Prevalence and Association Factors of Depression and Anxiety in Head and Neck Cancer Patients

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Objective: To evaluate the prevalence of depression and anxiety in head and neck cancer patients and investigate the relationship of the associating factors.

Materials and Methods: A cross-sectional study with self-completed questionnaire was conducted. Univariate and multivariate analyses with logistic regression were performed to assess the associated factors.

Results: Total of 293 patients (71.7% male, 28.3% female) were enrolled. The mean ± SD age was 58.25±14.28 years. The prevalence of anxiety was 17.75% and depression was 16.04%. Diagnostic time >12 month (adjusted OR 4.79, 95% CI 1.48 to 15.54, p=0.009), and perception of disfigurement (adjusted OR 4.68, 95% CI 1.42 to 15.38, p=0.011) were associated with anxiety. Education level had a direct positive correlation with anxiety prevention (adjusted OR 95% CI 0.13, 0.03 to 0.57, p=0.006 and adjusted OR 0.07, 95% CI 0.01 to 0.48, p=0.007 for education level lower Bachelor degree and Bachelor degree or higher, respectively). For depression, patient age >65 years (adjusted OR 4.09, 95% CI 1.6 to 10.46, p=0.003), group staging 4 (adjusted OR 3.12, 95% CI 1.2 to 8.08, p=0.019), and fatigue (adjusted OR 5.7, 95% CI 1.92 to 16.93, p=0.002) were related to depression. While married status was a protective factor of depression (adjusted OR 0.38, 95% CI 0.16 to 0.94, p=0.037).

Conclusion: Diagnostic time >12 months, and perception of disfigurement were associated with anxiety. Age >65 years, group staging 4, and fatigue were related to depression.

Keywords: Depression and anxiety, Head and neck cancer

Head and neck cancer (HNC) is the 7th most common cancer worldwide[1]. It is a devastating disease causing poor functional performance status in patients including speech, swallowing, cosmesis and disturbance of quality of life. HNC disease and treatment effects also causes patients to suffer from dysfunction and disfigurement. Therefore, physical or emotional stress is common at some point during the disease course. The review of literature shows that the prevalence of depression and anxiety in HNC patients worldwide ranges from 7% to 58%[2]. The study of Kim et al demonstrated that the prevalence of pretreatment depression was 24.9% and showed a significant correlation between pretreatment depression and survival outcome in HNC patients[3]. Moreover, the AJCC 8th[4] edition stated that "Depression adversely affects quality of life and survival. Notation of a previous or current diagnosis of depression should be recorded in the medical record".

Some previous studies regarding depression and anxiety in HNC patients had focused on demographic, psychosocial, or disease predictors. However, to the authors' knowledge, a paucity of studies that objectively address the prevalence of depression and anxiety in Thai population or any associating factors has not been declared.

The aim of the present study was to evaluate the prevalence of depression and anxiety in HNC patients and to investigate the relationship between demographics, disease, physical and psychosocial factors, and depression or anxiety among these patients.

Materials and Methods

Institutional ethical approval was obtained from the Ethical Committee of the Faculty of Medicine,

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Chulalongkorn University (IRB No. 139/59). Informed consent was obtained for experimentation with human subjects. Privacy rights of human subjects were always observed. The authors declare they have no conflict of interest with respect to the research study.

Patients

A single-center cross-sectional study with self-completed questionnaire was performed. The inclusion criteria were as follows: 1) patients confirmed diagnosis of cancer in head and neck region without receiving any prior definite treatments, 2) age ≥18 years, 3) HNC patients with confirmed recurrent disease. Illiterate patients in Thai language, patients with co-existing depression or anxiety according to the DSM-V criteria, patients in follow-up period after completing a course of definitive treatment, or patients without cooperation to complete the questionnaire were excluded. The study was conducted at the Department of Otolaryngology, Faculty of Medicine, Chulalongkorn University between July 2016 and June 2017.

