Original Article

Quality of Life, Anxiety, and Depression in the Head-and-Neck Cancer Patients, Undergoing Intensity-Modulated Radiotherapy Treatment

Maria Nikoloudi, Ioannis Lymvaios[1], Anna Zygogianni[2], Efi Parpa, Dimitra-Aspasia Strikou[3], Eleni Tsilika, Vassilios Kouloulias[3], Kyriaki Mystakidou

Department of Radiology, Pain Relief and Palliative Care Unit, School of Medicine, Areteion Hospital, National and Kapodistrian University of Athens, [1]Unit of Thalassemia, General Hospital of Corinthia, Corinthia, [2]Department of Radiology, School of Medicine, Areteion Hospital, National and Kapodistrian University of Athens, [3]Department of Radiology, Radiotherapy Unit, School of Medicine, Attikon University Hospital, National and Kapodistrian University of Athens, Greece

Abstract

Aims: The aim of this study is to investigate and compare distress and quality-of-life parameters among head-and-neck cancer patients who underwent intensity-modulated radiotherapy (IMRT). **Subjects and Methods:** The patients' sample consists of 55 individuals under IMRT treatment. Three questionnaires (Quality of Life Questionnaire [QLQ]-C30 and QLQ-H and N35) of the European Organization for the Research and Treatment of Cancer and the Greek Hospital Anxiety and Depression Scales were used. **Results:** Functioning and symptoms scales measured a week before the scheduled treatment worsen significantly until the end of the treatment and at the 3-month follow-up, tend to revert to their pretreatment values. **Conclusions:** Our results showed that all parameters (functioning scales, symptoms scales, and G-HAD subscales) worsen from the start to the end treatment and tend to revert to their pretreatment values after a 3-month period.

Keywords: Anxiety, depression, intensity-modulated radiotherapy, quality of life

Introduction

Head-and-neck cancer (HNC) is presented with diverse clinical and pathological features depending on patient characteristics and heterogeneous epidemiology. It arises from the mucosa of the oral cavity, oropharynx, hypopharynx, larynx, sinonasal tract, and nasopharynx, with head-and-neck squamous cell carcinoma (HNSCC) being the most common histologic type.[1] According to estimates of cancer incidence and mortality produced by the International Agency for the Research on Cancer,[2] there will be approximately 835,000 new cases and 430,000 HNC deaths worldwide in 2018 with an incidence and death rate of around 4.6%. A large proportion of oral, pharyngeal, and especially laryngeal cancers are attributed to tobacco smoking and alcohol drinking[3] while patients with HNSCC often do not have a history of tobacco or alcohol use, but instead their tumors are positive for oncogenic forms of the human papillomavirus, particularly the 16 type.[1] A recent analysis of international variations in HNC incidence rates presented significant heterogeneity in trends by subsite, country, and sex, and the authors attributed this fact mostly to the prevalence or decline of smoking and alcohol consumption.[4]

For patients with HNC, there are many treatment options that range in intensity from single-modality therapy to concurrent radiotherapy (RT) with targeted agents or chemotherapy to induction chemotherapy followed by concurrent chemoradiotherapy.[5] Advanced technologies in RT include two-dimensional RT, three-dimensional conformal RT, and intensity-modulated RT (IMRT).[6] The most

Access this article online

Quick Response Code:

Website: www.jpalliativecare.com

DOI: 10.4103/IJPC.IJPC_168_19

Address for correspondence: Prof. Kyriaki Mystakidou, 27 Korinthias St, 115 26 Athens, Greece. E-mail: mistakidou@yahoo.com

Submitted: 15-Sep-19 **Accepted:** 02-Nov-19
Published: 28-Jan-20

How to cite this article: Nikoloudi M, Lymvaios I, Zygogianni A, Parpa E, Strikou DA, Tsilika E, *et al*. Quality of life, anxiety, and depression in the head-and-neck cancer patients, undergoing intensity-modulated radiotherapy treatment. Indian J Palliat Care 2020;26:54-9.

