on the Neck Node status. All these patients undergo post-operative radiotherapy. Some pts where surgery is not possible, or RT and surgery carry same 3/5-year survival primary RT will be administered. While surgery addresses the bulk of the tumour radiotherapy takes care of the margins [1].

Radiotherapy causes significant morbidity to the patient even though it is a effective curative option in substantial cases with varied stages of the tumour. Radiation toxicity significantly brings down the quality of life with severe psychosocial impact also. Patients treated with RT take a long time to recover from its

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## Original Research Article

toxicity which further deteriorates the recovery from the ill effects of the primary tumour itself [2].

Many standardised qualities of life questionnaires are available out of which EORTC is a well-accepted and peer reviewed tool of assessment.

EORTC QLQ 30 measures the general clinical features of any cancer and specific EORTC H&N 35 is designed for Head and Neck cancer.

The study is aimed at determining the quality of life and associated co-morbidities in patients treated with Postoperative Radiotherapy status for Hypopharyngeal Cancers [1, 2].

## Materials and Methods

**Study setting, type, duration:** The study was undertaken in the Dept of ENT, Mandya Institute of Medical Sciences, Mandya.

The study was a Prospective study with Descriptive analysis based on EORTC questionnaire.

The study was carried out for a period of 2 years from October 2015 to September 2017

**Ethical consideration:** The study was started after permission from the Institutional Ethical Committee.

The study does not involve any interventions or procedures. It is a purely questionnaire-based study.

**Sampling:** Purposive sampling technique was used sample size was 202

**Inclusion criteria:** 1. Patients with Squamous Cell carcinoma of various subsites of Hypopharynx who have undergone Radiotherapy

### Exclusion criteria

1. Patients with radiation toxicity following radiotherapy for SCC Hypopharynx
2. Patients not willing to participate in the study
3. Patients who are not able to comprehend the EORTC questionnaire inspite of assistance.

**Methods, data collection, procedure-** The study was a prospective study with descriptive analysis approved by Ethical committee of Mandya Institute of Medical Sciences, Mandya.

Two hundred and two patients seen in ENT, head and neck surgery department after postoperative radiotherapy for hypopharyngeal squamous cell cancers at Mandya Institute of Medical Sciences were included in the study.

Inclusion criteria were, patients above the age of 20 years, 6 weeks after radiotherapy with pyriform fossa, Posterior pharyngeal wall and post cricoid region squamous cell carcinoma.

Patients who were unable to comprehend the questionnaire even after adequate support were excluded from the study.

A detailed history, socio demographic details were collected followed by clinical examination and all the data was recorded on a pre-prepared chart.

Patient consent was taken and comprehension to understand the questionnaire was assessed.

Patients with difficulty to understand the questionnaire and those who were not interested were duly excluded.

English and Kannada translation of general quality of life (EORTC QLQ-C30) was used followed by specific (EORTC QLQ H&N 35) head and neck questionnaire.

**Data analysis and interpretation:** Data was entered into Microsoft Excel (Windows 7; Version 2007) and analyses were done using the statistical package for Social Sciences (SPSS) for Windows software (version 22.0; SPSS Inc, Chicago).

Descriptive statistics such as mean and standard deviation (SD) for continuous variables, frequencies and percentages were calculated for categorical variables were determined.

Association between Variables was analyzed by using Chi-Square test for categorical variables.

Comparison of mean of quantitative variables were analyzed using ANOVA and Kruskal Wallis after checking the data for normality distribution by using Shapiro-Wilk Test.

Bar charts and Pie charts were used for visual representation of the analyzed data.

Level of significance was set at 0.05.

## Results

Table-1: Association between carcinoma type and bio-social characteristics (N=202).

