The Journal of Laryngology & Otology (2017), ***131***, *760–767*.

doi:10.1017/S0022215117001098

MAIN ARTICLE

Human papillomavirus tumour status is not associated with a positive depression screen for patients with oropharyngeal cancer

J R QUALLIOTINE[1,2], J A CALIFANO[1,2,3], R J LI[1,4], D GOLD[3], B MESSING[3], G LEE[3], P HA[1,3,5], C FAKHRY[1,3]

[1]*Department of Otolaryngology–Head and Neck Surgery, Johns Hopkins University School of Medicine, Baltimore, Maryland,* [2]*Division of Otolaryngology–Head and Neck Surgery, Department of Surgery, University of California, San Diego,* [3]*Milton J Dance Jr Head and Neck Center, Greater Baltimore Medical Center, Maryland,* [4]*Department of Otolaryngology–Head and Neck Surgery, Oregon Health and Science University, Portland, and* [5]*Department of Otolaryngology–Head and Neck Surgery, University of California, San Francisco, USA*

Abstract

Background: Several risk factors for depression in patients with oropharyngeal cancer have been determined. However, it is unknown whether human papillomavirus associated oropharyngeal cancer, which has a distinct clinico-demographic profile, modulates this risk.

Methods: A retrospective analysis was conducted of patients with oropharyngeal cancer. These patients had completed a 10-item depression screening questionnaire before receiving treatment for their disease from 2011 to 2014. Associations between patient or disease characteristics and depression screening questionnaire results were investigated.

Results: The study comprised 69 patients, 31 (44.9 per cent) of whom screened positive for depression. There were no significant differences in distributions of clinico-demographic or histopathological characteristics, including human papillomavirus tumour status, by depression screen result.

Conclusion: This population has a high risk for depression, but no obvious risk factors, including human papillomavirus tumour status, were associated with an elevated risk. This inability to risk-stratify patients by clinico-demographic or disease characteristics emphasises the importance of regular depression screening for all patients in this population.

Key words: Oropharyngeal Neoplasms; Squamous Cell Carcinoma; Head And Neck Cancer; Papillomaviridae; Depression

Introduction

The diagnosis of cancer can have a profound impact on a patient's psychosocial state. It is well established that the prevalence of depression is higher among patients with cancer compared to the general population.[1,2] Head and neck cancer patients have an even higher rate of depression, ranging from 15 to 54 per cent,[3–5] than non-head and neck cancer patients, ranging from 8 to 24 per cent.[2] The unique ways in which head and neck cancer can interfere with basic human function and challenge the patient's ability to participate in activities so essential to the human experience, such as eating, speaking and breathing, help to explain these higher rates of depression. Beyond negatively impacting quality of life,[6] depression in patients with head and neck cancer has been shown to adversely affect length of hospital stays, adherence to treatment and self-care abilities.[7–9] Furthermore, higher suicide rates have been observed relative to the general population, and the rates are among the highest of all populations with medical illnesses.[10] Recent analyses, both prospective and systematic reviews, have demonstrated that depression decreases overall survival in patients with head and neck cancer.[6,11]

Despite the high prevalence and important consequences of depression in patients with cancer, several studies have demonstrated that depression is underdiagnosed and under-treated in these populations.[12] Many barriers to diagnosis have been recognised, including lack of time in a busy oncological setting, inadequate competence in diagnosing and treating depression, lack of specialised training in the specific psychological needs of this patient population, the overlap of depression with somatic symptoms of

Accepted for publication 18 February 2017 First published online 19 July 2017

cancer, and patient reluctance to discuss psychosocial wellbeing.[12,13] To address these barriers, comprehensive cancer centres have introduced the use of self-report instruments, which have been validated as effective tools for the universal screening of depression in the cancer population.[2,14]

In the general population, risk factors for developing depression include female sex, marital divorce, unemployment, family history, traumatic life events and chronic medical illness.[15] In head and neck cancer specifically, risk factors include female sex, living alone and current tobacco use.[16,17] It is unknown whether human papillomavirus (HPV) associated oropharyngeal cancer affects the risk for depression. Human papillomavirus associated oropharyngeal cancer has a unique profile with regard to demographic and clinical factors. These patients are more likely than HPV-negative oropharyngeal cancer patients to be male, white and of a younger age, and less likely to use tobacco or alcohol.[18] Additionally, patient worries regarding the sexual transmission of HPV, the latency of infection and their partner's risk, among other issues, have been postulated to be specific to HPV-associated oropharyngeal cancer.[19]

Although HPV-associated oropharyngeal cancer has a distinct profile and patient concerns, whether this population has a different risk of depression has not been explored. This study aimed to investigate the primary hypothesis that clinico-demographic, social or oropharyngeal cancer disease characteristics, including HPV tumour status, affect a patient's risk for screening positive for depression on a self-report instrument.