commonly utilized treatment is IMRT, which yields excellent survival outcomes and achieves high rate of locoregional control for HNC.[7-10] In addition, the method achieves high conformality of dose distribution and is associated with reduced late overall toxicity.[11]

However, as with almost any cancer treatment, some issues arise. According to many studies, psychological distress (i.e., anxiety and depression), as well as quality-of-life (QOL) issues, do make their appearance as early as the start of RT, and might persist throughout the treatment, or long after the end of it,[12,13] affecting not only the patients but also their caregivers.[12] For example, RT causes physical (e.g., xerostomia) and functional (e.g., dysgeusia) impairments.[14,15] In addition, psychological distress in the form of anxiety and depression in HNC patients is particularly high ranging from 14% to 52%.[16,17]

The number of younger patients that present HNC is increasing, but at the same time, technological advances in the delivery of radical treatment give the potential to significantly improve patient outcomes.[18] As a result, QOL of HNC patients is a critical issue. Not only these patients must face a potentially lethal illness but also they must also learn to cope with the consequences on their physical appearance and body functions.[19]

Since it is recognized that QOL research in HNC has some limitations there has been a shift from measuring general QOL to measuring health-related QOL (HRQOL), which reflects the effect of disease and disease treatment on general wellbeing.[20] It includes patients' appraisal of their current level of functioning, as well as satisfaction with it, compared to what they believe is ideal.[21] The temporal variations of QOL and anxiety are not well documented among HNC patients. The aim of the present study is to record and compare distress and QOL parameters at pretreatment, at the end of RT and at 3-month follow-up intervals.

Subjects and Methods

The study was conducted at the Radiation Oncology Centre, Iaso General Hospital in Athens, from February to November 2016. The sample consisted of sixty (n = 60) patients with HNC that would be following IMRT. Five patients (~8%) were excluded as they did not complete the questionnaires after the end of the treatment; thus, the final sample consisted of 55 (n = 55) cancer patients. Criteria for inclusion were as follows: Ca diagnosis at the oral cavity, oropharynx, sub-pharynx/larynx, and nasopharynx, tumors either operable or inoperable, age >18 years, exclusively received IMRT. Criteria for exclusion were re-irradiation treatment.

Each participant completed the questionnaires three times, once at the first visit to the clinic, right after the treatment ended, and finally at a 3-month follow-up. The questionnaires were answered by each individual alone in a private clinic room, with the help and presence of a trained research assistant, if needed. All participants were capable of understanding the procedures and signed informed consent. The aforementioned study was conducted according to the Declaration of Helsinki Principles and to the guidelines for Good Clinical Practice, while it has been approved by The Hospital's Ethics Committee.

European Organization for the Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ)-C30 is an integrated, modular approach for evaluating the generic aspects of QOL of cancer patients participating in clinical trials. It is designed to measure physical, psychological, and social functions. It is composed of both multi-item scales (physical, role, social, emotional, and cognitive functioning) and nine single items (pain, fatigue, financial impact, appetite loss, nausea/vomiting, diarrhea, constipation, sleep disturbance, and QOL). In the present study, the Greek version of the instrument was used.[22]

EORTC QLQ-H and N 35 is a site-specific module of the core questionnaire EORTC QLQ-C30 designed for disorders, most likely seen in HNC patients, which considerably reduce their QOL. It consists of 7 multi-item scales, measuring pain in the mouth, problems with swallowing, senses, speech, social eating and social contact, and 11 single-item scales, assessing problems with teeth, mouth opening, dry mouth, sticky saliva, coughing, feeling ill, as well as use of analgesics, nutritional supplements, feeding tube, and finally, weight gain and weight loss.[23] The questionnaire has been translated and validated in the Greek population.[24]

