Health-related quality of life assessment for head-and-neck cancer patients during and at 3 months after radiotherapy – A prospective, analytical questionnaire-based study

ABSTRACT

Introduction: Health-related quality of life (HRQoL) is a more specific area of QoL that deals with the evaluation and assessment of the impact of the disease and its treatment-related morbidities on a patient's physical, psychological, and social aspects. The aim of the present study was to assess the HRQoL of patients with head-and-neck cancer (HNCs) during and at 3 months after completion of radiotherapy (RT) by intensity-modulated RT.

Materials and Methods: This study was a prospective, longitudinal, observational, and self-completed questionnaire-based study that included 120 patients with HNC who underwent intensity-modulated RT. The questionnaire had adequate internal consistency. The questionnaires were given to each patient at the beginning of treatment (pretreatment), weekly visits during the course of RT (at the end of 1st, 2nd, 3rd, 4th, 5th, and 6th week), on the day of completion of RT, and then finally at 3 months after completion of RT. Thus, a total of successive nine time points were assessed.

Results and Conclusions: One hundred and eleven patients completed the questionnaires at all nine time points. HRQoL usually decreases during treatment and then increases to pretreatment levels by 3 months after treatment. The Quality of Life Questionnaire, Core Module and Quality of Life Questionnaire, Head and Neck Module were found to be both valid and reliable. There was a significant QoL reduction for the patients throughout treatment in relation to functions and symptoms in the treatment of HNC. However, all the functions and most of the symptoms returned to baseline at the 3-month follow-up.

Keywords: Head-and-neck cancer, health-related quality of life, oral cancer, quality of life, radiotherapy

INTRODUCTION

Head-and-neck cancers (HNCs) account for 30% of all cancer cases in India. The treatment of these cancers involves a multidisciplinary approach. Not only is the treatment of these cancers complex, but HNCs also have the highest incidence of treatment-related morbidities among all the cancers. Although the patients may be disease free in their regular follow-up visits, treatment-related morbidities often continue to have a devastating impact on their quality of life (QoL). It is all the more important in the Indian subcontinent, where patients often present with advanced stage and hence undergo extensive surgeries, followed by radiotherapy (RT) with large radiation portals, which in turn...
results in even lower QoL. Hence, in recent ongoing clinical trials and studies, QoL has been considered important and is included as one of the outcomes.

“Health-related QoL” (HRQoL) is a more specific area of QoL that deals with the evaluation and assessment of the impact of the disease and its treatment-related morbidities on a patient’s physical, psychological, and social aspects. Knowing HRQoL helps clinicians to understand a patient’s perception about the disease and the impact of adverse effects of therapy, which then enables them to appropriately modify treatment strategies and facilitates the aftercare and rehabilitation services for the patients. The aim of the present study was to assess the HRQoL of patients with HNCs during and at 3 months after completion of RT by intensity-modulated RT (IMRT) technique.

MATERIALS AND METHODS

This study was a prospective, longitudinal, observational, and self-completed questionnaire-based study that included 120 patients with HNC who underwent IMRT. The study was approved by the ethical committee of the authors’ institute, and patients provided written consent. The inclusion criteria were: over 18 years of age; locally advanced squamous cell carcinoma HNC with primary tumor sites in the oral cavity, oropharynx, larynx, and hypopharynx; and IMRT delivered as radical or adjuvant therapy with or without concurrent chemotherapy. Exclusion criteria were: any ongoing mental or cognitive impairment that limits the ability to comprehend the questionnaires, previously diagnosed and treated for HNC, and previously treated with RT in the head-and-neck region.