Materials and methods

Patient selection

Patients who were diagnosed with oropharyngeal cancer between October 2011 and September 2014, and who completed the 10-item Center for Epidemiologic Studies Depression Scale ('CES-D 10'), a self-report instrument, before receiving treatment for their disease at Johns Hopkins Head and Neck Surgery at Greater Baltimore Medical Center, were eligible for this study. All patients are requested to complete the survey as part of the clinic check-in process. Patients aged less than 18 years or those with histological diagnoses other than squamous cell carcinoma were excluded from this analysis. This was a single institution retrospective review, which was approved by the hospital institutional review board.

Clinical data

The retrospective abstraction of eligible patients' medical records was performed. Clinico-demographic variables of interest at the time of diagnosis included: age, gender, race, major co-morbidities (history of stroke, coronary artery disease, diabetes mellitus, other cancer, chronic hepatitis, chronic obstructive pulmonary disease, heart failure, liver failure, chronic kidney disease, rheumatoid arthritis, sarcoidosis or Crohn's disease), number of prescribed medications, use of antidepressants, and whether the patient was being treated for primary or recurrent disease. Social variables of interest included: tobacco use, alcohol use, marital status and employment status. Histopathological variables of interest included HPV tumour status, and tumour–node–metastasis (TNM) classifications and overall stage as defined by the American Joint Committee on Cancer.[20]

Human papillomavirus tumour status

Human papillomavirus tumour status was determined by HPV in situ hybridisation or p16 immunohistochemistry (an established surrogate marker for HPV in oropharyngeal cancer), as clinically available.[21] Human papillomavirus tumour status was routinely evaluated for all oropharyngeal cancer cases, in keeping with clinical care.

Depression screening instrument

As part of routine clinic workflow, all patients are asked to complete the Center for Epidemiologic Studies Depression Scale, a 10-item self-report questionnaire developed to screen for depression symptoms experienced in the previous week. This questionnaire is a shorter version of the full 20-item ('CES-D') and revised ('CESD-R') Center for Epidemiologic Studies Depression Scales.[22,23] Each item is scored on a Likert-type scale from 0 to 3, indicating how frequently in the previous week the patient experienced each symptom. For example, for 'I felt fearful', a score of 0 represents rarely (less than 1 day), 1 represents sometimes (1–2 days), 2 represents occasionally (3–4 days) and 3 represents all of the time (5–7 days). A cut-off score of 10 constitutes a positive screening result.[24,25] The 10 questions on the survey are as follows: (1) I was bothered by things that usually don't bother me; (2) I had trouble keeping my mind on what I was doing; (3) I felt depressed; (4) I felt that everything I did was an effort; (5) I felt hopeful about the future; (6) I felt fearful; (7) My sleep was restless; (8) I was happy; (9) I felt lonely; and (10) I could not 'get going'.

Analysis and statistical methods

Descriptive statistics were reported in terms of numbers and frequencies for categorical variables, and medians and ranges for continuous variables. Chi-square tests were used for categorical data and Mann–Whitney tests were used for the comparison of medians. Simple logistic regression was performed to analyse relationships between clinico-demographic, social or histopathological variables and Center for Epidemiologic Studies Depression Scale responses (using a cut-off value of 10 for positive screening), and findings were reported as odds ratios and 95 per cent confidence intervals. A similar analysis was performed to evaluate associations between variables of

https://doi.org/10.1017/S0022215117001098 Published online by Cambridge University Press

interest and responses to individual Center for Epidemiologic Studies Depression Scale items, comparing item scores of 0 or 1 to item scores of 2 or 3, in order to investigate the internal consistency of the screening tool. Two-sided *p*-values of less than 0.05 were considered statistically significant. Data analysis was performed using Microsoft Excel®, 2010.