Hospital Anxiety and Depression Scales (HADS) is a well-established self-assessment mood scale questionnaire widely used to identify caseness (possible and probable) of anxiety disorders and depression among patients in nonpsychiatric hospital clinics. It is divided into two subscales with seven items relating to anxiety and seven items relating to depression.[25] Each item uses a four-point Likert scale (ranging from 0 to 3) and the responses are summed. Higher scores indicate the likelihood of anxiety or depressive symptoms. A score of ≤7 indicates a noncase, a score of 8–10 indicates a doubtful case, and a score of ≥11 indicates a definite case.[26] It has also been translated and validated in the Greek population (G-HADS) of cancer patients.[27]

Basic descriptive statistics were computed for sociodemographic variables, means, standard deviations, and ranges for all scale variables measured in the study. For the examination of the normal distribution of the data, Kolmogorov–Smirnov test and the normal probability plot have been used. Basic descriptive statistics, like mean with standard deviation, and percentage were then computed. T-test for independent samples, Chi-square or Fisher's exact tests was then used for quantitative and categorical sociodemographic characteristics. ANOVA analysis was also conducted to determine differences between the three different time intervals and associated measurements. Statistical significance was set at $P < 0.05$ level. To conduct the analysis, the tool used was the statistical software SPSS Statistics for Windows, version 17.00 (SPSS Inc., Chicago, Ill, USA).

Results

Patient characteristics

Patient sociodemographic and clinical characteristics are presented in Table 1. Thirty-nine (65.0%) of the patients were males and 21 (35.0%) females, with the mean age being 61.35 ± 14.37 years. Twenty-one (35.0%) of them had a university degree and forty (66.7%) were married. In the majority of the cases (27 patients – 45.0%), the tumor was located in the oral cavity, followed by the hypopharynx-larynx area (23.0%).

Quality-of-life scales

In the present study, the focus was on functioning scales and global health status of the EORTC QLQ-C30 and the symptoms subscales of EORTC QLQ-H and N 35. For the functioning scales and global health status, high mean scores show a better functioning response. Results, presented in Table 2, show that functioning performance of patients undergoing IMRT treatment follows the same pattern. The score at the end of the treatment interval is significantly worse compared to base score, and both differ with the 3-month interval which produced the best values. Accordingly, the pattern is almost the same in the 14 symptoms scales [Table 3], of EORTC QLQ-H and N 35 (for symptoms scales, high mean scores indicate worst symptoms response). Patient's scores at first measurement worsen ($P < 0.001$) at the end of the treatment and tend to revert to pretreatment levels after the 3 months interval. The majority (7/14) of symptom scores is somewhat above baseline, one is at baseline levels, while six symptoms (social eating and contact, teeth, stick saliva, coughing, and felt ill) have scores below the baseline. The coughing parameter, in particular, is the only one almost nonexistent after the 3 months.

Greek-Hospital Anxiety and Depression anxiety and depression in radiotherapy

Patient's anxiety levels rise at the end of treatment and revert to pretreatment levels at the 3 months interval [Table 4]. The trend is the same for depression [Table 4]. All pair comparisons are significant between time intervals. Depression seems to be affected more severely not only in terms of the mean score at the end of treatment and after the 3-month period but also as a percentage of participants scoring above the 7 threshold at the end of treatment and above 11 (definite cases) at the 3-month reevaluation [Table 5].

Table 1: Sociodemographic and clinical characteristics of the participants

	Total, *n* (%)
Sex	
Male	39 (65.0)
Female	21 (35.0)
Education	
Elementary or high school	39 (65.0)
University	21 (35.0)
Marital status	
Married	40 (66.7)
Single	20 (33.3)
Location	
Oral cavity	27 (45.0)
Oropharynx	6 (10.0)
Hyporharynx - larynx	23 (38.3)
Nasopharynx	4 (6.7)
M-stage	
0	60 (100.0)
T-stage	
1	7 (11.7)
2	23 (38.3)
3	24 (40.0)
4	6 (10.0)
N-stage	
0-1	44 (74.6)
2-3-x	15 (25.4)
Radiotherapy	
Baseline	60 (100.0)
End of treatment	55 (91.7)
Three months follow-up	55 (91.7)
Age, mean±SD	61.35±14.37

