Clinical Investigation

Emotional Quality of Life After Radiation Therapy for Oropharyngeal Carcinoma

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Abstract

Purpose: Substantial research exists on the physical toxicities from radiation therapy (RT) for oropharyngeal cancers, but emotional quality of life is understudied. The purpose of this study is to map the effects and time course of radiation-related changes in mood and anxiety and to investigate the physical factors that drive these changes.

Methods and materials: We prospectively collected University of Washington Quality of Life questionnaires and identified patients with oropharyngeal cancer who were treated with curative-intent RT between 2013 and 2016 and had completed questionnaires within 12 months after RT (n = 69). We analyzed swallow, saliva, taste, chewing, speech, pain, mood, and anxiety scores, using a scale from 0 to 100. We conducted a multivariate regression analysis to identify physical functioning predictors of worse emotional scores.

Results: Physical functioning scores declined from before RT to 3 months after RT and then began improving but did not rebound to baseline levels within 12 months. Patient mood slightly declined, but anxiety improved immediately after RT, with both generally improving such that scores were higher at the 12-month follow-up than at initial consult. Analysis showed that longer duration of treatment is associated with a higher likelihood of worse mood scores at 12 months (odds ratio [OR], 1.446; P < .01). Worse swallow score is associated with a greater likelihood of worse mood score at 3 months (OR, 0.971; P < .01) and 12 months (OR, 0.975; P < .01). A worse taste score is associated with a greater likelihood of worse anxiety score at 3 months (OR, 0.979; P < .05) and 12 months (OR, 0.982; P < .05).

Conclusions: Emotional changes are associated with certain treatment-associated toxicities. A patient’s emotional health is complex and likely multifactorial in nature. Our study identified key associations and time points to potentially intervene upon.

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Introduction

Head and neck cancers (HNCs) represent the sixth most common malignancy worldwide, with the oropharynx being the most commonly affected site.1,2 Several treatment modalities exist for the treatment of oropharyngeal carcinoma (OPC),3 and the majority of patients will require multimodal therapy including radiation therapy (RT).4 Secondary to the functional anatomy of the head and neck, there is significant treatment-related morbidity, including mucositis, xerostomia, dysphagia, dysgeusia, odynophagia, and depression. These toxicities follow different trajectories, occurring and evolving variably over the first year after RT.5 Despite the widespread acknowledgment that HNC treatment is associated with significant functional impairment and toxicity,6 the impact of toxicity and disease status on health-related quality of life (HRQoL) and functional status remains poorly studied.

Xerostomia and dysphagia have emerged as important determinants of HRQoL in HNC survivors.6 Newer techniques such as intensity modulated RT have shown improvements in HRQoL (specifically xerostomia and dysphagia) because these techniques allow for protection of the anatomic structures that are necessary for saliva production and swallowing.8,9 Although these newer techniques have helped ameliorate the severity of toxic effects, eating remains a problem exacerbated by chronic dysgeusia.10,11 Not only does dysgeusia adversely affect nutritional status, it also directly influences patient mood and mitigates feelings of pleasure. Palatable food stimulates dopamine release in the brain, producing the feeling of pleasure.12 Therefore, processes that negatively affect taste, such as saliva production, swallowing, and difficulties chewing, may also adversely affect psychosocial functioning.

In fact, psychological distress after diagnosis and treatment of HNC is common but underdiagnosed.13 Within the first 3 months after diagnosis, major depressive disorder is identified in up to half of patients with HNC.14-17 After RT, the prevalence of major depressive disorder decreases to 8% to 44% depending on the time point.18-20 Chen et al identified the proportions of patients who reported mild or severe depression as 17%, 15%, and 13% at 1, 3, and 5 years after treatment.21 In contrast, anxiety levels are the highest before treatment, decline immediately after treatment, and return to pretreatment levels 1 year after completion of RT.22 Mood reflects the present emotional state, whereas anxiety is future-oriented and associated with the anticipation of imminent danger.23 Psychological distress associated with HNC does not always meet the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition, criteria for a psychiatric diagnosis. Therefore, recognizing subclinical deviations in mood and anxiety is important and exploring the time course of toxicities after RT is crucial in identifying the critical time point for intervention to mitigate the aforementioned physical factors that drive changes in mood and anxiety. An adequate and timely intervention can improve HRQoL.