Results

Study population

The clinico-demographic, social and histopathological characteristics of the study population are summarised by HPV tumour status in Table I. In total, there were 65 patients with known HPV tumour status who were eligible for analysis. The majority of patients were HPV-positive ($n = 50$, 76.9 per cent). Median age was 59.9 years (range, 44–88 years). Overall, this population was mostly white ($n = 57$, 87.7 per cent), male ($n = 55$, 84.6 per cent) and married ($n = 49$, 75.4 per cent), with advanced American Joint Committee on Cancer stage (III or IV, $n = 61$, 93.8 per cent). Most patients ($n = 57$, 87.7 per cent) were not taking antidepressants, and nearly all ($n = 63$, 96.9 per cent) were being treated for primary malignancy rather than for recurrent disease. Patients with HPV-associated oropharyngeal cancer were less likely to use tobacco ($p = 0.03$) or alcohol ($p = 0.01$) at the time of diagnosis than patients with HPV-negative oropharyngeal cancer. A lower proportion of HPV-associated oropharyngeal cancer patients than HPV-negative oropharyngeal cancer patients reported using antidepressants (8 *vs* 27 per cent, $p = 0.05$).

Patient characteristics and depression

The distribution of clinico-demographic, social and histopathological characteristics of the study population stratified by Center for Epidemiologic Studies Depression Scale screening results are presented in Table II. Overall, 44.9 per cent of the population screened positive for depression, with a questionnaire cut-off value of 10. None of the characteristics analysed were found to be significantly associated with the questionnaire result, including HPV tumour status ($p > 0.1$ for all).

Patient characteristics and questionnaire domains

Relationships between patients' clinical characteristics at the time of diagnosis and each individual depression screening questionnaire item were investigated (tables not included). These analyses were not powered to detect true associations, but were nonetheless performed as exploratory analyses. Each Center for Epidemiologic Studies Depression Scale item assesses patients' feelings in the previous week. Current tobacco use ($p = 0.0005$), unemployment ($p = 0.03$) and higher TNM stage ($p = 0.03$) were associated with the domain of irritability: 'I was bothered by things that don't usually bother me'. Current tobacco use ($p = 0.02$) and unemployment ($p = 0.01$) were associated with the item 'I felt that everything I did was an effort'. Current tobacco use ($p = 0.04$), no spouse ($p = 0.04$) and higher tumour (T) classification ($p = 0.04$) were associated with the domain of helplessness: 'I [did not] feel hopeful about the future'. Higher nodal (N) classification ($p = 0.04$) was associated with the item 'I felt fearful'. Employment ($p = 0.03$) was associated with the item 'I was happy'. Not having a spouse ($p = 0.05$) was associated with feeling 'lonely'.

No significant associations were found between individual questionnaire items and other variables of interest, including HPV tumour status, as shown in Figure 1.

Discussion

In this study, the association of clinico-demographic, social and histopathological characteristics among patients with oropharyngeal cancer was evaluated in terms of the risk of depression, as determined by the Center for Epidemiologic Studies Depression Scale self-report instrument. This analysis highlights the high risk of depression among oropharyngeal cancer patients and specifically among HPV-associated oropharyngeal cancer patients. Indeed, 44.9 per cent of patients screened positive for a risk of depression. Of note, there was no association between any clinical or demographic characteristic, including HPV tumour status, and depression screening risk.

The prevalence of patients with oropharyngeal cancer who screen positive for a risk of depression in this study is similar to previous analyses of populations with head and neck cancer of all subsites.[3–5] It is important to reiterate that this prevalence is significantly greater than that for the general population,[1] and for all cancer types on average.[2] An analysis by Tu *et al.* demonstrated that over 60 per cent of those patients who screen positive for depression are found to have a depressive disorder on psychiatric evaluation with a specialist, with major depressive disorder diagnosed in 22 per cent of cases.[26] It has been demonstrated in head and neck cancer populations that pre-treatment depression is significantly associated with worse survival, worse pre-treatment nutrition, lower pre-treatment quality of life,[6] worse post-operative functional performance status, lower adjuvant treatment completion rates, longer hospital stay and a higher incidence of narcotic dependence,[5] and is associated with post-treatment depression.[3,27,28] Given this high prevalence of depression in head and neck cancer patients, and the clinically significant consequences, beyond treating patients known to be depressed, some have advocated the prophylactic treatment of all patients using antidepressant medications.[29]

Despite a distinct clinico-demographic profile and unique concerns regarding the sexual transmission of the aetiological agent, this analysis found no significant difference in Center for Epidemiologic Studies Depression Scale positivity by HPV tumour status.

https://doi.org/10.1017/S0022215117001098 Published online by Cambridge University Press