SD: Standard deviation

Discussion

Results show an overall decrease in HRQOL at the end of treatment, but after the 3-month period HRQOL tends to revert to its pretreatment values. All the functioning scales and global health follow the same pattern. They deteriorate at the end of RT, but after a 3-month period their values are even better than those originally measured. The fluctuation of role functioning scale was the most intense since its value dropped to half at the end of RT treatment. A similar observation was made from Loorents *et al*.,[13] while examining HRQOL after RT in HNC patients. They noted that the largest decrease was reported in role and social functioning. They also noted that while there was an improvement after a 3-month period, baseline levels were reached at 12 months.[13] Hammerlid *et al*.,[28] that had their baseline at the time of diagnosis, also found that role functioning had the largest deterioration after 3 months. They also noted that after a year since diagnosis, not all values had reached baseline values, something that was recorded at the 3-year follow-up.[28]

The impairment of neurocognitive function due to radiation doses delivered to the central nervous system by RT is a long recognized and potentially debilitating sequel to brain irradiation.[18] IMRT, in particular, has given rise to concerns regarding the possibility of increased late normal tissue toxicity and increased rates of malignancies.[18] At a prospective study in patients with nasopharyngeal carcinoma that evaluated the effects of IMRT on neurocognitive function, results indicated a general lowering of the cognitive functioning scores after RT and that the radiation dose to the temporal lobes was positively correlated with the grade of the cognitive decline.[29] The authors evaluated cognitive function with Cognitive Abilities Screening Instrument 12 months after the initiation

Table 2: Functioning scales and global health of the European Organization for the Research and Treatment of Cancer 130 Quality of Life Questionnaire-C30, at 1st week of intensity-modulated radiotherapy, at the end of intensity-modulated radiotherapy, and at 3-month follow-up

	Mean±SD			*P*
	1st week	End of treatment	12 weeks	
Physical functioning	77.44±22.20	57.67±20.20	80.67±19.97	<0.00119
Role functioning	68.61±33.06	34.44±34.56	74.17±27.86	<0.00112
Emotional functioning	70.28±26.07	54.31±27.42	79.72±21.17	<0.00120
Cognitive	92.78±15.15	78.89±16.77	93.89±14.38	<0.00165
Social functioning	74.44±29.82	58.61±35.19	76.94±20.83	<0.00115
Global health	54.86±29.24	35.56±26.30	69.86±17.02	<0.00147

SD: Standard deviation

Table 3: Symptoms scales of the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire-head and neck 35 at 1st week of Intensity-modulated radiotherapy, at the end of intensity-modulated radiotherapy, and at 3-month follow-up

	Mean±SD			*P*
	1st week	End of treatment	12 weeks	
Pain head and neck	18.33±14.70	65.42±16.65	19.58±11.57	<0.001
Swallowing	8.75±9.63	62.78±28.72	9.72±17.57	<0.001
Senses problems	5.83±12.59	53.89±16.34	13.61±13.20	<0.001
Speech problems	11.48±21.06	61.11±23.37	13.15±23.01	<0.001
Social eating	18.33±19.27	65.83±23.90	13.19±15.21	<0.001
Social contact	17.89±23.08	49.44±29.44	13.89±23.49	<0.001
Teeth	11.67±16.03	16.11±30.37	3.89±10.79	<0.001
Opening mouth	18.89±23.26	60.56±40.94	21.11±23.74	<0.001
Dry mouth	12.22±18.38	78.89±28.76	18.89±24.06	<0.001
Sticky Saliva	13.89±25.52	54.44±26.01	11.67±20.19	<0.001
Coughing	8.89±19.28	26.11±34.77	0.56±4.30	<0.001
Taste alteration	1.00±0.00	2.00±0.00	1.00±0.00	<0.001
Stomatitis	1.32±0.47	2.87±0.34	1.62±0.49	<0.001
Felt Ill	26.11±30.74	60.56±31.59	22.22±25.05	<0.001