Procedures and outcomes

The questionnaire was allocated to each patient attended the interdepartmental conference for treatment consensus. The questionnaire is composed of four parts as follows:

1. Demographic data including age, sex, marital status, education level, and children living at home

2. Disease data including primary site, number of comorbidities, tumor size, group staging, time since diagnosis, tracheostomy, and gastrostomy (In this part, all the data were rechecked and confirmed with medical records by the researcher after collecting the questionnaire)

3. Physical and psychosocial data including disease perception, pain, dyspnea, dysphagia/ aspiration, sleep disturbance, fatigue, social support, financial support, and perception of disfigurement

4. Thai hospital anxiety and depression scale (Thai HADS) consisted of 14 questions divided into two domains

4.1 Anxiety domain composed of questions in odd number (questions number 1, 3, 5, 7, 9, 11, 13).

4.2 Depression domain composed of questions in even number (questions number 2, 4, 6, 8, 10, 12, 14).

In each question, the scale ranged from 0 (minimum) to 3 (maximum) varying to severity of the symptoms. Total scores in each domain were 21.

Classification: 1) Score 0 to 10 points were classified as non-case group. 2) Score ≥11 points were classified as case group.

Thai HADS had good reliability and validity for both anxiety and depression sub-scales. At the cut-off point at ≥11, which was the best cut-off point, the sensitivity of anxiety sub-scales were 100% and 85.71%, respectively. Specificity was 86% for anxiety and 91.3% for depression[5].

Sample size calculation

The authors used Z=1.96 while Z² were the abscissa of the normal curve that cuts off an area α at the tail. The estimated proportion of an attribute that was present in the population (p)=0.25 were set according to the previous study of Haisfield-Wolfe et al[6] showing 25% of the prevalence of depression. The acceptable of sampling error (e) value was 0.05. Sample size of 288 patients were established.

Statistical analysis

Stata Statistical Software, version 16 (StataCorp LLC, College Station, TX, USA) was used to perform statistical analyses. The authors expressed continuous data as mean ± standard deviation (SD). Categorical data was represented as count and percentage. Odds ratio (OR) was used to estimate the occurrence of outcome of interest. Univariate and multivariate analyses using logistic regression was also applied to determine the independent predictors of anxiety and depression. Significant level was set at p-value less than 0.05.

Results

A total of 293 patients (210 male: 71.7%, 83 female: 28.3%) were enrolled in the present study. The demographic, disease, physical and psychosocial characteristics of the patients were represented in Table 1. The prevalence of anxiety was 17.75% (52 of total 293 patients) and depression was 16.04% (47 of total 293 patients).

The association between anxiety/depression and studied factors was performed with univariate and multivariate analyses using logistic regression. The univariate analysis of anxiety was shown in Table 2, and the univariate analysis of depression was shown in Table 3. The statistically significant factors from univariate analysis (as shown in Table 2, 3) were used for multivariate analysis. The multivariate analysis of anxiety and depression was presented in Table 4.

The multivariate analysis revealed a significant correlation between anxiety and time since diagnosis

Table 1. Demographic, disease, physical-psychosocial characteristics

Factors	n (%)	Factors	n (%)
Age (year); mean±SD	58.25±14.28	Time since diagnosis (month); mean±SD	6.98±10.64
Median (min, max)	59 (19, 92)	Median (min, max)	3 (0, 72)
≤65 years	198 (67.6)	≤12 months	218 (74.4)
>65 years	95 (32.4)	>12 months	31 (10.6)
Sex		Tracheostomy	
Male	210 (71.7)	No	120 (41.0)
Female	83 (28.3)	Yes	30 (10.2)
Marital status		Gastrostomy	
Unmarried	103 (35.2)	No	135 (46.1)
Married	176 (60.1)	Yes	2 (3.1)
Education level		Disease perception	
No	19 (6.5)	No	27 (9.2)
< Bachelor degree	183 (62.5)	Yes	209 (71.3)
≥ Bachelor degree	52 (17.7)	Pain	
Employment status		No	87 (29.7)
No	127 (43.3)	Yes (mild)	70 (23.9)
Yes	156 (53.2)	Yes (moderate)	72 (24.6)
Children living at home		Yes (severe)	57 (19.5)
No	57 (19.5)	Dyspnea	
Yes	215 (3.4)	No	155 (52.9)
Primary site		Yes	130 (44.4)
Oral cavity	63 (21.5)	Dysphagia/aspiration	
Pharynx (OP/HP)	56 (19.1)	No	139 (47.4)
Glottis	38 (13.0)	Yes	147 (50.2)
Nose & paranasal sinus	23 (7.8)	Sleep disturbance	
Nasopharynx	70 (23.9)	No	138 (47.1)
Others*	41 (14.0)	Yes	150 (51.2)
Number of comorbidities		Fatigue	
No	123 (42.0)	No	139 (47.4)
Yes	126 (43.0)	Yes	150 (51.2)
Tumor size		Social support	
<T4	175 (59.7)	No	26 (8.9)
T4	100 (34.1)	Yes	251 (85.7)
Group staging		Financial support	
<4	129 (44)	No	32 (10.9)
4	146 (49.8)	Yes	251 (85.7)
		Perception of disfigurement	
		Yes	150 (51.2)
		No	130 (44.4)