TABLE I
CHARACTERISTICS OF OROPHARYNGEAL SCC* PATIENTS AT TIME OF DIAGNOSIS BY HPV TUMOUR STATUS†

Characteristic	Overall ($n = 65$)	HPV-positive ($n = 50$)	HPV-negative ($n = 15$)	p‡
Age (median (range); years)	59.9 (44–88)	59.8 (44–74)	61.9 (53–88)	0.5**
Race (*n* (%))				
– White	57 (87.7)	44 (88.0)	13 (86.7)	0.9
– Other	8 (12.3)	6 (12.0)	2 (13.3)	
Sex (*n* (%))				
– Male	55 (84.6)	44 (88.0)	11 (73.3)	0.2
– Female	10 (15.4)	6 (12.0)	4 (26.7)	
Current tobacco use (*n* (%))				
– Yes	20 (30.8)	12 (24.0)	8 (53.3)	0.03§
– No	45 (69.2)	38 (76.0)	7 (46.7)	
Current alcohol use (*n* (%))				
– Yes	22 (33.8)	13 (26.0)	9 (60.0)	0.01§
– No	43 (66.2)	37 (74.0)	6 (40.0)	
Marital status (*n* (%))				
– Spouse	49 (75.4)	37 (74.0)	12 (80.0)	0.6
– No spouse	16 (24.6)	13 (26.0)	3 (20.0)	
Employed (*n* (%))				
– Yes	40 (61.5)	33 (66.0)	7 (46.7)	0.2
– No	25 (38.5)	17 (34.0)	8 (53.3)	
Major co-morbidities (*n* (%))				
– Yes	31 (47.7)	21 (42.0)	10 (66.7)	0.09
– No	34 (52.3)	29 (58.0)	5 (33.3)	
Number of prescribed medications (median (range))	3 (0–14)	2.5 (0–10)	3 (0–14)	0.1**
Taking antidepressant (*n* (%))				
– Yes	8 (12.3)	4 (8.0)	4 (26.7)	0.05§
– No	57 (87.7)	46 (92.0)	11 (73.3)	
Primary *vs* recurrent disease (*n* (%))				
– Primary	63 (96.9)	49 (98.0)	14 (93.3)	0.4
– Recurrent	2 (3.1)	1 (2.0)	1 (6.7)	
Tumour (T) classification (*n* (%))				
– T_1	19 (29.2)	16 (32.0)	3 (20.0)	0.4
– T_2	30 (46.2)	21 (42.0)	9 (60.0)	
– T_3	7 (10.8)	7 (14.0)	0 (0.0)	
– T_4	4 (6.2)	3 (6.0)	1 (6.7)	
– T_X	5 (7.7)	3 (6.0)	2 (13.3)	
Nodal (N) classification (*n* (%))				
– N_0	5 (7.7)	3 (6.0)	2 (13.3)	0.2
– N_1	12 (18.5)	7 (14.0)	5 (33.3)	
– N_{2a}	5 (7.7)	3 (6.0)	2 (13.3)	
– N_{2b}	35 (53.8)	30 (60.0)	5 (33.3)	
– N_{2c}	8 (12.3)	7 (14.0)	1 (6.7)	
Metastasis (M) classification (*n* (%))				
– M_0	65 (100.0)	50 (100.0)	15 (100.0)	–
– M_1	0 (0.0)	0 (0.0)	0 (0.0)	
Overall AJCC stage (*n* (%))				
– I or II	4 (6.2)	2 (4.0)	2 (13.3)	0.2
– III or IV	61 (93.8)	48 (96.0)	13 (86.7)	

*Excluding four cases with an unknown human papillomavirus (HPV) tumour status. †Human papillomavirus tumour status determined by p16 immunohistochemistry and/or HPV16 in situ hybridisation. ‡Determined using the chi-square test, unless otherwise indicated. **Determined using the Mann–Whitney test. §Indicates statistical significance ($p < 0.05$). SCC = squamous cell carcinoma; HPV = human papillomavirus; AJCC = American Joint Committee on Cancer

This was true not only for the overall depression screening questionnaire result, using a cut-off value of 10, but also for our exploratory analysis of each individual questionnaire item. Milbury *et al*. have suggested that HPV-associated oropharyngeal cancer does not confer significantly more psychosocial stress relative to HPV-negative oropharyngeal cancer; these authors found similar distress levels between patients who self-identified as HPV-positive and those who were unsure of their HPV tumour status.[30] A similar finding was demonstrated in a study that compared major depression rates by HPV tumour status in patients who were undergoing radiotherapy.[31] A smaller proportion of HPV-positive than HPV-negative patients were on antidepressants, yet the risk of depression was similar regardless of HPV tumour status. Therefore, while the possibility of anxieties specific to malignancy caused by sexually transmitted infection and to concerns regarding transmission remains, the risk of depression (as assessed by the available screening tool) is similar.