SD: Standard deviation

Table 4: Greek-Hospital Anxiety and Depression subscales at 1st week of intensity-modulated radiotherapy, at the end of intensity-modulated radiotherapy and at 3 months follow-up

	Mean±SD			*P*
	1st week	End of treatment	12 weeks	
G-HAD anxiety	6.46±3.31	8.08±4.39	6.36±3.44	<0.00115
G-HAD depression	5.86±3.38	10.17±4.94	6.32±3.94	<0.00120

G-HAD: Greek-Hospital Anxiety and Depression, SD: Standard deviation

of RT. In another study[30] that the Das-Naglieri cognitive assessment system was used for evaluation, no change in cognitive function after IMRT was recorded between the start of treatment and within a week after 6–7 weeks of RT. However, concerns were raised for long-term consequences.

Symptoms examined with questionnaire EORTC QLQ-H and N 35 seemed to be more severe at the end of RT and this is in accordance with other studies.[31] In our study, dry mouth had the largest mean score at the end of RT (78.89). Xerostomia-related symptoms were usually cited as the most prevalent complications in HNC survivors postRT, but since IMRT became the standard RT modality for HNC patients, oral-related symptoms seem to have been reduced.[32]

Besides physical symptoms, psychological symptoms including depression, irritability, loss of self-esteem, and social symptoms, including relationship disorders, work issues, and sense of uselessness, result negatively in daily life.[19] Anxiety and depression as consequences of RT are two core variables studied in the current paper. Anxiety but especially depression scores significantly increased when measured at the end of treatment and decreased at the 3-month reevaluation. The effect on depression was more profound and its score did not return to the initial baseline values, as opposed to anxiety levels that, at the end of the 12 weeks, were similar to pretreatment levels. Percentages of participants who presented mild-to-severe depression in the post-RT setting were also higher compared with anxiety scores, respectively, and in other studies,[30,33] but it has been recorded that in the long-term anxiety scores

Table 5: Percentage of participants scoring <7 (no case), 8-10 (doubtful case) and ≥11 (definite case) at Greek-Hospital Anxiety and Depression subscales at the 1st week of intensity-modulated radiotherapy, at the end of intensity-modulated radiotherapy and at 3-month follow-up

Score	Mean±SD		
	1st week (%)	End of treatment (%)	12 weeks (%)
G-HAD anxiety			
<7	76.62	38.21	76.62
8-10	13.36	40.08	11.69
≥11	10.02	21.71	11.69
G-HAD depression			
<7	71.61	33.20	74.95
8-10	15.03	13.36	3.34
≥11	13.36	53.44	21.71

G-HAD: Greek-Hospital Anxiety and Depression, SD: Standard deviation

are higher compared to depression.[33] This is in accordance with Givens *et al*.,[34] who assessed among others HRQOL parameters associated with concurrent chemoradiation therapy in patients with HNC. Symptoms of depression were measured using the Beck Depression Inventory. At the last available follow-up visit (as many as 8 years after diagnosis) although patients' mental health was found to be poorer than that of the general population, only 4.4% of the patients' sample was experiencing moderate or severe depression.[34]