This study aimed to investigate the trajectory of emotional impairment from treatment-related toxicity among patients who underwent RT for OPC. We tested the hypothesis that emotional quality of life (eQoL) as measured by mood and anxiety would decrease with a decline in physical function, specifically changes in swallowing and saliva. Importantly, we elucidated the physical predictors of worse psychosocial health in patients with OPC treated with RT to understand when medical or supportive intervention might be the most effective.

Methods and Materials

This study was a retrospective examination of previously collected survey and medical record data and was approved by our institutional review board.

Study population

We identified 69 patients who were treated for OPC with curative-intent RT between 2013 and 2016 and had follow-up up to 3 years. These patients had completed the University of Washington Quality of Life (UW-QoL) questionnaires prospectively at the time of the initial consultation. More specifically, patients completed the questionnaire before treatment and at 3, 6, 9, and 12 months after termination of RT and did not have cancer recurrence at their last follow-up in 2016. For patients who had surgery before starting RT, the initial questionnaire was completed after surgery but before starting RT. Tables 1 and 2 provide demographic and treatment characteristics, respectively, summarized with descriptive statistics. Cancer staging is based on the American Joint Committee on Cancer 7th edition.

Screening instrument

The UW-QoL (version 4) is a previously validated (average criterion validity of 0.849; reliability >0.90) instrument used in patients with HNC and consists of 12 question domains that reflect HRQoL based on patients’ responses.24,25 The questionnaire’s high internal validity reflects each item’s ability to provides a similar quality-of-life measurement, which further allows for internal comparisons.26 The 12 domains include pain, appearance, activity, recreation, swallowing, chewing, speech, shoulder, taste, saliva, mood, and anxiety. The domains
are followed by either 4 or 5 options, ranging from no symptoms to severe symptoms associated with that domain. The response options are scored evenly from 0 to 100, with 0 being the worst level and 100 representing the healthy level of that domain. Scoring is scaled to reflect the number of possible responses and to allow for direct comparisons between the domains. For example, mood can be indicated by 1 of 5 options, with a score of 0 for extremely depressed, 25 for somewhat depressed, 50 for neither in a good mood nor depressed, 75 for generally good, and 100 for mood is excellent. Anxiety is indicated by 1 of 4 responses: 0 for very anxious, 30 for anxious, 70 for a little anxious, and 100 for not anxious.24

Statistical analysis

We chose the physical domains of swallow, taste, saliva, speech, chewing, and pain and the emotional domains of mood and anxiety for the multivariable logistic regression analysis. These physical domains were the most concerning in our patient population. Physical and emotional domains were analyzed separately. Scores at each time point before (0) and after (3, 6, 9, and 12 months) treatment for the 8 domains were averaged across subjects to create a plot of the time course of changes in physical outcomes versus emotional outcomes. A plot of the time course of changes in the rest of the UW-QoL domains was also created; however, these domains could not be included in the regression analysis because of our small sample size. Including these domains would lead to overfitting of the statistical model.

Multivariable logistic regressions were used to determine whether patient/disease characteristics and treatment characteristics were associated with the likelihood of having high levels of anxiety or mood. We subdivided patients with percutaneous endoscopic gastrostomy (PEG) into those who received it prophylactically versus as-needed during or after treatment. We ran Fisher’s exact tests to test for a relationship between reason for PEG placement and mood/anxiety as well to investigate whether there is a difference in mood/anxiety in patients who underwent surgery versus chemoradiation. In addition, we ran a $\chi^2$ test to assess mood/anxiety based on human papillomavirus infection status. Worse levels of anxiety and mood were defined as equaling 1 if very

| Table 1 (continued) |
|---------------------|
| Characteristics (n = 69) | Frequency (%) |
| 3 | 1 (1.4) |
| Metastasized | 2 (2.9) |
| Human papillomavirus positive (any subtype) | 43 (62.3) |