Our analysis demonstrates no significant difference in risk of depression (as defined by the Center for Epidemiologic Studies Depression Scale) for other clinico-demographic, social or histopathological characteristics in oropharyngeal cancer patients. This

https://doi.org/10.1017/S0022215117001098 Published online by Cambridge University Press

TABLE II
CHARACTERISTICS OF OROPHARYNGEAL SCC PATIENTS AT TIME OF DIAGNOSIS BY CES-D 10 SCORE*

Characteristic	CES-D 10 score			Univariate binomial regression		
	Positive (*n*) (total *n* = 31)	Negative (*n*) (total *n* = 38)	% positive	OR	95% CI	*p*
Age				1.67	0.64–4.35	0.3
– >60 years	17	16	51.5			
– ≤60 years	14	22	38.9			
Race				1.02	0.25–4.19	1.0
– White	27	33	45.0			
– Other	4	5	44.4			
Sex				1.27	0.32–4.96	0.7
– Male	27	32	45.8			
– Female	4	6	40.0			
Current tobacco use				2.33	0.83–6.54	0.1
– Yes	13	9	59.1			
– No	18	29	38.3			
Current alcohol use				1.78	0.66–4.77	0.2
– Yes	14	12	53.8			
– No	17	26	39.5			
Marital status				0.65	0.23–1.88	0.4
– Spouse	21	29	42.0			
– No spouse	10	9	52.6			
Employed				0.81	0.31–2.13	0.7
– Yes	18	24	42.9			
– No	13	14	48.1			
Major co-morbidities				1.35	0.52–3.49	0.5
– Yes	17	18	48.6			
– No	14	20	41.2			
Number of prescribed medications				0.68	0.26–1.77	0.4
– >2	15	22	40.5			
– ≤2	16	16	50.0			
Taking antidepressant				1.27	0.33–4.86	0.7
– Yes	5	5	50.0			
– No	26	33	44.1			
Primary *vs* recurrent disease				1.67	0.14–19.29	0.7
– Primary	30	36	45.5			
– Recurrent	1	2	33.3			
HPV tumour status†				0.78	0.30–2.02	0.6
– Positive	21	29	42.0			
– Negative	8	7	53.3			
Tumour (T) classification‡				1.26	0.36–4.43	0.7
– T_3, T_4	23	29	44.2			
– T_1, T_2	6	6	50.0			
Nodal (N) classification				1.00	0.35–2.83	1.0
– N_2	9	11	45.0			
– N_0, N_1	22	27	44.9			
Metastasis (M) classification				–	–	–
– M_1	0	0				
– M_0	31	38	44.9			
Overall AJCC stage				0.80	0.15–4.27	0.8
– III or IV	3	3	50.0			
– I or II	28	35	44.4			

*Score of 10 or greater is considered positive for depression. †Determined by p16 immunohistochemistry and/or HPV16 in situ hybridisation, excluding four cases with an unknown HPV tumour status. ‡Excludes 5 T_X cases, in which tumour classification was unknown. SCC = squamous cell carcinoma; CES-D 10 = 10-item Center for Epidemiologic Studies Depression Scale; OR = odds ratio; CI = confidence interval; HPV = human papillomavirus; AJCC = American Joint Committee on Cancer

result is somewhat unexpected, as a recent analysis demonstrated significant associations between depression and: smoking, alcohol use, T_{3-4} tumour classification and greater than three prescribed medications.[32] However, that analysis compared pre-treatment characteristics to post-treatment depression (median follow up of 39 months) using a different self-report instrument, the Hospital Anxiety Depression Scale, in patients with head and neck cancer including all subsites. Employment in particular was shown to be associated with depression and decreased function in German head and neck cancer survivors five years after diagnosis.[33] Our exploratory analyses for associations between individual questionnaire items and characteristics found that employment status and tobacco use were associated with three items each.

Overall, the literature on associations between depression and clinico-demographic and social characteristics, such as age, sex, smoking, alcohol use, marital status and employment, have been inconsistent,[3,16,17] and larger collective analyses would aid investigation of these issues.

https://doi.org/10.1017/S0022215117001098 Published online by Cambridge University Press