OP=oropharynx; HP=hypopharynx; SD=standard deviation

* Unknown primary, thyroid, salivary gland, external acoustic canal

>12 months (adjusted OR 4.79, 95% CI 1.48 to 15.54, p=0.009), and perception of disfigurement (adjusted OR 4.68, 95% CI 1.42 to 15.38, p=0.011). While, education level had a direct positive correlation with anxiety prevention (adjusted OR 0.13, 95% CI 0.03 to 0.57, p=0.006 and adjusted OR 0.07, 95% CI 0.01

Table 2. Univariate analysis of anxiety

Factors	Anxiety (n=52); n (%)	No anxiety (n=241); n (%)	OR, 95% CI	p-value
Age (year)				
≤65 year	31 (59.6)	167 (69.3)	Reference	1
>65 year	21 (40.4)	74 (30.7)	1.53, 0.78 to 2.95	0.176
Sex				
Male	36 (69.2)	174 (72.2)	Reference	1
Female	16 (30.8)	67 (27.8)	1.15, 0.56 to 2.3	0.667
Marital status				
Unmarried	19 (36.5)	84 (34.9)	Reference	1
Married	27 (51.9)	149 (61.8)	0.67, 0.35 to 1.28	0.186
Education level				
No	7 (13.5)	12 (5.0)	Reference	1
< Bachelor degree	30 (57.7)	153 (63.5)	0.78, 0.41 to 1.52	0.434
≥ Bachelor degree	7 (13.5)	45 (18.7)	0.68, 0.24 to 1.65	0.372
Employment status				
No	25 (48.1)	102 (42.3)	Reference	1
Yes	26 (50)	130 (53.9)	0.85, 0.45 to 1.63	0.605
Children living at home				
No	6 (11.5)	51 (21.2)	Reference	1
Yes	41 (78.8)	174 (72.2)	1.44, 0.67 to 3.28	0.325
Primary site				
Oral cavity	8 (15.4)	55 (22.8)	0.61, 0.24 to 1.43	0.237
Pharynx (OP/HP)	9 (17.3)	47 (19.5)	0.86, 0.35 to 1.96	0.715
Glottis	5 (9.6)	33 (13.7)	0.67, 0.19 to 1.86	0.427
Nose & paranasal sinus	8 (15.4)	15 (6.2)	2.74, 0.94 to 7.36	0.026*
Nasopharynx	12 (23.1)	58 (24.1)	0.95, 0.42 to 1.99	0.879
Others	10 (19.2)	31 (12.9)	1.61, 0.65 to 3.7	0.23
Number of comorbidities				
No	18 (34.6)	105 (43.6)	Reference	1
Yes	23 (44.2)	103 (42.7)	1.06, 0.55 to 2.03	0.844
Tumor size				
<T4	24 (46.2)	151 (62.7)	Reference	1
T4	23 (44.2)	77 (32.0)	1.69, 0.87 to 3.24	0.09
Group staging				
<4	15 (28.8)	114 (47.3)	Reference	1
4	32 (61.5)	114 (47.3)	1.78, 0.93 to 3.48	0.063
Time since diagnosis				
≤12 month	33 (63.5)	185 (76.8)	Reference	1
>12 month	11 (21.2)	20 (8.3)	2.96, 1.18 to 7.05	0.006*
Tracheostomy				
No	18 (34.6)	102 (42.3)	Reference	1
Yes	6 (11.5)	24 (10.0)	1.18, 0.37 to 3.18	0.733
Gastrostomy				
No	20 (38.5)	115 (47.7)	Reference	1
Yes	3 (5.8)	6 (2.5)	2.4, 0.37 to 11.65	0.214
Disease Perception				
No	6 (11.5)	21 (8.7)	Reference	1
Yes	38 (73.1)	171 (71.0)	1.11, 0.55 to 2.36	0.759
Pain				
No	13 (25.0)	74 (30.7)	Reference	1
Yes (mild)	4 (7.7)	66 (27.4)	0.22, 0.06 to 0.64	0.003*
Yes (moderate)	13 (25.0)	59 (24.5)	1.03, 0.47 to 2.13	0.937
Yes (severe)	20 (38.5)	37 (15.4)	3.45, 1.67 to 6.96	<0.001*
Dyspnea				
No	19 (36.5)	136 (56.4)	Reference	1
Yes	31 (59.6)	99 (41.1)	2.12, 1.1 to 4.11	0.015*
Dysphagia/aspiration				
No	21 (40.4)	118 (49.0)	Reference	1
Yes	30 (57.7)	117 (48.5)	1.45, 0.76 to 2.79	0.232
Sleep disturbance				
No	13 (25.0)	125 (51.9)	Reference	1
Yes	39 (75.0)	111 (46.1)	3.51, 1.72 to 7.52	<0.001*
Fatigue				
No	9 (17.3)	130 (53.9)	Reference	1
Yes	42 (80.8)	108 (44.8)	5.17, 2.4 to 12.05	<0.001*
Social support				
No	4 (7.7)	22 (9.1)	Reference	1
Yes	43 (82.7)	208 (86.3)	0.76, 0.32 to 1.94	0.5
Financial support				
No	5 (9.6)	27 (11.2)	Reference	1
Yes	44 (84.6)	207 (85.9)	0.9, 0.38 to 2.42	0.812
Perception of disfigurement				
Yes	42 (80.8)	108 (44.8)	5.17, 2.4 to 12.05	<0.001*
No	8 (15.4)	122 (50.6)	Reference	1
Depression (Y2)				
Non-case depression	28 (53.8)	218 (90.5)	Reference	1
Case depression	24 (46.2)	23 (9.5)	8.12, 3.81 to 17.2	<0.001*