| Table 1  |
|----------|
| Patient and disease characteristics |
| Characteristics (n = 69) | Frequency (%) |
| Age, mean (Standard deviation) | 58 (9.0) |
| Women | 18 (26.1) |
| Race |
| Caucasian | 42 (60.8) |
| African American | 11 (15.9) |
| Hispanic | 4 (5.8) |
| Asian | 2 (2.9) |
| Other | 10 (14.5) |
| Marital status |
| Single | 8 (11.6) |
| Unmarried, in a relationship | 4 (5.8) |
| Married | 40 (60) |
| Divorced | 10 (14.5) |
| Separated | 3 (4.3) |
| Widowed | 4 (5.8) |
| Living situation |
| Alone | 21 (30.4) |
| With partner/wife | 27 (39.1) |
| With family | 21 (30.4) |
| Health insurance |
| Medicaid | 11 (15.9) |
| New York Medicare | 4 (5.8) |
| Other Medicare | 7 (10.1) |
| Private insurance | 41 (59.4) |
| Alcohol use |
| Never | 25 (36.2) |
| Active: social | 31 (44.9) |
| Active: moderate | 14 (20.3) |
| Active: heavy/abuse | 6 (8.7) |
| Former: moderate | 3 (4.3) |
| Former: heavy/abuse | 2 (2.9) |
| Charlson comorbidity index | 3 (2.8) |
| Primary site |
| Tonsil | 17 (24.6) |
| Tongue base | 26 (37.7) |
| Oropharynx/unspecified | 26 (37.7) |
| Stage (American Joint Commission on Cancer, 7th Edition) |
| I | 4 (5.8) |
| II | 7 (10.1) |
| III | 12 (17.4) |
| IVA | 41 (59.4) |
| IVB | 5 (7.2) |
| T stage |
| 0 | 2 (2.8) |
| 1 | 18 (26.1) |
| 2 | 28 (40.6) |
| 3 | 6 (8.7) |
| 4a | 11 (15.9) |
| 4b | 4 (5.8) |
| N stage |
| 0 | 15 (21.7) |
| 1 | 12 (17.4) |
| 2a | 5 (7.2) |
| 2b | 24 (34.8) |
| 2c | 12 (17.4) |
anxious/anxious or extremely depressed/somewhat depressed and 0 if otherwise. Similarly, a longitudinal logistic regression model was used to analyze repeated responses to the UW-QoL questionnaire across time, looking in particular at the association between physical domains (swallow, taste, saliva, speech, chewing, and pain) on mood and anxiety at the 3- and 12-month follow-up posttreatment. This model was fit using the generalized estimating equations methodology, which allows for the specification of within-group correlation structures of the panel. In other words, we assume that the responses of an individual to the questionnaire over time are more correlated than those between different individuals. From the logistic regression, we estimated predicted probabilities and set the levels of confounding variables, such as radiation dosage, frequency of definitive radiation, and frequency of chemotherapy, to the mean values. We then graphed the length of RT and predicted probabilities. Analyses were conducted using Stata, version 15.

**Results**

Table 1 summarizes the patient and disease characteristics, and Table 2 summarizes the treatment characteristics for the 69 patients with OPC who had UW-QoL questionnaires completed for at least 12 months of follow-up. The sample consisted of 51 men and 18 women with a mean age of 58.3 years. Of these patients, 53.6% received RT after surgery, and 46.4% received definitive radiation with a mean radiation dose of 63 Gy and mean treatment duration of 44.7 days. Approximately 16% of patients had stage I/II cancer, 17% had stage III, and 67% had stage IVA/IVB. Of the 51 patients with active alcohol use, 6 reported a severe mood score (>50) and 17 reported a severe anxiety score (>50) before starting radiation treatment (Figs 1 and 2). After 12 months after RT, we have follow-up data for 52% of the patients, of whom 88% returned to baseline or better mood.

At consult (0 months), anxiety was greater (worse) than mood, as evident from an average anxiety score of 63 and a mood score of 75. After RT, mood scores declined slightly, but anxiety scores improved so that at the 3-month follow-up, levels were approximately equal with an anxiety score of 73.3 and a mood score of 74.1. Both domains improved at the same rate over the next 3 months. However, anxiety slightly worsened between 6 and 9 months, whereas mood continued to improve. Thus, at the 12-month follow-up, anxiety remained mildly worse than mood, but both were better than the pretreatment levels (Fig 3).

