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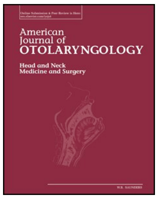

Comparison of psychosocial factors over time among HPV+ oropharyngeal cancer and tobacco-related oral cavity cancer patients[☆,☆☆]

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ABSTRACT

Introduction: The role of human papilloma virus (HPV) in the pathogenesis of *oropharyngeal* squamous cell carcinoma (OPSCC) is well documented, as is the excellent prognosis of patients with HPV-associated disease; in contrast, *oral cavity* squamous cell carcinoma (OCSCC) is associated with tobacco and alcohol use and has a worse prognosis. While causative factors, staging, and treatment guidelines differ between these cancer subsets, few studies have compared psychosocial factors in these groups.

Objective: To explore differences in psychosocial factors between HPV+ OPSCC patients versus OCSCC smokers.

Methods: A prospective cohort study at a single multidisciplinary, tertiary care HNC center was completed with recruitment from 2010 to 2013 using self-administered questionnaires before treatment and at 12 months. Patients were included with a diagnosis of HPV+ OPSCC or OCSCC with a smoking history. 38 (21 HPV+ OPSCC/17 OCSCC) met criteria. The main outcomes included self-efficacy, symptom severity, cancer worry, and depression.

Results: A total of 38 (21 HPV+ OPSCC/17 OCSCC) patients (mean age: 57 [32–76], 73.7% male, 78.9% Caucasian, 71% stage IV) met inclusion criteria. OPSCC patients tended to be of male sex, Caucasian race, and single. Furthermore, OPSCC patients were more likely than OCSCC patients to have private insurance, be employed, and use alcohol and tobacco less frequently. Regarding psychosocial factors, HPV+ OPSCC patients reported lower symptom severity (2.7 versus 3.3), depression (12.0 versus 14.0) and cancer worry (2.8 versus 3.2) at baseline compared to OCSCC patients. Depression decreased significantly over time in OPSCC patients (12.0 to 9.9; effect size: −3.2 (95% CI: −5.9 to −0.4)). Although not statistically significant, cancer worry decreased in both groups (2.8 to 2.4 and 3.2 to 2.7, respectively, effect sizes: −0.3 (95% CI: −0.7–0.08) and −0.6 (95% CI: −1.2–0.05), respectively). No statistically significant differences in patterns of change over time were noted between groups.

Conclusions and relevance: This pilot study highlighted a pattern of reduced quality of life parameters in OCSCC patients at baseline with similar improvements over time compared to the OPSCC cohort. Although different in cancer etiology and treatment plans, HPV+ OPSCC and tobacco-related OCSCC patients both require multidisciplinary cancer care plans that address psychosocial concerns.

Level of evidence: 2B

Abbreviations: HPV, human papilloma virus; HNC, head and neck cancer; QoL, quality of life; OPSCC, oropharyngeal squamous cell carcinoma; OCSCC, oral cavity squamous cell carcinoma

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1. Introduction

Head and neck cancers (HNC) affect over 600,000 patients yearly worldwide [1]. Additionally, squamous cell carcinoma accounts for over 90% of oral or oropharynx cancers within the United States [2]. However, a dramatic shift in the HNC patient population has occurred. Over the past three decades, the number of cases of HNC related to alcohol and tobacco has decreased while the number of cases related to the human papilloma virus (HPV) has increased [3]. While advancements in treatments for patients with HNC have impacted outcomes, survival beyond 5 years has not improved [4–6]. In response to the high mortality of HNC, treatment modalities have become both targeted and aggressive.

While aggressive therapies may improve patient survival, symptoms and toxicities commonly arise and affect a patient's quality of life (QoL) [7–9]. Patients with HNC experience changes in physical and emotional well-being during their care. For example, during HNC radiotherapy treatments, patients may experience high levels of psychosocial distress [10]. Additionally, physical symptoms such as xerostomia and dysphagia are commonly encountered throughout a patient's cancer course [11]. Furthermore, patients at different points in their cancer care or who have different types of HNC may differ in their reported QoL [12]. Therefore, identifying unique factors associated with HNC patients' QoL may direct the implementation of customized patient care plans to meet each patient's needs.