Conclusions

All studied parameters (functioning scales, symptoms scales, and G-HAD subscales) worsen from the start to the end treatment and tend to revert to their pretreatment values after a 3-month period. Health-related QOL aspects, psychological difficulties, and HNC patients' concerns should be recorded regularly during and after the treatment. Multidisciplinary teams can then evaluate each individual patient needs and decide on specific ways of support and intervention.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Marur S, D'Souza G, Westra WH, Forastiere AA. HPV-associated head and neck cancer: A virus-related cancer epidemic. Lancet Oncol 2010;11:781-9.
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A, *et al.* Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424.
3. Hashibe M, Brennan P, Chuang SC, Boccia S, Castellsague X, Chen C, *et al.* Interaction between tobacco and alcohol use and the risk of head and neck cancer: Pooled analysis in the international head and neck cancer epidemiology consortium. Cancer Epidemiol Biomarkers Prev 2009;18:541-50.
4. Simard EP, Torre LA, Jemal A. International trends in head and neck cancer incidence rates: Differences by country, sex and anatomic site. Oral Oncol 2014;50:387-403.
5. Rose BS, Jeong JH, Nath SK, Lu SM, Mell LK. Population-based study of competing mortality in head and neck cancer. J Clin Oncol 2011;29:3503-9.
6. Jang-Chun L, Jing-Min H, Yee-Min J, Dai-Wei L, Chang-Ming C, Chun-Shu L, *et al.* Comparisons of quality of life for patients with nasopharyngeal carcinoma after treatment with different RT technologies. Acta Otorhinolaryngol Ital 2014;34:241-6.
7. Sun X, Su S, Chen C, Han F, Zhao C, Xiao W, *et al.* Long-term outcomes of intensity-modulated radiotherapy for 868 patients with nasopharyngeal carcinoma: An analysis of survival and treatment toxicities. Radiother Oncol 2014;110:398-403.
8. Ng WT, Lee MC, Hung WM, Choi CW, Lee KC, Chan OS, *et al.* Clinical outcomes and patterns of failure after intensity-modulated radiotherapy for nasopharyngeal carcinoma. Int J Radiat Oncol Biol Phys 2011;79:420-8.
9. Kerr P, Myers CL, Butler J, Alessa M, Lambert P, Cooke AL. Prospective functional outcomes in sequential population based cohorts of stage III/IV oropharyngeal carcinoma patients treated with 3D conformal vs. intensity modulated radiotherapy. J Otolaryngol Head Neck Surg 2015;44:17.
10. Au KH, Ngan RK, Ng AW, Poon DM, Ng WT, Yuen KT, *et al.* Treatment outcomes of nasopharyngeal carcinoma in modern era after intensity modulated radiotherapy (IMRT) in Hong Kong: A report of 3328 patients (HKNPCSG 1301 study). Oral Oncol 2018;77:16-21.
11. Gomez-Millan J, Fernández JR, Medina Carmona JA. Current status of IMRT in head and neck cancer. Rep Pract Oncol Radiother 2013;18:371-5.
12. Badr H, Gupta V, Sikora A, Posner M. Psychological distress in patients and caregivers over the course of radiotherapy for head and neck cancer. Oral Oncol 2014;50:1005-11.
13. Loorents V, Rosell J, Salgado Willner H, Börjeson S. Health-related quality of life up to 1 year after radiotherapy in patients with head and neck cancer (HNC). Springerplus 2016;5:669.
14. Memtsa PT, Tolia M, Tzitzikas I, Bizakis J, Pistevou-Gombaki K, Charalambidou M, *et al.* Assessment of xerostomia and its impact on quality of life in head and neck cancer patients undergoing radiation therapy. Mol Clin Oncol 2017;6:789-93.
15. Baharvand M, ShoalehSaadi N, Barakian R, Moghaddam EJ. Taste alteration and impact on quality of life after head and neck radiotherapy. J Oral Pathol Med 2013;42:106-12.
16. Haisfield-Wolfe ME, McGuire DB, Soeken K, Geiger-Brown J, De Forge BR. Prevalence and correlates of depression among patients with head and neck cancer: A systematic review of implications for research. Oncol Nurs Forum 2009;36:E107-25.
17. Kanatas A, Ghazali N, Lowe D, Rogers SN. The identification of mood and anxiety concerns using the patients concerns inventory following head and neck cancer. Int J Oral Maxillofac Surg 2012;41:429-36.
18. Welsh LC, Dunlop AW, McGovern T, McQuaid D, Dean JA, Gulliford SL, *et al.* Neurocognitive function after (chemo)-radiotherapy for head and neck cancer. Clin Oncol (R Coll Radiol) 2014;26:765-75.
19. Babin E, Sigston E, Hitier M, Dehesdin D, Marie JP, Choussy O.