Physical toxicities followed the opposite trajectory. Swallow, taste, saliva, chewing, and pain scores decreased from pretreatment to 3 months after treatment, but speech remained at baseline levels. All improved at about the same rate over the next 9 months, and swallow, speech, chewing, and pain scores reached pretreatment levels by the end of 12 months (Fig 4). The time course of changes in other physical toxicities related to appearance, activity, recreation, and shoulder followed similar
trajectories, with shoulder remaining at baseline after RT. (Fig. E1; available online at www.redjournal.org; available online at https://doi.org/10.1016/j.adro.2019.05.001).

A multivariate regression analyzed predictors of worse anxiety and mood scores. Table 3 shows that there is no significant association between worse emotional status and patient/disease characteristics within 12 months after termination of treatment. For PEG placement, neither prophylactic nor as-needed placement was found to be significantly associated with worse mood or anxiety after treatment. No significant difference in anxiety or mood was found between patients who received surgery versus chemoradiation ($P = .128$ for anxiety; $P = .070$ for mood). Similarly, the results of $\chi^2$ test indicate that there is no statistically significant relationship between anxiety or mood and human papillomavirus infection status ($P = .089$ for anxiety; $P = .731$ for mood).

When considering treatment characteristics (Table 4), longer duration of treatment is more likely to be associated with worse mood (odds ratio [OR], 1.446; 95% confidence interval [CI], 1.10-1.90; $P < .01$). From the logistic regression, we estimated predicted probabilities and found

![Figure 1](image1.png)  **Figure 1** Alcohol use and frequency of mood score $>50$. This graph illustrates the amount of alcohol use and the number of patients reporting mood score $>50$ at each time point. No mood data corresponds to no follow-up at that specific time point.

![Figure 2](image2.png)  **Figure 2** Alcohol use and frequency of anxiety score $>50$. This graph illustrates the amount of alcohol use and the number of patients reporting anxiety score $>50$ at each time point. No anxiety data corresponds to no follow-up at that specific time point.
that an individual with mean levels of definitive radiation, mean levels of radiation dosage, and mean levels of chemotherapy had worse mood if treatment lasted >50 days (Fig. E2; available online at www.redjournal.org; available online at https://doi.org/10.1016/j.adro.2019.05.001). With regard to physical functioning and anxiety (Table E1; available online at www.redjournal.org; available online at https://doi.org/10.1016/j.adro.2019.05.001), a decline in taste scores was associated with worse anxiety scores at 3 months (OR, 0.979; 95% CI, 0.96-1.00; P < .05) and at 12 months (OR, 0.982; 95% CI, 0.97-1.00; P < .05). Worse saliva score was associated with being slightly less likely to have worse anxiety scores at 12 months (OR, 1.023; 95% CI, 1.01-1.04; P < .05).

With regard to physical functioning and mood (Table E2; available online at www.redjournal.org; available online at https://doi.org/10.1016/j.adro.2019.05.001), a decline in taste scores was associated with worse anxiety scores at 3 months (OR, 0.979; 95% CI, 0.96-1.00; P < .05) and at 12 months (OR, 0.982; 95% CI, 0.97-1.00; P < .05). Worse saliva score was associated with being slightly less likely to have worse anxiety scores at 12 months (OR, 1.023; 95% CI, 1.01-1.04; P < .05).

Figure 3  Changes in mood and anxiety after radiation therapy in patients with oropharyngeal carcinoma. This figure illustrates changes in University of Washington—Quality of Life scores for mood and anxiety after radiation treatment in patients.