HNC affects multiple different regions of the head and neck and risk factors vary by cancer site. The role of the human papilloma virus (HPV) in the pathogenesis of oropharyngeal squamous cell carcinoma (OPSCC) is well documented, as is the comparatively improved survival of patients with HPV-associated disease [13]. Patients with HPV related disease are younger, have fewer comorbid conditions, and have lower rates of tobacco and alcohol abuse [3]. In contrast, oral cavity squamous cell carcinoma (OCSCC) is associated with tobacco and alcohol use [14,15]. As clinical management (i.e., staging and treatment) of the two groups evolves, it becomes important to also understand patient experiences. Specifically, the 2018 AJCC staging specifies a new staging algorithm for HPV+ OPSCC which will allow for the proper intensity of therapy to be determined for these patients [16]. While etiology, presentation, staging, treatment, and survival differ between OPSCC and OCSCC patients, recent research has shown mixed results regarding whether psychosocial factors differ by HNC type [17–21]. Thus, it remains unknown whether patient experiences and outcomes differ between these two groups.

Therefore, this pilot study was performed to explore demographic, behavioral, and psychosocial factors in HPV+ OPSCC patients and tobacco-related OCSCC patients. This study used prospective, self-reported measures of depression, cancer worry, health behaviors, self-efficacy, and tobacco and alcohol use at diagnosis and at a 12-month follow-up and evaluated potential differences in psychosocial factors between the HPV+ OPSCC patients and OCSCC tobacco users. These findings will help providers understand whether differences exist between these two patient populations and how to best address each patient's comprehensive care needs.

2. Methods

This study was approved by the Institutional Review Board at the Medical University of South Carolina. Recruitment and data collection methods have been described previously [22]. Briefly, patients were prospectively enrolled after diagnosis of a new head and neck malignancy at a tertiary care HNC center from 2010 to 2013. Participants were excluded if they had recurrent cancer or could not speak English. After completing consent procedures, participants completed surveys at baseline and at a 12-month follow-up by mail or telephone and received a gift card to thank them for their participation.

2.1. Measures

2.1.1. Demographic factors

Sex, age, race, employment status, marital status, health insurance and years of education were assessed at baseline.

2.1.2. Clinical factors

Symptom severity was assessed with the 13-item MD Anderson Symptom Inventory [23] at baseline and follow-up. An average severity score was calculated ranging from 0 to 10; higher scores indicated worse symptom severity. Type of cancer, overall cancer stage and comorbid health conditions were collected from medical records.

2.1.3. Behavioral factors

Patients reported lifetime and current cigarette smoking. Patients were classified into ‘Never’, ‘Former’ (smoked $>$ 100 cigarettes in their lifetime but quit $>$ 1 month ago), or ‘Current/Recent’ ($\leq$1 month ago) smoking categories. Current alcohol use, frequency, and amount (number of drinks) were also assessed. Drinking status was categorized as none, light (1–4 times monthly, 1–2 drinks per occasion), regular (1–4 times monthly, 3–4 drinks per occasion, or $\geq$2 times weekly, 1–2 drinks per occasion), and heavy ($\geq$2 times weekly), 3–4 drinks per occasion, or any binge drinking ($\geq$5 drinks on one occasion).

2.1.4. Psychosocial factors

Depression was measured using the 10-item Center for Epidemiologic Studies-Depression Scale [24,25] at both timepoints. Summary scores ranged from 0 to 30 with higher scores indicating higher depression. Cancer worry was assessed at baseline and follow-up using the 5-item Assessment of Survivor Concerns instrument [26] assessing worry about health and cancer recurrence (range 1–4; higher scores indicating higher worry). Each patient's self-efficacy for coping with cancer was assessed at baseline using the 14-item Cancer Behavior Inventory [27–29]. Self-efficacy summary scores were calculated (range 14–126).