OP=Oropharynx, HP=Hypopharynx; OR=odds ratio; CI=confident interval

A p-value corresponds to Binary logistic regression, * Significant at p<0.05

Table 3. Univariate analysis of depression

Factors	Depression (n=47); n (%)	No depression (n=246); n (%)	OR, 95% CI	p-value
Age (year)				
≤ 65 year	22 (46.8)	176 (71.5)	Reference	1
>65 year	25 (53.2)	70 (28.5)	2.86, 1.44 to 5.68	0.001*
Sex				
Male	34 (72.3)	176 (71.5)	1.04, 0.5 to 2.28	0.912
Female	13 (27.7)	70 (28.5)	Reference	1
Marital status				
Unmarried	20 (42.6)	83 (33.7)	Reference	1
Married	20 (42.6)	156 (63.4)	0.43, 0.21 to 0.84	0.008*
Education level				
No	5 (10.6)	14 (5.7)	Reference	1
< Bachelor degree	28 (59.6)	155 (63.0)	0.87, 0.44 to 1.74	0.656
≥ Bachelor degree	4 (8.5)	48 (19.5)	0.38, 0.1 to 1.14	0.071
Employment status				
No	29 (61.7)	98 (39.8)	2.43, 1.23 to 4.91	0.006*
Yes	17 (36.2)	139 (56.5)	Reference	1
Children living at home				
No	8 (17.0)	49 (19.9)	Reference	1
Yes	36 (76.6)	179 (72.8)	1.22, 0.57 to 2.83	0.586
Primary site				
Oral cavity	9 (19.1)	54 (22.0)	0.84, 0.34 to 1.92	0.668
Pharynx (OP/HP)	14 (29.8)	42 (17.1)	2.06, 0.93 to 4.36	0.042*
Glottis	4 (8.5)	34 (13.8)	0.58, 0.14 to 1.76	0.321
Nose & paranasal sinus	5 (10.6)	18 (7.3)	1.51, 0.41 to 4.52	0.438
Nasopharynx	10 (21.3)	60 (24.4)	0.84, 0.35 to 1.85	0.647
Others	5 (10.6)	36 (14.6)	0.69, 0.2 to 1.93	0.469
Number of comorbidities				
No	15 (31.9)	108 (43.9)	Reference	1
Yes	21 (44.7)	105 (42.7)	1.08, 0.55 to 2.13	0.8
Tumor size				
<T4	21 (44.7)	154 (62.6)	Reference	1
T4	23 (48.9)	77 (31.3)	2.1, 1.06 to 4.15	0.02*
Group staging				
<4	9 (19.1)	120 (48.8)	Reference	1
4	35 (74.5)	111 (45.1)	3.55, 1.69 to 7.85	<0.001*
Time since diagnosis				
≤12 month	33 (70.2)	185 (75.2)	Reference	1
>12 month	6 (12.8)	25 (10.2)	1.29, 0.41 to 3.5	0.595
Tracheostomy				
No	16 (34)	104 (42.3)	Reference	1
Yes	6 (12.8)	24 (9.8)	1.35, 0.43 to 3.68	0.533
Gastrostomy				
No	18 (38.3)	117 (47.6)	Reference	1
Yes	4 (8.5)	5 (2.0)	4.48, 0.85 to 21.6	0.018*
Disease perception				
No	3 (6.4)	24 (9.8)	Reference	1