Figure 4  Changes in physical functioning after radiation therapy in patients with oropharyngeal carcinoma. This figure illustrates changes in University of Washington—Quality of Life scores for swallowing, saliva, taste, pain, chewing, and speech after radiation treatment in patients.
Table 3  Baseline predictors of worse emotional status (patient/disease characteristics)

| Variable                             | Worse anxiety | Worse mood |
|--------------------------------------|---------------|------------|
| Alcohol - heavy/abuse                | 1.335         | 2.923      |
| (0.25-7.23)                          | (0.55-15.44)  |            |
| Percutaneous endoscopic gastrostomy status | 1.150         | 2.080      |
| (0.32-4.19)                          | (0.47-9.12)   |            |
| Stage IV                             | 1.755         | 0.710      |
| (0.09-32.81)                         | (0.04-14.19)  |            |
| T classification: 3 or 4             | 0.736         | 1.454      |
| (0.15-3.55)                          | (0.26-8.15)   |            |
| N classification: 2 or 3             | 1.104         | 0.608      |
| (0.08-15.28)                         | (0.04-9.52)   |            |
| Observations                         | 62            | 62         |

Data are exponentiated coefficients; 95% confidence intervals in parentheses

https://doi.org/10.1016/j.adro.2019.05.001), a decline in swallow scores was associated with being more likely to have worse mood scores at 3 months (OR, 0.971; 95% CI, 0.95-0.99; \( P < .01 \)) and 12 months (OR, 0.975; 95% CI, 0.96-0.99; \( P < .01 \)).

Discussion

Using the validated UW-QoL questionnaire and robust follow-up data, we conducted a retrospective multivariate study to identify predictors of poor mood and increased anxiety after RT in patients with OPC. This study not only identified the physical factors associated with a decline in psychosocial functioning but also mapped out the time course of these factors for up to 1 year to understand how emotional function changes in response to a decline or improvement in physical function. Thus, this study provides a broadly applicable understanding of the interrelationship between the physical and emotional domains of the UW-QoL.

Overall, emotional quality of life improved despite a decline in physical function.\(^{28}\) Compared with pretreatment levels, anxiety levels improved within 3 months and remained lower for subsequent time points after treatment. In contrast, mood initially declined by a few points after treatment and then slowly improved after 3 months. Among the physical toxicity domains, shoulder and speech were the only 2 that remained at baseline levels immediately after RT, perhaps because these domains are less reflective of radiation toxicity and more related to surgical outcomes. Among the patient and treatment characteristics studied, longer treatment duration (specifically treatments >50 days) was significantly associated with worse mood but not anxiety scores after RT. Other variables did not yield a significant association with worse mood or anxiety.

A study of 67 Chinese patients treated with primary RT for stage I or II nasopharyngeal cancer used the Beck Anxiety Inventory, Beck Depression Inventory, Rotterdam Symptom Checklist, Perceived Stress Scale, and 36-item Short-Form Health Survey and showed that the period from before to 2 months after RT is the most vulnerable to physical and emotional decline. Recovery of emotional functions was evident by the end of the first year after RT despite lower physical symptom scores.\(^{29}\) To our knowledge, the current study is the first to present similar findings in patients with OPC who were treated with RT for different stages of disease.

This study further provides a clear time line of the physical and subclinical eQoL after RT for patients with OPC. Most importantly, we identified dysphagia and taste as the primary factors associated with worse psychosocial functioning. Mood is primarily affected by dysphagia such that only poor swallowing function at 3 months after RT is associated with worse mood; this association remains significant 12 months after treatment. A study of patients with HNC found recovery in swallowing and related functions to be coupled with recovery in psychosocial functioning, albeit at a slower rate than improvement in eQoL.\(^{30}\) Another prospective study of 101 patients with HNC showed elevated prevalence of clinical depression 3 months after radiation but lower prevalence at 18-month follow-up in association with changes in physical symptoms, which included xerostomia and dysphagia.\(^{22}\) However, these studies investigated quality of life in patients with HNC, not specifically OPC, and the latter considered only depression reaching clinical threshold in its analysis. Our study adds to the OPC literature by showing toxicities that predict subthreshold mood decline in specific patients.