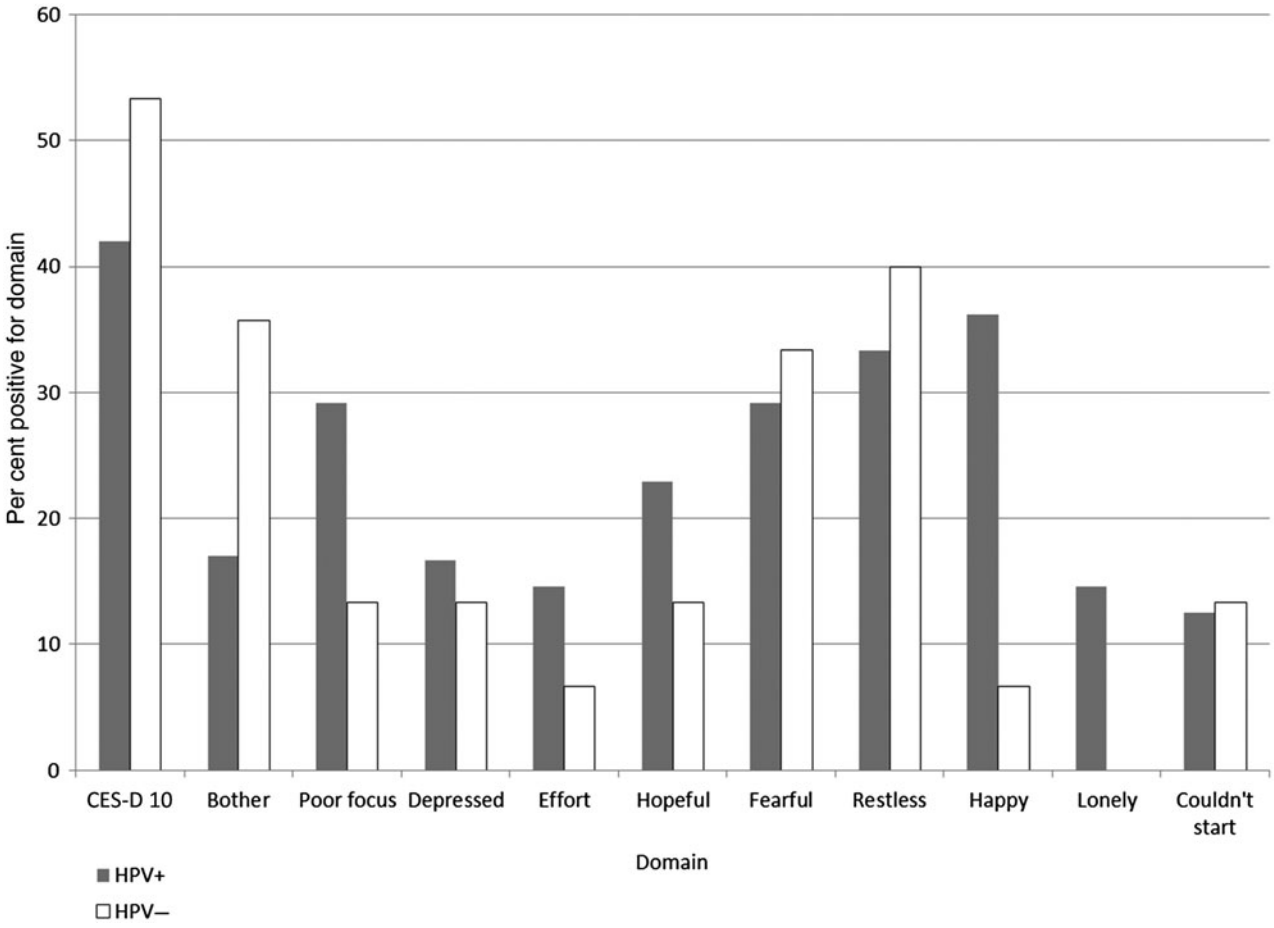

FIG. 1

Graph showing no associations between human papillomavirus (HPV) tumour status and overall 10-item Center for Epidemiologic Studies Depression Scale (CES-D 10) score and individual domain items. *P*-values were greater than 0.05 for each comparison. The 10 domain items are as follows: (1) bother – I was bothered by things that usually don't bother me; (2) poor focus – I had trouble keeping my mind on what I was doing; (3) depressed – I felt depressed; (4) effort – I felt that everything I did was an effort; (5) hopeful – I felt hopeful about the future; (6) fearful – I felt fearful; (7) restless – my sleep was restless; (8) happy – I was happy; (9) lonely – I felt lonely; (10) couldn't start – I could not 'get going'.

We believe that these results emphasise the importance of depression screening tools, including the 10-item Center for Epidemiologic Studies Depression Scale, given that neither socio-demographic nor histopathological factors are associated with depression screening positivity. A standardised screening tool, not patient characteristics, allows the clinician to predict depression in their patients a priori. At our institution, when a patient screens positive for a risk of depression using the 10-item Center for Epidemiologic Studies Depression Scale questionnaire, they are counselled by our oncology social work team, given information about support groups and, if necessary, referred to a mental health provider.