Parameter	Carcinoma Type			P value
	Piriform fossa (n=121) n (%)	Post cricoid (n=11) n (%)	Post pharyngeal (n=70) n (%)	
<b>Age (in Years)</b>				
≤ 50	15 (12.4)	2 (18.2)	2 (2.9)	0.077
51-60	33 (27.3)	4 (36.4)	14 (20.0)	
61-70	46 (38.0)	5 (45.5)	34 (48.6)	
>70	27 (22.3)	0	20 (28.6)	
<b>Mean (SD)</b>	63.2 (10.2)	60.3 (7.2)	66.6 (7.7)	64.2 (9.4)
<b>Sex</b>				
Female	41 (33.9)	0	19 (27.1)	0.153
Male	80 (66.1)	11 (100.0)	51 (72.9)	
<b>Smoking</b>				
Non-Smoker	28 (23.1)	0	7 (10.0)	0.061
Tobacco Chewing	3 (10.7)	1 (9.1)	12 (17.1)	
Smoker	80 (66.1)	10 (90.9)	51 (72.9)	
<b>Socio-Economic Status</b>				
APL	11 (9.1)	2 (18.2)	11 (15.7)	0.491
BPL	110 (90.9)	9 (81.8)	59 (84.3)	
<b>Alcoholic</b>				
Yes	58 (47.9)	11 (100.0)	46 (65.7)	0.001*
No	63 (52.1)	0	24 (34.3)	
Chi-Square Test, P Value *Significant				

Table-2: Association between Carcinoma Type and Staging &amp; Mode of Intervention (N=202)

Parameter	Carcinoma Type			P value
	Piriform fossa (n=121) n (%)	Post cricoid (n=11) n (%)	Post pharyngeal (n=70) n (%)	
<b>Staging</b>				
1	9 (7.4)	3 (27.3)	9 (12.9)	<0.001*
2	22 (18.2)	1 (9.1)	39 (55.7)	
3	47 (38.8)	2 (18.2)	14 (20.0)	
4A	9 (7.4)	2 (18.2)	2 (2.9)	
4B	13 (10.7)	2 (18.2)	1 (1.4)	
4C	21 (17.4)	1 (9.1)	5 (7.1)	
<b>Mode of intervention</b>				
Palliative Radio	21 (17.4)	1 (9.1)	5 (7.1)	0.137
Post op Radio	92 (76.0)	10 (90.9)	56 (80.0)	
Primary Radio	8 (6.6)	0	9 (12.9)	
Chi-Square Test, P Value *Significant				

**Table-3: Association between carcinoma type and EORTC 30 scoring (N=202)**

Parameter	Carcinoma Type			P value
	Piriform fossa (n=121) Mean (SD)	Post cricoid (n=11) Mean (SD)	Post pharyngeal (n=70) Mean (SD)	
Appetite Loss	3.17 (0.73)	1.82 (0.75)	2.03 (0.85)	<0.001*
Physical Functioning	3.28 (0.73)	2.45 (1.12)	2.07 (0.76)	<0.001*
Role Functioning	3.31 (0.65)	3.55 (0.52)	2.19 (0.78)	<0.001*
Emotional	3.66 (0.47)	3.18 (0.75)	3.01 (0.71)	<0.001*
Cognitive	3.17 (0.68)	3.18 (0.87)	2.74 (0.63)	<0.001*
Social	3.21 (0.76)	3.55 (0.52)	2.86 (0.64)	0.001*
Fatigue	3.40 (0.66)	3.27 (0.64)	3.16 (0.71)	0.066
Nausea/Vomiting	2.42 (0.92)	2.18 (1.16)	2.11 (0.64)	0.054
Pain in the Throat	3.42 (0.57)	3.27 (0.64)	3.51 (0.63)	0.337
Dyspnoea	3.45 (0.53)	3.45 (0.52)	3.31 (0.67)	0.308
Insomnia	3.64 (0.51)	3.18 (0.60)	3.31 (0.77)	0.001*
Appetite Loss	3.60 (0.51)	3.55 (0.52)	3.50 (0.50)	0.460
Constipation	2.07 (1.30)	3.00 (0.89)	2.10 (1.20)	0.064
Diarrhoea	2.26 (1.34)	1.00 (-)	2.30 (1.32)	0.008*
Financial Problems	3.36 (0.77)	2.91 (0.94)	3.59 (0.60)	0.008*
<b>Total</b>	47.40 (3.11)	43.55 (3.35)	41.80 (2.70)	<0.001*
ANOVA, P Value *Significant				