2.2. Statistical analysis

Demographic, clinical, and behavioral factors were summarized at baseline and compared between the two patient groups using Fisher's exact test for categorical results, and the two-sample *t*-test or Wilcoxon rank-sum test for continuous results. Depression, symptom severity, and cancer worry scores were summarized using means and standard deviations for each group and time point (baseline and 12-months). Paired *t*-tests were used to compare baseline and 12-month depression, symptom, and worry scores within patient group (OPSCC and OCSCC). Average change from baseline to 12-months was compared across groups for the same outcomes using two-sample *t*-tests. We further assessed the change in scores from baseline to 12-months between groups in a linear regression model adjusting for baseline score and for each of the factors in Table 1 one at a time (results not shown). None of those results contradicted the results from the two-sample *t*-tests that are reported. All tests used two-sided $\alpha = 0.05$ for determining statistical significance.

3. Results

There were a total of 78 potential patients with HNC enrolled in the parent study; 38 patients met criteria based on diagnosis, enrolled and completed baseline and 12-month follow-up surveys in this study. Of these, a total of 21 patients (55.2%) had HPV+ OPSCC cancer, and a total of 17 patients who had a smoking history had OCSCC cancer and this group was included in this analysis. HPV status was determined by HPV DNA in-situ hybridization or, more commonly, p16 testing.

Table 1

Comparison of demographic, clinical, and behavioral factors in HPV+ oropharynx versus tobacco-related oral cavity head and neck cancer patients.

Characteristic	Total cohort N = 38	HPV+ OPSCC cohort N = 21	OCSCC smoker cohort N = 17	p-value[a] or average difference with [95% CI]
All (%)	100%	–	–	
Demographic factors				
Age, mean [range]	57 [32–76]	58.2 [49–76]	55.0 [32–76]	3.2 [−3.4–9.7]
Sex (% female)	26.3	9.5	47.1	0.02
Race (% Caucasian)	78.9	85.7	70.6	0.31
Education (% ≤ high school education)	18.4	14.3	23.5	0.68
Marital status (% partnered)	54.3	44.4	61.1	0.51
Health insurance (%)				0.34
Self-pay/medicaid	31.6	23.8	41.2	–
Private (any)	55.2	66.7	41.2	–
Public (medicare only/military)	13.2	9.5	17.6	–
Employment status (%)				0.71
Employed	36.8	42.8	29.4	–
Retired	39.4	38.1	41.1	–
Unemployed/disability	23.7	19.0	29.4	–
Clinical factors				
Treatment received, N (%)[b]				
Surgery (S)	30 (81)	13 (65)	17 (100)	0.01
Chemotherapy (C)	23 (64)	16 (84)	7 (41)	0.01
Radiation (R)	26 (70)	17 (85)	9 (53)	0.07
All combinations				0.03
S + R	6 (17)	2 (11)	4 (24)	–
C + R	5 (14)	5 (26)	0 (0)	–
S + C + R	14 (39)	9 (47)	5 (29)	–
Other	11 (31)	3 (16)	8 (47)	–
T stage, N (%)				0.007
T0–T1	8 (23)	1 (6)	7 (41)	–
T2–T3	15 (43)	12 (67)	3 (18)	–
T4	12 (34)	5 (28)	7 (41)	–
Missing	3	2	0	
N stage, N (%)				0.01
N0	5 (14)	0 (0)	5 (31)	–
N1–N2	29 (83)	18 (95)	11 (69)	–
N3	1 (3)	1 (5)	0 (0)	–
Missing	3	2	1	
Overall cancer stage (% stage IV)	71.1	76.2	64.7	0.48
Number of comorbid conditions, mean [range]	2.9 [0 − 13]	2.3 [0–6]	3.7 [0–13]	1.4 [−0.4–3.1]
Behavioral factors				
Alcohol use (% regular/heavy drinkers)	65.8	57.1	76.5	0.31
Current smoker (% current/recent smokers)	47.3	38.1	58.8	0.33

HPV: human papilloma virus; OPSCC: oropharyngeal squamous cell carcinoma; OCSCC oral cavity squamous cell carcinoma.