The Hindi language versions of the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 and QLQ-H and N35 questionnaires were obtained from the QoL Unit, EORTC Data Center in Brussels, Belgium. The EORTC QLQ-C30 questionnaire consisted of five functional scales that includes physical, role, cognitive, emotional, and social; three symptom scales that include fatigue, pain, and nausea/vomiting; a global QoL scale; and six single-item scales that assess the presence of symptomatic problems associated with teeth, mouth opening, dry mouth (xerostomia), sticky saliva, coughing, and feeling ill. All of the scales pertaining to the EORTC QLQ-C30 and QLQ-H and N35 range from zero to 100. A high score for a functional or global HR-QoL scale indicates a relatively high/healthy level of functioning or global QoL, whereas a high score for a symptom scale indicates the presence of a symptom or problem(s). The questionnaires were given to each patient at the beginning of treatment (pretreatment), weekly visits during the course of RT (at the end of 1st, 2nd, 3rd, 4th, 5th, and 6th week), on the day of completion of RT, and then finally at 3 months after completion of RT. Thus, a total of successive nine time points were assessed.

Statistical methods

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS version 20, SPSS Inc., Chicago, IL, USA). Continuous variables were presented using the mean, standard deviation, and median. Categorical variables were expressed as frequencies and percentages. Cronbach’s α-coefficient was used to confirm the internal consistency of the questions. The associations between different quantitative variables were assessed using the Mann–Whitney U-test (for two samples). A one-way analysis of variance was used to determine whether there were any statistically significant differences between the means of three or more independent (unrelated) groups. A dependent t-test (paired-samples t-test) was used to compare the means between the two related groups on the same continuous, dependent variable.

RESULTS

Of 120 patients recruited for the study, 111 completed the questionnaires at all nine time points. Three patients discontinued RT, and six defaulted at the 3-month follow-up visit; hence, these nine patients were excluded from the analysis. Pretreatment characteristics are presented in Table 1. Reliability coefficients and descriptive statistics for the EORTC QLQ-C30 and EORTC QLQ-H and N35 were performed using Cronbach’s α-coefficient. The questionnaire had adequate internal consistency. The differences in HRQoL mean scores at various time points during the course of treatment are presented in Tables 2 and 3.

DISCUSSION

In QoL research, there is no questionnaire that has been accepted as the gold standard. Various QoL questionnaires are available for use. For this study, the EORTC QLQ-C30 version 3.0 and the QLQ-H and N35 were used. The questionnaires had adequate reliability, with the QLQ-C30 displaying higher internal consistency than the QLQ-H and N35.
Global QoL deteriorated significantly during RT. It improved significantly from the end of RT to 3-month post-RT; however, there was no significant change in global QoL at 3 months when compared with baseline scores. Rathod et al. have shown that global QoL recovered rapidly during the 6 months after completion of RT. Global QoL represents the overall status of the patient’s health with respect to physical and psychological symptoms. Decreases in global QoL are associated with increases in symptoms such as pain, nausea, vomiting, difficulty in swallowing, and so forth. Improvement in global QoL at follow-up could be due to patients’ adjustment to their lifestyle such as maintaining a healthy lifestyle or starting normal activities and keeping busy with day-to-day activities.

Physical, role, emotional, cognitive, and social functioning deteriorated significantly during RT. These improved significantly from the end of RT to 3-month post-RT; however, there was no significant change in functional scores at 3 months when compared with baseline scores. de Graeff et al. prospectively evaluated the QoL of HNCs and then improved after treatment. Lohith et al. have also shown that the mean score of functions declined during treatment and then improved after treatment. However, in their study,
### Table 3: Mean score of quality of life questionnaire, head and neck module of patients at successive time points