**Table-4: Association between Carcinoma Type and EORTC 35 Scoring (N=202)**

Parameter	Carcinoma Type			P value
	Piriform fossa (n=121) Mean (SD)	Post cricoid (n=11) Mean (SD)	Post pharyngeal (n=70) Mean (SD)	
Pain	3.45 (0.56)	3.27 (0.64)	3.44 (0.55)	0.593
Difficulty in swallowing	3.00 (0.79)	3.82 (0.40)	3.60 (0.54)	<0.001*
Decreased senses	3.14 (0.72)	3.45 (0.52)	2.81 (0.59)	0.001*
Change in speech	3.28 (0.64)	3.82 (0.40)	3.53 (0.50)	0.001*
Social eating disturbed	3.46 (0.56)	3.36 (0.67)	3.34 (0.50)	0.379
Changes in social contact	3.50 (0.56)	3.64 (0.50)	3.34 (0.61)	0.264
Sexuality	3.57 (0.53)	3.55 (0.52)	3.37 (0.72)	0.002*
Toothache	3.17 (0.65)	2.82 (0.60)	3.24 (0.75)	0.003*
Opening mouth	3.49 (0.60)	3.27 (0.64)	3.41 (0.55)	0.097
Dry mouth	3.29 (0.60)	3.45 (0.52)	3.30 (0.62)	0.535
Sticky saliva	3.58 (0.51)	3.64 (0.50)	3.20 (0.69)	0.459
Coughed	3.40 (0.66)	3.18 (0.60)	3.60 (0.54)	0.033*
Felt ill	3.33 (0.73)	3.64 (0.50)	3.44 (0.62)	0.261
<b>Total</b>	43.67 (2.67)	44.91 (1.51)	43.97 (2.26)	0.251
ANOVA / Kruskal Wallis Test, P Value *Significant				

**Table-5: Association between Carcinoma Type and Last week history (N=202)**

Parameter	Carcinoma Type			P value
	Piriform fossa (n=121) n (%)	Post cricoid (n=11) n (%)	Post pharyngeal (n=70) n (%)	
Pain killers	101 (83.5)	7 (63.6)	58 (82.9)	0.254
Nutritional supplements	54 (44.6)	7 (63.6)	34 (48.6)	0.457
Feeding tube	37 (30.6)	5 (45.5)	27 (38.6)	0.383
Weight loss	56 (46.3)	3 (27.3)	27 (38.6)	0.334
Weight gain	65 (53.7)	8 (72.7)	43 (61.4)	0.334
<b>VAS 1</b>				
1	80 (66.1)	7 (63.6)	56 (80.0)	0.110
2	41 (33.9)	4 (36.4)	14 (20.0)	
<b>VAS 2</b>				
1	88 (72.7)	8 (72.7)	49 (70.0)	0.219
2	33 (27.3)	3 (27.3)	18 (25.7)	
3	0	0	3 (4.3)	
Chi-Square Test, P Value Not Significant				

Piriform fossa squamous cell cancers dominate the other two subsites of hypopharynx significantly. They form the bulk of tumours of not just hypopharynx but of Head and Neck malignancies. About 67.7% (121) are tumours of Piriform Fossa. Post cricoid cancers constitute only 3% (11) of the total number of cases. Posterior Pharyngeal wall squamous cell cancers are not so uncommon forming 28.3% (70) of the total cases.

Even though it is a potential space which gives scope for tumour growth, because the piriform fossa has good lymphatic drainage and neck nodal presentation is quite early, inspite of this diagnosis in Stage I is only 7% and maximum presented in advanced stage (stage III 47% and Stage IV 21%). Most of the posterior pharyngeal wall and post cricoid region cancers present late and they become poor surgical candidates. Even CRT carries poor outcome and Five-year survival rates are not encouraging. (PPW-Stage III, IV 20%) and (PCR Stage III-18.2%).

76% of patients had undergone some form of surgery (total or partial laryngectomy, debulking surgery) and 21% had received radiotherapy as primary modality treatment. CRT and CRT with surgery were also employed in 8% and 2% of patients respectively.

EORTC QLQ 30 assessment of symptoms for PFS, PPW, PCR showed that Global quality of life had deteriorated significantly. In all the three subsites of hypopharyngeal cancers quality of life was poor (PFS 3.28, PPW 2.45, PCR 2.07; <0.001). Dyspnoea and odynophagia were the most important symptoms which crippled the patients irrespective of the subsite in which cancer presented (PFS 3.35, PPW 3.35, PCR 3.31 ;<0.001)

Psychological, cognitive, social functions though were affected there was not much difference amongst the individual subsites (PFS3.66, PPW3.18, PCR3.01 ;0.001). Almost all the patients had significant financial problems (PFS 3.36, PPW2.91, PCR 3.59;0.001).