[a] To examine the association between clinical group (HPV+ oropharynx versus oral cavity) and sociodemographic, clinical and behavioral factors, Fisher's exact test used for categorical variables.

[b] Missing treatment information not included.

3.1. Sociodemographic and clinical factors

The majority of participants were male (73.7%), Caucasian (78.9%), and had stage IV cancer (71.1%) (Table 1). Participants varied widely in regard to health insurance and employment status. (Table 1). The HPV+ OPSCC and OCSCC cohorts were similar in age and race distribution but the OCSCC group had more females (47.1% versus 9.5% of patients; p = .02; Table 1). While no significant differences were found by group in other demographic factors, the OCSCC cohort had a higher percentage on Medicaid or self-pay and were more likely to be unemployed or on disability. The HPV+ OPSCC cohort more commonly presented with T2 or T3 cancers as compared to the OCSCC cohort (67% versus 18%, p = .007). Stage IV cancer was seen in 76.2% of the HPV+ cohort compared to 64.7% of the OCSCC cohort (p = .48) (Table 1). Treatment type varied by group with 100% of patients in the OCSCC smoker cohort receiving surgical treatment (p = .01) and more HPV+ OPSCC patients receiving both chemotherapy and radiation or surgery, chemotherapy, and radiation as compared to the OCSCC cohort (p = .03) (Table 1).

3.2. Behavioral and psychosocial factors at diagnosis

Regarding behavioral factors, 57.1% of the HPV+ cohort reported regular/heavy alcohol use compared to 76.5% of the patients in the OCSCC cohort (p = .31) at baseline. Fewer HPV+ patients reported a current or former smoking history than OCSCC patients (38.1 versus 58.8%, p = .33) (Table 1). At baseline, the HPV+ OPSCC patients had a mean symptom severity score of 2.7 (SD: 1.65) as compared to a mean symptom score of 3.3 (SD: 2.33) in the OCSCC cohort (p = .37). At baseline, the HPV+ OPSCC patients had a mean depression score of 12.0 (SD: 6.58) as compared to a mean depression score of 14.0 (SD: 7.78) in the OCSCC cohort (p = .41). At baseline, the HPV+ OPSCC patients had a mean cancer worry score of 2.80 (SD: 0.90) as compared to a mean cancer worry score of 3.25 (SD: 0.75) in the OCSCC cohort (p = .10). Finally, at baseline the HPV+ OPSCC patients reported self-efficacy scores of 97.8 (SD: 17.7) as compared to 96.3 (SD: 16.8) in the OCSCC cohort (p = .79).

3.3. Psychosocial factors over time

Symptom severity increased from baseline to 12 months for the HPV

Table 2
Comparison of psychosocial factors in HPV+ oropharynx versus oral cavity head and neck cancer patients, baseline to 12-months.

	HPV+ OPSCC cohort		OCSCC smoker cohort		
	N	Mean ± sd	N	Mean ± sd	Effect size with [95% CI] (p-value[b])
MDASI score, Mean ± sd					
Baseline	18	2.7 ± 1.65	16	3.3 ± 2.33	
12-Months	15	2.8 ± 1.54	13	3.0 ± 2.95	
Paired difference (95% CI)		−0.1 (−1.0–0.9)		0.1 (−1.2–1.3)	−0.2 [−1.6–1.4] (0.87)
p-Value[a]		0.91		0.91	
CESD score, Mean ± sd					
Baseline	21	12.0 ± 6.58	17	14.0 ± 7.78	
12-Months	16	9.9 ± 5.44	15	9.73 ± 7.55	
Paired difference (95% CI)		−3.2 (−5.9 to −0.4)		−4.6 (−10.3–1.1)	−1.4 [−7.6–4.7] (0.64)
p-Value[a]		0.03		0.10	
Cancer worry score, Mean ± sd					
Baseline	21	2.8 ± 0.90	16	3.2 ± 0.75	
12-Months	16	2.4 ± 0.82	15	2.7 ± 1.08	
Paired difference (95% CI)		−0.3 (−0.7–0.08)		−0.6 (−1.2–0.05)	−0.3 [−1.0–0.4] (0.38)
p-Value[a]		0.11		0.07	

HPV: human papilloma virus; OPSCC: oropharyngeal squamous cell carcinoma; OCSCC oral cavity squamous cell carcinoma; MDASI: MD Anderson Symptom Inventory; CESD: Center for Epidemiologic Studies Depression Scale.