The Center for Epidemiologic Studies Depression Scale is one of the most widely used instruments in the field of psychiatric epidemiology. It was shown to be strongly associated with depression in a meta-analysis of 76 prospective studies evaluating self-report tools.[22,34] The shorter 10-item Center for Epidemiologic Studies Depression Scale was utilised as part of the clinical workflow and was administered as part of routine clinical care for all new patient visits.

- **Patients with human papillomavirus (HPV) associated oropharyngeal cancer have a distinct clinico-demographic profile**
- **Whether HPV tumour status modulates risk for depression has not been adequately investigated**
- **This study demonstrated a 44.9 per cent prevalence of risk for depression overall**
- **There was no association between any characteristic measured, including HPV tumour status, and depression risk**
- **Regular depression screening is important, as clinico-demographic and histopathological variables are unable to predict depression risk**

https://doi.org/10.1017/S0022215117001098 Published online by Cambridge University Press

This study has important limitations, including its retrospective design and psychometric method of only using a self-report screening instrument without confirmation with psychiatric evaluation by a specialist. Nevertheless, this analysis does address a substantial gap in the literature regarding whether the characteristics of oropharyngeal cancer patients are associated with a greater risk of depression, specifically for patients with HPV-associated disease.

The analyses of associations between individual Center for Epidemiologic Studies Depression Scale items and patient characteristics were not sufficiently powered to detect true associations, but were nonetheless performed as exploratory analyses to inform further investigations. Future analyses should follow this population through treatment to investigate how various treatment modalities modulate risk for the HPV-associated oropharyngeal cancer population.