Loss of appetite, insomnia, constipation and diarrhoea were also the major constituent symptoms. Head and Neck 35 EORTC questionnaire shows significant alterations in quality of life due to local complications and also sequelae of residual disease. Swallowing and Social eating were affected badly because of severe mucositis and post-surgical scarring and complications involving flap healing (PFS 3.0, PPW 3.82, PCR 3.60;<0.001).

When the same QLQ 30 and 35 questionnaires were applied to assess the quality of living in different stages of hypopharyngeal cancers individually, Role functioning was found to be very poor, probably due to morbidity of surgery and radiation toxicity (PFS 3.31, PPW 3.55, PCR 2.90;<0.001).

Fatigue and pain universally were present irrespective of the stage of the disease but score were higher in advanced stages, due to cancer catabolism and neurotoxicity (Stage III 61.4, Stage IV 79.1;<0.001). Dyspnoea, insomnia and appetite loss also prevailed upon in the late stages of disease following RT (PFS 3,64, PPW 3.38; PCR 3.31;<0.001).

Late stages of the disease post radiotherapy showed significant alterations in Speech (Stage III 59.2, Stage IV 70.9;<0.001), Taste and Smell (Stage IV 70.9;<0.001). Dry mouth and sticky saliva was present in all stages of disease with increasing severity following radiotherapy due to salivary glandular necrosis and fibrosis, (Stage IV 80.1;<0.001)

## Discussion

Poor quality life secondary to Radiation toxicity lasts for years together and can be never ending since radiation induces irreversible changes at molecular level and stimulates accelerated fibrosis. Even though tissue or organ preservation is achieved with good control of micrometastasis at the margins, the damage is long lasting which cripples the life of the patient. The preserved anatomy of the organ is poor physiologically and rehabilitation has to be simultaneously carried out along with improvement of nutrition and general condition, taking care of the comorbidities.

In the present study with 202 patients who had undergone RT for Hypopharyngeal cancers on whom EORTC QLQ 30 and H&N 35 were applied, morbidity was observed due to RT itself other than the Primary disease as well as Surgery.

Wang Leung S, in their multivariate analysis proved that the variables of gender, annual family income, tumor site, AJCC stage, treatment methods, and RT technique were prognosticators for QLQ-C30 results, so were tumor site and RT technique for H&N35. Significant difference ( $p < 0.05$ ) of HR-QoL outcome by different RT techniques was observed at 2 of the 15 scales in QLQ-C30 and 10 of the 13 scales in H&N35.

Compared with 2DRT, 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. The technological advance of RT substantially improves the head-and-neck related symptoms and broad aspects of HR-QoL for HNC survivors [1].

Bjordal, Hammerlid, in a study on QLQ in RT pts found compliance rate was high, and the questionnaires were well accepted by the patients. The QLQ-H & N35, in conjunction with the QLQ-C30, provides a valuable tool for the assessment of health-related quality of life in clinical studies of H&N cancer patients before, during, and after treatment with radiotherapy, surgery, or chemotherapy [2].

Dyspnoea formed one of the important symptoms in cancers of all the three subsites of hypopharynx. de Graffe A., mentions that there was a significant but temporary deterioration of physical functioning, fatigue and most head and neck symptoms. Speech was the only symptom which improved. Patients with T2 tumors had significantly worse physical symptoms compared with patients with T1 tumors. There was a high level of depressive symptomatology at baseline, followed by an improvement after treatment. After radiotherapy for laryngeal cancer, a temporary deterioration of physical functioning and symptoms occurs, mostly caused by side effects of treatment. Despite physical deterioration, there is an improvement of emotional functioning and mood after treatment, probably as a result of psychological adaptation and coping processes [3].

Generalised symptoms of malignancies like Insomnia, Loss of appetite, Constipation and Diarrhoea were universally present. Bjordal K et al., Seventy-eight percent of the patients who were alive after 12 months filled in all questionnaires (218/280). The general trend was that HRQL deteriorated significantly during treatment, followed by a slow recovery until the 12-month follow-up with few exceptions (senses, dry mouth, and sexuality).