With regard to increased anxiety, taste is found to be the primary associated physical factor. Worse taste at 3 and 12 months after RT is associated with increased

Table 4  Baseline predictors of worse emotional status (treatment characteristics)

| Variable            | Worse anxiety | Worse mood |
|---------------------|---------------|------------|
| Definitive radiation| 4.288         | 2.030      |
| (0.80-23.09)        | (0.40-10.19)  |            |
| Any chemotherapy    | 0.485         | 0.925      |
| (0.11-2.18)         | (0.21-3.99)   |            |
| Dosage (cGy)        | 0.999         | 0.998      |
| (1.00-1.00)         | (1.00-1.00)   |            |
| Elapsed days        | 1.065         | 1.446*     |
| (0.88-1.29)         | (1.10-1.90)   |            |
| Observations        | 68            | 68         |

Data are exponentiated coefficients; 95% confidence intervals in parentheses

\(^*\) \( P < .01 \)
anxiety. Taste impairment is found to have significant effect on patients’ quality of life because it is associated with a decrease in appetite and weight loss.\textsuperscript{31} Improvement in taste is noted 3 weeks after completion of RT, but a full recovery of taste function does not always occur.\textsuperscript{31} We add to this literature by elucidating the impact of taste impairment on eQoL. Our results suggest that recovery in taste primarily improves anxiety but has no effect on mood. Interestingly, improvement in anxiety is also slightly associated with a decline in salivary production. This finding is not consistent with literature; some studies of patients with HNC show no significant change in anxiety over time.\textsuperscript{18,32,33} Further studies are warranted to understand our finding because no previous study has tracked the time course of subclinical anxiety after RT in patients with OPC.

Although there is substantial research on HRQoL during and after RT in patients with HNC, few studies have assessed the trajectories of physical and emotional symptoms, specifically in patients with OPC. Using the European Organization for Research and Treatment of Cancer Quality of Life questionnaires and Hospital Anxiety and Depression Scale, Moubayed et al identified factors related to patient and disease characteristics, such as smoking, alcohol use, T stage, and medication use, that are predictors of long-term depression and quality of life after RT.\textsuperscript{34} Our study does not corroborate these findings, but it adds to the limited literature on eQoL in patients with OPC by identifying physical symptom predictors of worse mood and increased anxiety levels within 12 months after treatment to allow clinicians to identify specific time points of intervention to address physical toxicities and thereby improve eQoL. This study is among the first to differentiate physical predictors of emotional changes within patients with OPC after RT and analyze their trajectories. With these findings, clinicians can be better prepared to encourage patients, specifically those undergoing longer treatments, to use mental health and social services at appropriate times after treatment.

A number of limitations of this study should be noted. Foremost, we are drawing conclusions based on responses to a single question that assesses a particular quality of life domain. This is an important limitation, but we want to highlight that the UW-QoL is a validated instrument that has been widely used in HNC research. More importantly, particular domains of the UW-QoL have been correlated with similar metrics on other questionnaires.\textsuperscript{35,36}

Second, we lack objective evaluation, such as video-fluoroscopy, to evaluate swallowing function and instruments to assess other physical and emotional factors. Of note, physical factors are not necessarily mutually exclusive because changes in saliva and taste affect swallowing. Moreover, our study is focused on a relatively small sample of relatively heterogeneous patients with OPC. More than half of these patients had pre-RT surgery, which makes it difficult to separate radiation-related effects and complications, such as PEG placement, from surgical effects. The higher rate of PEG in our study is an institution-specific finding, which makes results difficult to generalize. In addition, the finding of a correlation between longer treatment and worse mood needs to be corroborated with further studies because no other patient and treatment characteristics yielded significant associations.

The current study highlights the complex nature of emotional health in patients undergoing cancer treatment. Although we identify associations between physical domains and eQoL, patients’ ultimate emotional health is driven by a number of factors. We aim to incorporate these findings into the development of a new questionnaire that can better assess these factors and provide a more nuanced understanding of the complex emotional changes within patients with OPC.

Additionally, future studies in this area are necessary to investigate the time course of symptoms for longer follow-up to account for the heterogeneity of treatment characteristics. These studies should also incorporate objective measurements of functional outcomes. Further studies are also needed to understand the effectiveness of specific interventions, such as supportive oncology care, pharmacologic therapeutics, and mindfulness and relaxation therapies, on mood and anxiety levels, specifically whether interventions are effective in preventing decline or accelerating the recovery of eQoL.