References

1 Waraich P, Goldner EM, Somers J, Hsu L. Prevalence and incidence studies of mood disorders: a systematic review of the literature. *Can J Psychiatry* 2004;**49**:124–38
2 Krebber AM, Buffart LM, Kleijn G, Riepma IC, De Bree R, Leemans CR *et al*. Prevalence of depression in cancer patients: a meta-analysis of diagnostic interviews and self-report instruments. *Psychooncology* 2014;**23**:121–30
3 Neilson KA, Pollard AC, Boonzaier AM, Corry J, Castle DJ, Mead KR *et al*. Psychological distress (depression and anxiety) in people with head and neck cancers. *Med J Aust* 2010;**193**:S48–51
4 Kugaya A, Akechi T, Okuyama T, Nakano T, Mikami I, Okamura H *et al*. Prevalence, predictive factors, and screening for psychologic distress in patients with newly diagnosed head and neck cancer. *Cancer* 2000;**88**:2817–23
5 Barber B, Dergousoff J, Nesbitt M, Mitchell N, Harris J, O'Connell D *et al*. Depression as a predictor of postoperative functional performance status (PFPS) and treatment adherence in head and neck cancer patients: a prospective study. *J Otolaryngol Head Neck Surg* 2015;**44**:38
6 Kim S-A, Roh J-L, Lee S-A, Lee S, Kim S-B, Choi S-H *et al*. Pretreatment depression as a prognostic indicator of survival and nutritional status in patients with head and neck cancer. *Cancer* 2016;**122**:131–40
7 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
8 Hall RC, Wise MG. The clinical and financial burden of mood disorders. Cost and outcome. *Psychosomatics* 1995;**36**:S11–18
9 Beck D, Koenig H. Minor depression: a review of the literature. *Int J Psychiatry Med* 1996;**26**:177–209
10 Yu GP, Mehta V, Branovan D, Huang Q, Schantz S. Non-cancer-related deaths from suicide, cardiovascular disease, and pneumonia in patients with oral cavity and oropharyngeal squamous carcinoma. *Arch Otolaryngol Head Neck Surg* 2012;**138**:25–32
11 Barber B, Dergousoff J, Slater L, Harris J, O'Connell D, El-Hakim H *et al*. Depression and survival in patients with head and neck cancer. *JAMA Otolaryngol Neck Surg* 2016;**142**:284–8
12 Newport DJ, Nemeroff CB. Review, assessment and treatment of depression in the cancer patient. *J Psychosom Res* 1998;**45**: 215–37
13 Söllner W, DeVries A, Steixner E, Lukas P, Sprinzl G, Rumpold G *et al*. How successful are oncologists in identifying patient distress, perceived social support, and need for psychosocial counselling? *Br J Cancer* 2001;**84**:179–85
14 Vodermaier A, Linden W, Siu C. Screening for emotional distress in cancer patients: a systematic review of assessment instruments. *J Natl Cancer Inst* 2009;**101**:1464–88
15 Hirschfeld R, Weissman M. Risk factors for major depression and bipolar disorder. In: Davis KL, Charney D, Coyle JT, Nemeroff C, eds. *Neuropsychopharmacology*. Philadelphia: Lippincott, Williams & Wilkins, 2002;1018–25
16 Katz MR, Irish JC, Devins GM, Rodin GM, Gullane PJ. Psychosocial adjustment in head and neck cancer: the impact of disfigurement, gender and social support. *Head Neck* 2003;**25**:103–12
17 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
18 Gillison ML, D'Souza G, Westra W, Sugar E, Xiao W, Begum S *et al*. Distinct risk factor profiles for human papillomavirus type 16-positive and human papillomavirus type 16-negative head and neck cancers. *J Natl Cancer Inst* 2008;**100**:407–20
19 Baxi SS, Shuman AG, Corner GW, Shuk E, Sherman EJ, Elkin EB *et al*. Sharing a diagnosis of HPV-related head and neck cancer: the emotions, the confusion, and what patients want to know. *Head Neck* 2013;**35**:1534–41
20 Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. Pharynx. In: Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A, eds. *AJCC Cancer Staging Manual*, 7th edn. New York: Springer, 2010;41–56
21 Begum S, Gillison ML, Ansari-Lari MA, Shah K, Westra WH. Detection of human papillomavirus in cervical lymph nodes: a highly effective strategy for localizing site of tumor origin. *Clin Cancer Res* 2003;**9**:6469–75
22 Eaton WW, Muntaner C, Smith C, Tien A, Ybarra M. Center for Epidemiologic Studies Depression Scale: Review and revision (CESD and CESD-R). In: Maruish ME, ed. *The Use of Psychological Testing for Treatment Planning and Outcomes Assessment*, 3rd edn. Mahwah, New Jersey: Lawrence Erlbaum, 2004;363–77
23 Irwin M, Artin KH, Oxman MN. Screening for depression in the older adult: criterion validity of the 10-item Center for Epidemiological Studies Depression Scale (CES-D). *Arch Intern Med* 1999;**159**:1701–4
24 Bjorgvinsson T, Kertz SJ, Bigda-Peyton JS, McCoy KL, Aderka IM. Psychometric properties of the CES-D-10 in a psychiatric sample. *Assessment* 2013;**20**:429–36
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**:77–84
26 Tu CH, Hsu MC, Chi SC, Lin HY, Yen YC. Routine depression screening and diagnosing strategy for cancer inpatients. *Psychooncology* 2014;**23**:1057–67
27 Adachi Y, Kimura H, Sato N, Nagashima W, Nakamura K, Aleksic B *et al*. Preoperative level of depression is a predictor of postoperative levels of depression in patients with head and neck cancer. *Jpn J Clin Oncol* 2014;**44**:311–17
28 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
29 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 Neck Surg* 2013;**139**:678–86
30 Milbury K, Rosenthal DI, El-Naggar A, Badr H. An exploratory study of the informational and psychosocial needs of patients with human papillomavirus-associated oropharyngeal cancer. *Oral Oncol* 2013;**49**:1067–71
31 Hess CB, Rash DL, Daly ME, Farwell DG, Bishop J, Vaughan AT *et al*. Competing causes of death and medical comorbidities among patients with human papillomavirus-positive vs human papillomavirus-negative oropharyngeal carcinoma and impact on adherence to radiotherapy. *JAMA Otolaryngol Head Neck Surg* 2014;**140**:312–16
32 Moubayed SP, Sampalis JS, Ayad T, Guertin L, Bissada E, Gologan OE *et al*. Predicting depression and quality of life among long-term head and neck cancer survivors. *Otolaryngol Head Neck Surg* 2015;**152**:91–7
33 Koch R, Wittekindt C, Altendorf-Hoffmann A, Singer S, Guntinas-Lichius O. Employment pathways and work-related issues in head and neck cancer survivors. *Head Neck* 2015;**37**: 585–93
34 Pinquart M, Duberstein P. Depression and cancer mortality: a meta-analysis. *Psychol Med* 2010;**40**:1797–810

Address for correspondence:
Dr Carole Fakhry,
Department of Otolaryngology – Head and Neck Surgery,
601 N Caroline Street,
JHOC 6th Floor,
Baltimore,
MD 21287, USA

Fax: +01 (410) 955 6526
E-mail: cfakhry@jhmi.edu

Dr C Fakhry takes responsibility for the integrity of the content of the paper
Competing interests: None declared

https://doi.org/10.1017/S0022215117001098 Published online by Cambridge University Press