Quality of life in head and neck cancers patients: Predictive factors, functional and psychosocial outcome. Eur Arch Otorhinolaryngol 2008;265:265-70.
20. Murphy BA, Ridner S, Wells N, Dietrich M. Quality of life research in head and neck cancer: A review of the current state of the science. Crit Rev Oncol Hematol 2007;62:251-67.
21. Megari K. Quality of life in chronic disease patients. Health Psychol Res 2013;1:e27.
22. Kyriaki M, Eleni T, Efi P, Ourania K, Vassilios S, Lambros V, *et al.* The EORTC core quality of life questionnaire (QLQ-C30, version 3.0) in terminally ill cancer patients under palliative care: Validity and reliability in a Hellenic sample. Int J Cancer 2001;94:135-9.
23. Singer S, Arraras JI, Chie WC, Fisher SE, Galalae R, Hammerlid E, *et al.* Performance of the EORTC questionnaire for the assessment of quality of life in head and neck cancer patients EORTC QLQ-H and amp; N35: A methodological review. Qual Life Res 2013;22:1927-41.
24. Nalbadian M, Nikolaidis V, Nikolaou A, Themelis C, Kouloulas A, Vital V. Psychometric properties of the EORTC head and neck-specific quality of life questionnaire in disease-free Greek patients with cancer of pharynx and larynx. Qual Life Res 2010;19:761-8.
25. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the hospital anxiety and depression scale. An updated literature review. J Psychosom Res 2002;52:69-77.
26. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67:361-70.
27. Mystakidou K, Tsilika E, Parpa E, Katsouda E, Galanos A, Vlahos L. The hospital anxiety and depression scale in Greek cancer patients: Psychometric analyses and applicability. Support Care Cancer 2004;12:821-5.
28. Hammerlid E, Silander E, Hörnestam L, Sullivan M. Health-related quality of life three years after diagnosis of head and neck cancer – A longitudinal study. Head Neck 2001;23:113-25.
29. Hsiao KY, Yeh SA, Chang CC, Tsai PC, Wu JM, Gau JS, *et al.* Cognitive function before and after intensity-modulated radiation therapy in patients with nasopharyngeal carcinoma: A prospective study. Int J Radiat Oncol Biol Phys 2010;77:722-6.
30. Mo YL, Li L, Qin L, Zhu XD, Qu S, Liang X, *et al.* Cognitive function, mood, and sleep quality in patients treated with intensity-modulated radiation therapy for nasopharyngeal cancer: A prospective study. Psychooncology 2014;23:1185-91.
31. Melo Filho MR, Rocha BA, Pires MB, Fonseca ES, Freitas EM, Martelli Junior H, *et al.* Quality of life of patients with head and neck cancer. Braz J Otorhinolaryngol 2013;79:82-8.
32. Wan Leung S, Lee TF, Chien CY, Chao PJ, Tsai WL, Fang FM. Health-related quality of life in 640 head and neck cancer survivors after radiotherapy using EORTC QLQ-C30 and QLQ-H and N35 questionnaires. BMC Cancer 2011;11:128.
33. Neilson K, Pollard A, Boonzaier A, Corry J, Castle D, Smith D, *et al.* A longitudinal study of distress (depression and anxiety) up to 18 months after radiotherapy for head and neck cancer. Psychooncology 2013;22:1843-8.
34. Givens DJ, Karnell LH, Gupta AK, Clamon GH, Pagedar NA, Chang KE, *et al.* Adverse events associated with concurrent chemoradiation therapy in patients with head and neck cancer. Arch Otolaryngol Head Neck Surg 2009;135:1209-17.