Conclusions

The present study shows improvement in mood and anxiety up to 12 months after RT despite worse physical outcomes. A decline in mood is found to be associated with dysphagia, with a greater likelihood of worse mood in patients undergoing treatments that last $\geq 50$ days. Improvement in anxiety, on the other hand, is found to be associated with improving taste function. Patients’ emotional health is likely to be the result of complex interactions between treatment toxicity, recovery, and emotion domains. These results further our understanding of patients with OPC who are at risk for mood and anxiety decline and identify key time points of intervention.

Supplementary data

Supplementary material for this article can be found at https://doi.org/10.1016/j.adro.2019.05.001.
References

1. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin.* 2005;55:74-108.
2. Pettig EM, D’Souza G. Epidemiology of head and neck cancer. *Surg Oncol Clin N Am.* 2015;24:379-396.
3. Roets E, Tukanova K, Govarts A, Specenier P. Quality of life in oropharyngeal cancer: A structured review of the literature. *Support Care Cancer.* 2018;26:2511-2518.
4. Arigis A, Eng C. Epidemiology, staging, and screening of head and neck cancer. *Cancer Treat Res.* 2011;145:15-60.
5. Murphy BA, Gilbert J. Dysphagia in head and neck cancer patients treated with radiation: Assessment, sequelae, and rehabilitation. *Semin Radiat Oncol.* 2009;19:35-42.
6. Murphy BA. Advances in quality of life and symptom management for head and neck cancer patients. *Curr Opin Oncol.* 2009;21:242-247.
7. Terrell JE, Ronis DL, Fowler KE, et al. Clinical predictors of quality of life in patients with head and neck cancer. *Arch Otolaryngol Head Neck Surg.* 2004;130:401-408.
8. Vainshtein JM, Moon DH, Feng FY, Chepeha DB, Eisbruch A, Stenmark MH. Long-term quality of life after swallowing and salivary-sparing chemosensory modulation radiation therapy in survivors of human papillomavirus-related oropharyngeal cancer. *Int J Radiat Oncol Biol Phys.* 2015;91:925-933.
9. Nutting CM, Morden JP, Harrington KJ, et al. Parotid-sparing intensity-modulated radiation therapy in head and neck cancer (PARSPORT): A phase 3 multicentre randomised controlled trial. *Lancet Oncol.* 2011;12:127-136.
10. Airoldi M, Garzano M, Raimondo L, et al. Functional and psychological evaluation after flap reconstruction plus radiotherapy in oral cancer. *Head Neck.* 2011;33:458-468.
11. O'Neill M, Henry DE, Flickinger JC, Smith R, Ferris RL, Gibson M. Posttreatment quality-of-life assessment in patients with head and neck cancer treated with intensity-modulated radiation therapy. *Am J Clin Oncol.* 2011;34:478-482.
12. Breslin PA, Spector AC. Mammalian taste perception. *Curr Biol.* 2008;18:R148-R155.
13. Lydiatt WM, Bessette D, Schmid KK, Sayles H, Burke WJ. Prevention of depression with escitalopram in patients undergoing treatment for head and neck cancer: Randomized, double-blind, placebo-controlled clinical trial. *JAMA Otolaryngol Head Neck Surg.* 2013;139:678-686.
14. Hammerlid E, Ahlner-Elmqvist M, Bjordal K, et al. A prospective multicentre study in Sweden and Norway of mental distress and psychiatric morbidity in head and neck cancer patients. *Br J Cancer.* 1999;80:766-774.
15. Hammerlid E, Mercke C, Sullivan M, Westin T. A prospective quality of life study of patients with oral or pharyngeal carcinoma treated with external beam irradiation with or without brachytherapy. *Oral Oncol.* 1997;33:189-196.
16. Hammerlid E, Silander E, Hornestam L, Sullivan M. Health-related quality of life three years after diagnosis of head and neck cancer: A longitudinal study. *Head Neck.* 2001;23:113-125.
17. Paula JM, Sononbe HM, Nicolussi AC, Zago MM, Sawada NO. Symptoms of depression in patients with cancer of the head and neck undergoing radiotherapy treatment: A prospective study. *Rev Lat Am Enfermagem.* 2012;20:362-368.