[a] One-sample *t*-test within group.

[b] Two-sample *t*-test between groups.

+ OPSCC patients and decreased for the OCSCC patients (Table 2) but these changes were not statistically significantly different. Depression decreased over time for the HPV+ OPSCC patients and OCSCC patients from baseline to 12 months (p = .03, effect size: −3.2 (95% CI: −5.9 to −0.4), and p = .10, effect size: −4.6 (−10.3–1.1) respectively). Finally, cancer worry decreased over time, though this finding was not statistically significant, in both the HPV+ OPSCC patients (p = .11, effect size: −0.3 (95% CI: −0.7–0.08)) and the OCSCC group (p = .07, effect size: −0.6 (95% CI: −1.2–0.05)) (Table 2). Patterns of change from baseline to 12 months in symptom severity, depression and cancer worry over time did not differ between the HPV+ OPSCC and OCSCC smoker cohorts.

4. Discussion

HNC poses both physical and mental challenges to affected patients. Growing research has highlighted that QoL is impacted by HNC and HNC treatments. For example, Al-Mamgani et al. found patients with OPSCC had reduced QoL during their cancer treatments [30]. Additionally, Thomas et al. noted xerostomia and post-operative appearance greatly impacted QoL in patients with OCSCC [31]. The current study used prospectively-collected, validated measures of QoL and psychosocial function to investigate the impact of OPSCC, specifically, whether HPV+ OPSCC patients have different QoL and/or psychosocial challenges relative to OCSCC patients who have a history of tobacco use.

A better understanding of potential differences in patients experiences by HPV status is important particularly as advances have been made in clinical management (e.g., cancer staging) [13,16]. Previous studies have hypothesized that HPV status may impact patient reported QoL, however results have been mixed. Dziegielewski et al. examined QoL 12 months after transoral robotic surgery for OPSCC using the Head and Neck Cancer Inventory (HNCI), and found no significant difference between the HPV+ and HPV− cohorts in any of the 10 domains evaluated [17]. On the other hand, Broglie et al., using EORTC questionnaires, found that HPV+ patients had significantly higher scores in physical and role functions as well as fewer complaints about feeling ill and pain [21]. Additionally, Maxwell et al. noted in 2013 that p16 HPV+ patients had better overall University of Washington QoL scores both at baseline and post-treatment [18]. Both Sharma et al., using the University of Washington QoL questionnaire, and Ringash et al., using the Functional Assessment of Cancer Therapy–Head and Neck questionnaire, found that HPV+ patients start with higher initial QoL, experience a greater immediate post-treatment drop in QoL, but eventually had the same or better QoL as HPV− patients a year or more after treatment [19,32]. Michaelsen et al. attempted a meta-analysis of the published data, but concluded there was insufficient data to effectively evaluate the long-term impact of HPV status on QoL [20].

In this study, at baseline, several key differences were noted between the two cohorts. The HPV+ cohort had a higher percentage of males, higher-educated patients, employed patients who were privately insured, and non-smokers and non-drinkers. Dahlstrom et al., noted similar findings for HPV+ OPSCC patients [33]. Regarding treatment therapies, as expected, all patients in the OCSCC smoker cohort received surgery as a part of their care. Surgical therapy is an essential part in the treatment of OCSCC [34]. Additionally, a higher number of patients in the HPV+ cohort received chemotherapy and radiation or surgery, chemotherapy, and radiation as compared to the OCSCC cohort. Chemotherapy and radiation are frequently utilized as a part of the de-intensification therapy approaches for HPV+ OPSCC patients [35].