Yes	34 (72.3)	175 (71.1)	1.06, 0.51 to 2.32	0.867
Pain				
No	8 (17.0)	79 (32.1)	Reference	1
Yes (mild)	3 (6.4)	67 (27.2)	0.18, 0.04 to 0.6	0.002*
Yes (moderate)	10 (21.3)	62 (25.2)	0.8, 0.34 to 1.77	0.567
Yes (severe)	23 (48.9)	34 (13.8)	5.98, 2.86 to 12.39	<0.001*
Dyspnea				
No	9 (19.1)	146 (59.3)	Reference	1
Yes	36 (76.6)	94 (38.2)	5.29, 2.47 to 12.04	<0.001*
Dysphagia/aspiration				
No	10 (21.3)	129 (52.4)	Reference	1
Yes	35 (74.5)	112 (45.5)	3.49, 1.67 to 7.72	<0.001*
Sleep disturbance				
No	8 (17.0)	130 (52.8)	Reference	1
Yes	39 (83.0)	111 (45.1)	5.93, 2.58 to 15.22	<0.001*
Fatigue				
No	6 (12.8)	133 (54.1)	Reference	1
Yes	40 (85.1)	110 (44.7)	7.06, 2.96 to 19.31	<0.001*
Social support				
No	3 (6.4)	23 (9.3)	Reference	1
Yes	42 (89.4)	209 (85.0)	1.49, 0.54 to 5.13	0.43
Financial support				
No	2 (4.3)	30 (12.2)	Reference	1
Yes	43 (91.5)	208 (84.6)	1.96, 0.65 to 7.95	0.214
Perception of disfigurement				
Yes	36 (76.6)	114 (46.3)	3.79, 1.78 to 8.61	<0.001*
No	9 (19.1)	121 (49.2)	Reference	1

OP=Oropharynx, HP=Hypopharynx; OR=odds ratio; CI=confident interval

A p-value corresponds to Binary logistic regression, * Significant at p<0.05

Table 4. The multivariate analysis of anxiety and depression

	Anxiety (stepwise method)		Depression (stepwise method)	
	Adjusted OR, 95% CI	p-value	Adjusted OR, 95% CI	p-value
Marital status: married			0.38, 0.16 to 0.94	0.037*
Group staging: 4			3.12, 1.2 to 8.08	0.019*
Education level				
No	Reference	1		
< Bachelor degree	0.13, 0.03 to 0.57	0.006*		
≥ Bachelor degree	0.07, 0.01 to 0.48	0.007*		
Nose & Paranasal sinus: yes	2.4, 0.59 to 9.77	0.221		
Time since diagnosis >12 months	4.79, 1.48 to 15.54	0.009*		
Pain				
No	Reference	1	Reference	1
Yes (mild)	0.12, 0.01 to 1.13	0.064	0.23, 0.04 to 1.23	0.085
Yes (moderate)	1.27, 0.37 to 4.35	0.702	0.55, 0.17 to 1.77	0.319
Yes (severe)	1.1, 0.3 to 4.07	0.887	2.4, 0.78 to 7.35	0.126
Perception of disfigurement: yes	4.68, 1.42 to 15.38	0.011*		
Fatigue: yes			5.7, 1.92 to 16.93	0.002*
Case depression: yes	2.23, 0.75 to 6.63	0.15		