| Items of scale | Pretreatment | Week 1 | Week 2 | Week 3 | Week 4 | Week 5 | Week 6 | End of RT | 3 months |
|----------------|--------------|-------|--------|--------|--------|--------|--------|----------|----------|
| Pain           | 22.31±22.42  | 20.74±22.43 | 14.52±23.37 | 27.43±24.77 | 29.74±26.32 | 20.38±26.37 | 21.56±20.94 | 55.54±34.36 | 62.98±31.60 |
| Swallowing     | 38.65±24.46  | 46.74±27.68 | 36.65±27.16 | 38.93±23.97 | 32.50±26.14 | 30.85±26.34 | 32.50±26.14 | 66.40±25.15 | 66.20±25.15 |
| Speech problems | 4.48±5.55    | 4.85±5.75  | 6.35±5.85  | 4.35±6.57   | 5.21±8.12   | 5.19±8.12   | 5.21±8.12   | 5.97±8.12   | 5.97±8.12   |
| Sensory problems | 0.167        | 0.024     | <0.005    | 0.001      | <0.005    | <0.005    | <0.005    | <0.005    | <0.005    |
| Trouble with social contact | 67.17±32.53 | 39.06±36.67 | 45.30±28.46 | 53.70±50.33 | 33.33±47.58 | 46.74±27.68 | 67.17±32.53 | 29.31±28.64 | 39.13±29.26 |
| Trouble with feeding | 20.04±25.59 | 20.38±24.98 | 0.00±0.00  | 0.00±0.00  | 0.00±0.00  | 0.00±0.00  | 0.00±0.00  | 0.00±0.00  | 0.00±0.00  |
| Less sexuality | 39.82±35.99  | 43.33±50.40 | 32.57±30.47 | 32.57±30.47 | 32.57±30.47 | 32.57±30.47 | 32.57±30.47 | 0.97±10.96  | 0.97±10.96  |
| Teeth | 25.07±29.07 | 24.88±25.46 | 28.89±26.54 | 36.15±31.68 | 45.63±32.45 | 62.61±38.14 | 66.62±32.48 | 45.63±32.45 | 62.61±38.14 |
| Opening mouth difficulty | 51.31±34.45 | 51.31±34.45 | 51.31±34.45 | 51.31±34.45 | 51.31±34.45 | 51.31±34.45 | 51.31±34.45 | 51.31±34.45 | 51.31±34.45 |
| Dry mouth | 35.09±28.93 | 35.09±28.93 | 35.09±28.93 | 35.09±28.93 | 35.09±28.93 | 35.09±28.93 | 35.09±28.93 | 35.09±28.93 | 35.09±28.93 |
| Difficulty swallowing | 0.00±0.00 | 0.00±0.00 | 0.00±0.00 | 0.00±0.00 | 0.00±0.00 | 0.00±0.00 | 0.00±0.00 | 0.00±0.00 | 0.00±0.00 |
| Coughing | 65.63±47.58 | 66.62±47.58 | 66.62±47.58 | 66.62±47.58 | 66.62±47.58 | 66.62±47.58 | 66.62±47.58 | 66.62±47.58 | 66.62±47.58 |
| Nutritional supplements | 0.00±0.00 | 0.00±0.00 | 0.00±0.00 | 0.00±0.00 | 0.00±0.00 | 0.00±0.00 | 0.00±0.00 | 0.00±0.00 | 0.00±0.00 |
| Weight loss | 71.02±29.79 | 71.02±29.79 | 71.02±29.79 | 71.02±29.79 | 71.02±29.79 | 71.02±29.79 | 71.02±29.79 | 71.02±29.79 | 71.02±29.79 |
| Weight gain | 0.00±0.00 | 0.00±0.00 | 0.00±0.00 | 0.00±0.00 | 0.00±0.00 | 0.00±0.00 | 0.00±0.00 | 0.00±0.00 | 0.00±0.00 |

**Change in mean score over time from pretreatment to end of RT and from end of RT to 3 months after RT calculated from paired *t*-test and 2-tailed *t*-test.**

**Change in mean score over time from pretreatment to end of RT calculated from repeated measures ANOVA of 35 patients, who completed RT in 7 weeks.**

**Change in mean score over time from pretreatment to end of RT calculated from repeated measures ANOVA of 35 patients, who completed RT in 7 weeks.**