Regarding QoL parameters, our study results highlighted that OCSCC smokers reported higher symptoms, cancer worry, and depression at baseline compared to the HPV+ OPSCC patients, although these results were not statistically significant. The higher symptom scores may partially be attributed to smoking as Sterba et al. noted HNC patients who were current/recent smokers had more issues with coughing, speech, and swallowing as compared to never smokers [36]. Additionally, the OCSCC group had lower self-efficacy scores compared to the HPV+ OPSCC patients. From baseline to 12-months after diagnosis, both groups demonstrated improvements in cancer worry although these results were not statistically significant for either cohort (Table 2). Neilson et al. in 2010 noted during treatment, HNC patients experienced a reduction in anxiety levels over time as compared to baseline [37]. HPV+ oropharyngeal patients also noted statistically significant improvements in depression (CESD) over time. This finding contrasts studies which noted HNC patients become more depressed during and after their treatment course [37,38]. No statistically significant improvements in symptoms (MDASI) were noted in either group over time. HNC patients have been known to experience more physical symptoms during or after their treatment course [39,40].

Overall, this pilot study provides insight on the QoL and psychosocial aspects of HPV+ OPSCC patients and OCSCC smokers. The results of this study demonstrate that both cohorts may benefit from supportive care interventions. Future larger scale studies are needed to further examine patterns of QoL over time. Additionally, future studies should more comprehensively examine QoL in HNC patients and assess functional status, social well-being, and other factors to guide intervention planning. Furthermore, the ability to longitudinally follow these patients beyond 12 months may provide further information regarding their psychosocial or QoL needs over time.

Of note, our study has some limitations. First, study enrollment began before routine HPV testing was available and some patients received tissue-based HPV testing after treatment. In addition, our control cohort is an imperfect proxy for HPV− OPSCC. We chose OCSCC smokers because of the well-established difference in demographics and risk factors as compared to HPV+ OPSCC patients. However, treatment paradigms for OCSCC and oropharynx tumors are different. Oropharynx tumors, regardless of HPV status, are frequently treated with less intense regimens. This difference may influence patient-reported QoL outcomes based on the primary tumor site and HPV status [41]. Additionally, the AJCC 8 staging system was not utilized in this study. Changes in overall cancer stage may impact the psychosocial factors examined in this study. Furthermore, information was not collected regarding if patients received treatment for depression or symptoms from other healthcare providers. Finally, generalizations are limited due to the sample size of this study.

5. Conclusion

This pilot study provides insight on the psychosocial needs of HPV+ OPSCC patients and OCSCC smokers. OCSCC smokers reported a pattern of higher levels of depression, cancer worry, and symptoms at diagnosis. HPV+ OPSCC patients experienced improvements in depression scores over time. Even though there is a clear survival advantage for patients with HPV-associated OPSCC, this study adds to the growing literature in this area and highlights that HNC patients face considerable psychosocial and functional challenges. Cancer clinicians including physicians, dentists, mental health experts, speech therapists, and social workers should work proactively to address the QoL and psychosocial needs for each patient regardless of HPV status during all phases of care.