OR=odds ratio; CI=confident interval

* Significant at p<0.05

to 0.48, p=0.007 for education level lower Bachelor degree and Bachelor degree or higher, respectively).

As a result of multivariate analysis in depression, a significant correlation between depression and age >65 years (adjusted OR 4.09, 95% CI 1.6 to 10.46, p=0.003), group staging 4 (adjusted OR 3.12, 95% CI 1.2 to 8.08, p=0.019), and fatigue (adjusted OR 5.7, 95% CI 1.92 to 16.93, p=0.002) was revealed. While married status was a protective factor of depression (adjusted OR 0.38, 95% CI 0.16 to 0.94, p=0.037).

Discussion

The prevalence of anxiety was 17.75% and depression was 16.04% in the studied population. The prevalence in the present study may seem inferior to the previously published reports. According to the literature, prevalence of anxiety or depression reported between 1984 and 2012 varied with a range of 7% to 58%. The 7% was the prevalence of severe anxiety shown in only one study, while the rest of the reports revealed the prevalence ranging from 15% to 58%[2].

A prospective observational study of Neilson et al performed to assess symptoms and identify the prevalence of depression and anxiety using the HADS in patients with HNC showed that probable cases of depression was 15% and anxiety was 20% at baseline.

In that study, the anxiety and depression rate was quite similar to the rate in the present studied population[7].

From the study, the factors associating with anxiety were time since diagnosis >12 months and perception of disfigurement. The systematic review of Manier et al[8] also supported the association between visible disfigurement and anxiety. The result of this study revealed that the HNC patients with perception of body image disturbance had an impact on psychosocial indices including anxiety[8]. In combination, the knowledge from both studies of the perception of image disfigurement should be taken into consideration to prevent anxiety in HNC patients[8].

Age >65 years, group staging 4, and fatigue were demonstrated as associated factors of depression in the present study, in contrast to married status which was recognized as a protective factor of depression. The trial of Chen et al[2] reported the variables that were significantly associated with post-radiation depression included employment status (working at enrollment), younger age (<55 years), single, and living alone (p<0.05, for all). The concordance of the presented study and Chen et al[2] study could be assumed that married status was considered as a protection of depression. However, the difference between these two studies was that in one, increased age showed

increase in developing depression, and the other study, younger age had a higher risk of depression[2].

The strengths of the present study are: 1) large study in single center of head and neck; 2) comprehensive factors contributing to anxiety or depression were assessed; 3) psychiatric distress, including depression and anxiety was emphasized; and 4) a well-validated questionnaire was used in the present study.

The limitation of the present research is a high rate of missing data at some points i.e., gastrostomy and tracheostomy questions. In addition, there were less variables in patient characteristics due to the tertiary medical nature of the authors' institution.

For clinical applicability: 1) HNC patients (especially with high Thai HADS scores) with identified associated factors should be assessed for other psychiatric symptoms (feelings and thoughts etc.), 2) early psychiatric intervention may be a clinical benefit to the patient survival outcome and for successful treatment of head-and-neck cancer.

Conclusion

The prevalence of anxiety and depression in HNC patients was 17.75% and 16.04%, respectively. Diagnostic time >12 months and perception of disfigurement were associated with anxiety, while education level had direct positive correlation with anxiety prevention. Age >65 years, group staging 4, and fatigue were related to depression, where married status was revealed as a protective factor.

What is already known on this topic?

Prevalence of depression and anxiety in HNC patient is higher than in normal general population. Some factors contribute to the physical and emotional stress in the disease course.

What this study adds?

The findings support the relationship between demographic/disease/physical and psychosocial factors and depression-and-anxiety among HNC patients.

Conflicts of interest

The authors declare no conflict of interest.

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