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role function decreased when compared to baseline. In their review article, Rogers et al. have shown that patients who have a preserved larynx have better outcomes in terms of depression, which leads to better role function. Rathod et al. have also shown that role function at a 3-month follow-up is almost the same as the pretreatment level. Rogers et al. found that there was a drop in social functioning throughout treatment and no improvement in social function until 12-month posttreatment. Lohith et al. demonstrated that there is an improvement in social functioning at 1- and 3-month posttreatment. Another study found no improvement in social functioning at 2-month posttreatment, but there was an improvement at 12-month posttreatment. Emotional and cognitive functions have also been shown to decline during treatment. The mean emotional function score in this study was less compared to another study.

In this study, we found that fatigue declined gradually during the course of RT and improved thereafter. The reasons for fatigue could be multifactorial and could include both mental and physical reasons. Nausea, vomiting, decreased appetite, and inability to take food result in fatigue. Decreases in mouth opening and mucositis are other factors that can lead to decreases in oral intake that can result in fatigue and generalized weakness. Pain in cancer patients and the disease itself could cause mental disturbances that lead to fatigue. There was a high correlation in our study: as the problems increased during RT, patients’ fatigue increased. In line with our study, Irvine et al. observed that fatigue worsened over the course of RT and was highest in the last week of treatment, but fatigue returned to pretreatment levels by 3 months after treatment.

We noticed an increase in nausea and vomiting in our study during treatment that gradually decreased 3-month postcompletion of treatment but did not reach pretreatment levels. The reason for this finding is that RT and chemotherapy both cause nausea and vomiting. Ackerstaff et al. evaluated the QoL in inoperable Stage IV head-and-neck patients undergoing concurrent chemoradiation and found that there was a significant increase in nausea and vomiting in the 7th-week assessment with IV cisplatin-based chemotherapy that improved over a 3-month period postcompletion of treatment and almost reached baseline at 12-month posttherapy.

Pain has been a major problem in HNC, as seen in our study. Pain in our study could have been caused by mucositis and the advanced stage of the disease. At the 3-month follow-up, the use of painkillers reduced significantly. A possible reason for this could be that at 3 months, the mucositis had resolved, and there was complete remission or reduction in the bulk of the disease. The other reason for pain could be psychological. Ackerstaff et al. also found that pain worsened during RT and improved after treatment, thereby lessening the need for painkillers. In some cases, pain is coincidental and may not be directly related to cancer. Possible causes could be coexisting dental carries, periodontal inflammation, ear infections, etc., which are common concerns, especially in India. The sleep disturbances found in our study can be explained by persisting pain and psychological suffering that lead to anxiety.

In contrast to this study, Melo Filho et al. found that insomnia gradually improved during treatment. The possible reasons for better sleep could be better counseling by caregivers, use of anti-anxiety medications, or a good support system available at home. Shuman et al. found that pain and xerostomia were major predictors of poor sleep quality among HNC patients.

This study found a gradual decline in dyspnea and swallowing. The reason for the difficulty in breathing could be edema due to RT or aspiration as swallowing difficulty increases. The other possible reason for dyspnea could be fatigue and nutritional deficiencies that lead to anemia. The problem of dyspnea improved during the 3 months after treatment, which contrasts with the study done by Loorents et al. They found that dyspnea remained a significant problem at 3 months after treatment but gradually improved over a 1-year period. The reason that dyspnea may have remained a problem could be the higher number of patients with HNCs in the oropharynx in their study compared to our study, in which a higher number of patients had an oral cavity lesion. Melo Filho et al. also found higher rates of dyspnea at the end of treatment that improved at the follow-up. Eisbruch et al. concluded that swallowing difficulty is present, and it promotes aspiration leading to breathing difficulty. The reasons for swallowing difficulty are tumor size, tumor site, mucositis, and edema. Persisting dysphagia during the follow-up period may be explained by the xerostomia.