18. Kohda R, Otsubo T, Kuwakado Y, et al. Prospective studies on mental status and quality of life in patients with head and neck cancer treated by radiation. *Psychooncology.* 2005;14:331-336.
19. de Leeuw JR, de Graeff A, Ros WJ, Blijham GH, Hordijk GJ, Winnubst JA. Prediction of depression 6 months to 3 years after treatment of head and neck cancer. *Head Neck.* 2001;23:892-898.
20. Karnell LH, Funk GF, Christensen AJ, Rosenthal EL, Magnuson JS. Persistent posttreatment depressive symptoms in patients with head and neck cancer. *Head Neck.* 2006;28:453-461.
21. Chen AM, Daly ME, Vazquez E, et al. Depression among long-term survivors of head and neck cancer treated with radiation therapy. *JAMA Otolaryngol Head Neck Surg.* 2013;139:885-889.
22. Neilson K, Pollard A, Boonzaaier A, et al. A longitudinal study of distress (depression and anxiety) up to 18 months after radiotherapy for head and neck cancer. *Psychooncology.* 2013;22:1843-1848.
23. Cosci F, Fava GA, Sonino N. Mood and anxiety disorders as early manifestations of medical illness: A systematic review. *Psychother Psychosom.* 2015;84:22-29.
24. Lowe D, Rogers S. University of Washington quality of life questionnaire (UW-QOL v4) Guidance for scoring and presentation. Available at: http://www.hancsupport.com/sites/default/files/assets/ UW-QOL-update_2012.pdf. Accessed August 1, 2018.
25. Hassan SJ, Weymuller EA Jr. Assessment of quality of life in head and neck cancer patients. *Head Neck.* 1993;15:485-496.
26. Weymuller EA Jr, Alsarrar R, Yveh B, Deleyiannis FWB, Coltrera M. Analysis of the performance characteristics of the University of Washington quality of life instrument and its modification (UW-QOL-R). *Arch Otolaryngol Head Neck Surg.* 2001;127:489-493.
27. Wang M, Kong L, Li Z, Zhang L. Covariance estimators for generalized estimating equations (GEE) in longitudinal analysis with small samples. *Stat Med.* 2016;35:1706-1721.
28. Amurd RJ, Chera BS. Misuse of quality of life evaluation in oncology studies: Reification, adaptation, and the U-shaped curve [e-pub ahead of print]. *Pract Radiat Oncol.* doi: 10.1016j.prro.2018.05.002. Accessed January 1, 2019.
29. Lee PW, Kwan TT, Kwong DL, et al. A prospective study of the impact of nasopharyngeal cancer and radiotherapy on the psycho-social condition of Chinese patients. *Cancer.* 2007;109:1344-1354.
30. Roe JW, Drinnan MJ, Carding PN, Harrington KJ, Nutting CM. Patient-reported outcomes following parotid-sparing intensity-modulated radiotherapy for head and neck cancer. How important is dysphagia? *Oral Oncol.* 2014;50:1182-1187.
31. Deshpande TS, Blanchard P, Wang L, Foote RL, Zhang X, Frank SJ. Radiation-related alterations of taste function in patients with head and neck cancer: A systematic review. *Curr Treat Options Oncol.* 2018;19:72.
32. Kelly C, Paleri V, Downs C, Shah R. Deterioration in quality of life and depressive symptoms during radiation therapy for head and neck cancer. *Otolaryngol Head Neck Surg.* 2007;136:108-111.
33. Rose P, Yates P. Quality of life experienced by patients receiving radiation treatment for cancers of the head and neck. *Cancer Nurs.* 2001;24:255-263.
34. Moubayed SP, Sampalis JS, Ayad T, et al. Predicting depression and quality of life among long-term head and neck cancer survivors. *Otolaryngol Head Neck Surg.* 2015;152:91-97.
35. Katre C, Johnson IA, Humphris GM, Lowe D, Rogers SN. Assessment of problems with appearance, following surgery for oral and oro-pharyngeal cancer using the University of Washington appearance domain and the Derriford appearance scale. *Oral Oncol.* 2008;44:927-934.
36. Rogers SN, Gwanne S, Lowe D, Humphris G, Yueh B, Weymuller EA Jr. The addition of mood and anxiety domains to the University of Washington quality of life scale. *Head Neck.* 2002;24:521-529.