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References

[1] Mehanna H, Paleri V, West CM, Nutting C. Head and neck cancer—part 1: epidemiology, presentation, and prevention. BMJ 2010;341:c4684.
[2] Chi AC, Day TA, Neville BW. Oral cavity and oropharyngeal squamous cell carcinoma—an update. CA Cancer J Clin 2015;65(5):401–21.
[3] Young D, Xiao CC, Murphy B, Moore M, Fakhry C, Day TA. Increase in head and neck cancer in younger patients due to human papillomavirus (HPV). Oral Oncol 2015;51(8):727–30.
[4] Baxi SS, Pinheiro LC, Patil SM, Pfister DG, Oeffinger KC, Elkin EB. Causes of death in long-term survivors of head and neck cancer. Cancer 2014;120(10):1507–13.
[5] Pulte D, Brenner H. Changes in survival in head and neck cancers in the late 20th and early 21st century: a period analysis. Oncologist 2010;15(9):994–1001.
[6] Skarsgard DP, Groome PA, Mackillop WJ, et al. Cancers of the upper aerodigestive tract in Ontario, Canada, and the United States. Cancer 2000;88(7):1728–38.
[7] Ringash J. Survivorship and quality of life in head and neck cancer. J Clin Oncol 2015;33(29):3322–7.
[8] Rogers LQ, Rao K, Malone J, et al. Factors associated with quality of life in outpatients with head and neck cancer 6 months after diagnosis. Head Neck 2009;31(9):1207–14.
[9] So WK, Chan RJ, Chan DN, et al. Quality-of-life among head and neck cancer survivors at one year after treatment—a systematic review. Eur J Cancer (Oxford, England: 1990) 2012;48(15):2391–408.
[10] Chen AM, Jennelle RL, Grady V, et al. Prospective study of psychosocial distress among patients undergoing radiotherapy for head and neck cancer. Int J Radiat Oncol Biol Phys 2009;73(1):187–93.
[11] Strojan P, Hutcheson KA, Eisbruch A, et al. Treatment of late sequelae after radiotherapy for head and neck cancer. Cancer Treat Rev 2017;59:79–92.
[12] Dwivedi RC, Chisholm EJ, Khan AS, et al. An exploratory study of the influence of clinico-demographic variables on swallowing and swallowing-related quality of life in a cohort of oral and oropharyngeal cancer patients treated with primary surgery. Eur Arch Otorhinolaryngol 2012;269(4):1233–9.
[13] Ang KK, Harris J, Wheeler R, et al. Human papillomavirus and survival of patients with oropharyngeal cancer. N Engl J Med 2010;363(1):24–35.
[14] Sujatha D, Hebbar PB, Pai A. Prevalence and correlation of oral lesions among tobacco smokers, tobacco chewers, areca nut and alcohol users. Asian Pac J Cancer Prev 2012;13(4):1633–7.
[15] Perry BJ, Zammit AP, Lewandowski AW, et al. Sites of origin of oral cavity cancer in nonsmokers vs smokers: possible evidence of dental trauma carcinogenesis and its importance compared with human papillomavirus. JAMA Otolaryngol Head Neck Surg 2015;141(1):5–11.
[16] Lydiatt WM, Patel SG, O'Sullivan B, et al. Head and Neck cancers—major changes in the American Joint Committee on cancer eighth edition cancer staging manual. CA Cancer J. Clin. 2017;67(2):122–37.
[17] Dziegielewski PT, Teknos TN, Durmus K, et al. Transoral robotic surgery for oropharyngeal cancer: long-term quality of life and functional outcomes. JAMA Otolaryngol Head Neck Surg 2013;139(11):1099–108.
[18] Maxwell JH, Mehta V, Wang H, et al. Quality of life in head and neck cancer patients: impact of HPV and primary treatment modality. Laryngoscope 2014;124(7):1592–7.
[19] Sharma A, Mendez E, Yueh B, et al. Human papillomavirus-positive oral cavity and oropharyngeal cancer patients do not have better quality-of-life trajectories. Otolaryngol Head Neck Surg 2012;146(5):739–45.
[20] Hoxbroe Michaelsen S, Gronhoj C, Hoxbroe Michaelsen J, Friborg J, von Buchwald C. Quality of life in survivors of oropharyngeal cancer: a systematic review and meta-analysis of 1366 patients. Eur J Cancer (Oxford, England: 1990) 2017;78:91–102.
[21] Broglie MA, Soltermann A, Haile SR, et al. Quality of life of oropharyngeal cancer patients with respect to treatment strategy and p16-positivity. Laryngoscope 2013;123(1):164–70.
[22] Sterba KR, Zapka J, Armeson KE, et al. Physical and emotional well-being and support in newly diagnosed head and neck cancer patient-caregiver dyads. J Psychosoc Oncol 2017:1–20.
[23] Cleeland CS, Mendoza TR, Wang XS, et al. Assessing symptom distress in cancer patients: the M.D. Anderson Symptom Inventory. Cancer 2000;89(7):1634–46.
[24] Radloff LS. The CES-D Scale: a self-report depression scale for research in the general population. Appl Psychol Measur 1977;1(3):385–401.
[25] Andresen EM, Malmgren JA, Carter WB, Patrick DL. Screening for depression in well older adults: evaluation of a short form of the CES-D (Center for Epidemiologic Studies Depression Scale). Am J Prev Med 1994;10(2):77–84.
[26] Gotay CC, Pagano IS. Assessment of Survivor Concerns (ASC): a newly proposed brief questionnaire. Health Qual Life Outcomes 2007;5:15.
[27] Heitzmann CA, Merluzzi TV, Jean-Pierre P, Roscoe JA, Kirsh KL, Passik SD. Assessing self-efficacy for coping with cancer: development and psychometric analysis of the brief version of the Cancer Behavior Inventory (CBI-B). Psychooncology 2011;20(3):302–12.
[28] Merluzzi TV, Martinez Sanchez MA. Assessment of self-efficacy and coping with cancer: development and validation of the cancer behavior inventory. Health Psychol 1997;16(2):163–70.
[29] Merluzzi TV, Nairn RC, Hegde K, Martinez Sanchez MA, Dunn L. Self-efficacy for coping with cancer: revision of the Cancer Behavior Inventory (version 2.0). Psychooncology 2001;10(3):206–17.
[30] Al-Mamgani A, van Rooij P, Tans L, Verduijn GM, Sewnaik A. Baatenburg de Jong RJ. A prospective evaluation of patient-reported quality-of-life after (chemo)radiation for oropharyngeal cancer: which patients are at risk of significant quality-of-life deterioration? Radiother Oncol 2013;106(3):359–63.
[31] Thomas L, Moore EJ, Olsen KD, Kasperbauer JL. Long-term quality of life in young adults treated for oral cavity squamous cell cancer. Ann Otol Rhinol Laryngol 2012;121(6):395–401.
[32] Ringash J, Fisher R, Peters L, et al. Effect of p16 status on the quality-of-life experience during chemoradiation for locally advanced oropharyngeal cancer: a substudy of randomized Trial Trans-Tasman Radiation Oncology Group (TROG) 02.02 (HeadSTART). Int J Radiat Oncol Biol Phys 2017;97(4):678–86.
[33] Dahlstrom KR, Bell D, Hanby D, et al. Socioeconomic characteristics of patients with