There was significant loss of appetite, loss of weight, and increase in usage of nutritional supplements in this study during RT, and there was improvement in appetite and weight gain at the 3-month follow-up after RT. The increased use of nutritional supplements continued in even at the 3-month follow-up. Newman et al. concluded that there was a significant weight loss during treatment and decline in eating that improved over a period of 18 months. Weight loss
during RT can be related to many factors, including loss of appetite, mucositis, difficulty in swallowing, loss of ability to perceive taste or smell, nausea, vomiting, and psychological complications such as depression. These things, in return, cause fatigue and impact the global QoL of the patients.

Constipation and diarrhea increased during RT. Mosel et al. found that constipation had one of the greatest negative impacts on HRQoL.

Financial difficulty also increases during the course of RT and returns to baseline at 3-month follow-up. Financial difficulty can lead to psychological distress, which in turn leads to insomnia. Costs are often incurred by the patients in developing countries like India, which potentially compromises their family's finances, savings, and future. Many times, the bread earner of the family is diagnosed with cancer, and this has a large impact on the family’s finances. A country that has a social system created by the government may lead to less of an impact on financial problems compared to countries that do not have a robust health-care policy.

Sense (smell and taste) gradually declined as the treatment progressed. The mean score gradually improved at the 3-month follow-up, many studies have similar findings. An impaired sense of taste is a common problem during radiation, chemotherapy, or both. It is believed that this decline in taste is due to the cumulative doses of radiation. These symptoms may have contributed to the progressive weight loss reported by the patients.

Speech problems occurred more during treatment in our study. At posttreatment at 3 months, speech problems had improved and returned almost to baseline. However, in a study done by Lohith et al., speech problems remain significant even at 3-month posttreatment. Patients also reported problems with social contact and social eating. Dry mouth, difficulty in swallowing, decreases in mouth opening, cough, edematous tongue, mucositis, and psychological disturbance are possible reasons for trouble with social contact, eating, and speech problems. Verdonck-de Leeuw et al. evaluated HRQoL from diagnosis to 2-year follow-up. Improvement over time was observed in social eating, social contact, and speech.

Mouth opening difficulties posed a major problem during treatment and at the follow-up. Sherman et al. have found that cancer patients have more opening mouth difficulty than a comparison group. It is recommended that exercise to prevent trismus should start before treatment and should be done 3–4 times a day. Improvement in mouth opening will lead to improvement in other symptoms such as speech, eating, social contact, and fatigue, and this will have a good overall impact on HRQoL.

Our findings suggest that there is much overlap in content areas covered by the different instrument categories (e.g., fatigue, mobility, sleep, and pain). This overlap in content areas results in difficulty in the interpretation of the clinical relevance of scores when symptoms are combined. Improvement in a few symptoms will lead to a tremendous improvement in overall HRQoL of patients. HRQoL is multifactorial; hence, the use of patient-reported outcomes will help us to know which symptoms or functions have the most negative effect on HRQoL, and we can address those concerns. This will improve patients' HRQoL, and they will be able to better cope with the treatment.

The limitation of this study is that the follow-up period was short. To accurately assess the HRQoL of treated HNC patients, a much longer follow-up period is needed.

CONCLUSIONS

HRQoL is a self-reported, subjective, multidimensional phenomenon that changes over time. It is an integral part of assessment of outcomes in HNC. HRQoL usually decreases during treatment and then increases to pretreatment levels by 3 months after treatment. The QLQ-C30 and QLQ-H and N35 were found to be both valid and reliable.

There was a significant QoL reduction for the patients throughout treatment in relation to functions and symptoms in the treatment of HNC. However, all the functions and most of the symptoms returned to baseline at the 3-month follow-up. It is necessary for the multidisciplinary team to use the information obtained in this investigation to build a broader care protocol, involving demands arising from symptoms and life situations.

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Conflicts of interest
There are no conflicts of interest.

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