Patients who later died reported worse HRQL at each assessment point compared with patients who filled in all six questionnaires, whereas those who dropped out of the study for other reasons were quite similar to patients who filled in all questionnaires. The patients with pharyngeal cancer in general reported worse HRQL compared with the other groups and did not reach pretreatment values in several domains. Stage was also an important factor for HRQL in patients with head and neck cancer. Detailed knowledge about the differences between groups and changes over time may aid us in the communication with patients and in the design of intervention studies focusing on improvement of the support and rehabilitation of patients with head and neck cancer [4]. Harrison L Bet al., At follow-up, annual incomes were similar to those at initial examination. Average PSS scores were 90 for eating in public, 96 for understandability of speech, and 68 for

normalcy of diet. > 30% xerostomia, difficulty swallowing, decreased energy, pain, worrying, insomnia, cough, drowsy, change in taste, and irritability. The overwhelming majority of patients achieved excellent functional status and quality of life and could maintain their pre-diagnosis earning potential and employment status after primary radiation for advanced base of tongue cancer [5, 6].

Epstein JB et al., assessed pain in the head and neck region. The measure was commonly embedded in quality of life studies. Most of these studies described pain in head and neck cancer (HNC) patients, which therefore became the focus of the report.

Pain is common in patients with HNC and is reported by approximately half of patients prior to cancer therapy, 81% during therapy, 70% at the end of therapy, and by 36% at 6 months after treatment. Pain is experienced beyond the 6-month period by approximately one third of patients and is typically more severe than pre-treatment cancer-induced pain [7].

More disturbing was the fact that all pts were poor financially and were unable to bear the cost of treatment as well as rehabilitation Martino and Ringash., state that ,common concerns of head and neck squamous cell cancer patients include concerns about illness and their future, general physical and emotional wellbeing, speech, body image, and financial issues.

Patients receiving radiotherapy report high levels of problems with swallowing, eating, and dry mouth. This article focuses on several of the most common and severe lasting issues for head and neck squamous cell cancer patients: impairments of overall quality of life, xerostomia, speech, and swallowing, focusing primarily on the tools and techniques for measuring such effects [8].

Gandhi AK et al., found that, female: male ratio was 17:83.42% of them were  $\geq 60$  years of age. Median value for SW, HO, WL, BL, PALMP, OM, and OS was 33.33 (100-0) while TA, CG, NV, DY, and HE had a median score of 0.00. Advanced HNCa has a significant burden of symptoms. These results would help in giving patients better symptom directed therapies and improve their QOL [9].

Cooper JS., in their book on Radiation toxicity states that, head and neck region is composed of numerous structures, each with an inherent response to radiation that is largely governed by the presence or absence of mucosa, salivary glands, or specialized organs within

that site. Irradiated mucocutaneous tissues demonstrate increased vascular permeability that leads to fibrin deposition, subsequent collagen formation, and eventual fibrosis. Irradiated salivary tissue degenerates after relatively small doses, leading to markedly diminished salivary output. This, in turn, effects the teeth by promoting dental decay which, in turn, effects the integrity of the mandible. Details of these changes are presented, including their pathophysiology, clinical syndromes, and potential treatment [10].

Poor physical functioning, Decreased Cognitive skills and Emotions along with low social life were present in all the patients. Schrloo et al. reported better emotional functioning at both follow-ups ( $p < 0.001$ ), worse social functioning at 12 months ( $p < 0.05$ ), and better global health status at 24 months ( $p < 0.05$ ). Patients' own implicit common-sense beliefs about their illness added small but significant amounts of variance to the prediction of QoL after 2 years.

Less belief in own behavior causing the illness predicted better functioning and better global health. Strong illness identity beliefs predicted worse functioning and worse global health. Negative perceptions about the duration of the illness (chronic timeline beliefs) and more negative perceived consequences also predicted worse QoL [11].

## Conclusion

Quality of life questionnaires provide an insight into the life of patients who suffer from morbidity of the disease as well as its treatment.

## What the study adds to the existing knowledge?

Thorough assessment of the condition of the patient in the post treatment status helps timely rehabilitation. Standardisation and updating of the questionnaire with advances in treatment and its implications in decreasing disease burden might be necessary.

## Author's contribution

**Dr. Nagavara Kalegowda Balaji:** Concept, study design and manuscript preparation.

**Dr. Ravi D.:** Concept, study design and manuscript preparation.

**Dr. M.H. Prasad:** Concept, study design and manuscript preparation.

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