oropharyngeal carcinoma according to tumor HPV status, patient smoking status, and sexual behavior. Oral Oncol 2015;51(9):832–8.

[34] Montero PH, Patel SG. Cancer of the oral cavity. Surg Oncol Clin N Am 2015;24(3):491–508.

[35] Spence T, Bruce J, Yip KW, Liu FF. HPV associated head and neck cancer. Cancer 2016;8(8).

[36] Sterba KR, Garrett-Mayer E, Carpenter MJ, et al. Smoking status and symptom burden in surgical head and neck cancer patients. Laryngoscope 2017;127(1):127–33.

[37] Neilson KA, Pollard AC, Boonzaier AM, et al. Psychological distress (depression and anxiety) in people with head and neck cancers. Med J Aust 2010;193(5 Suppl):S48–51.

[38] 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(1):108–11.

[39] Fang FM, Chien CY, Kuo SC, Chiu HC, Wang CJ. Changes in quality of life of head-and-neck cancer patients following postoperative radiotherapy. Acta Oncol (Stockholm, Sweden) 2004;43(6):571–8.

[40] Rathod S, Livergant J, Klein J, Witterick I, Ringash J. A systematic review of quality of life in head and neck cancer treated with surgery with or without adjuvant treatment. Oral Oncol 2015;51(10):888–900.

[41] Wang MB, Liu IY, Gornbein JA, Nguyen CT. HPV-positive oropharyngeal carcinoma: a systematic review of treatment and prognosis. Otolaryngol Head Neck Surg 2015;153(5):758–69.