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CLINICAL INVESTIGATION **Head and Neck**

PHYSICAL DISTRESS, EMOTIONAL STATUS, AND QUALITY OF LIFE IN PATIENTS WITH NASOPHARYNGEAL CANCER COMPLICATED BY POST-RADIOTHERAPY ENDOCRINOPATHY

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Purpose: To explore factors affecting quality of life (QOL) among patients with nasopharyngeal cancer (NPC) complicated by post-radiotherapy endocrinopathy.

Methods and Materials: This cross-sectional study was conducted in a tertiary medical center and involved a total of 43 post-radiotherapy, recurrence-free NPC patients with endocrinopathy. They performed self-assessment of their emotional status using the Beck Anxiety Inventory and Beck Depression Inventory–II, and their QoL with the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) questionnaire and the H&N35 cancer module.

Results: Emotional and cognitive functioning of EORTC QLQ-C30 were the most affected. Fatigue, insomnia, and pain were the main concerns. Of the patients, 22 (51.2%) had anxiety and 19 (44.2%) had depression. Both depression and anxiety were negatively correlated with functional scales and global QoL but positively correlated with symptom scales. Multiple linear regression analysis revealed that physical distress symptoms of QLQ-C30 and physical functioning were the significant predictors of global QoL. Emotional and social functioning could predict depression, whereas emotional and physical functioning were significant predictors of anxiety.

Conclusions: NPC patients with post-radiotherapy endocrinopathy exhibit impaired cognitive function and negative emotions. Symptoms of physical distress play an important role in QoL perception. Measurement of EORTC QLQ-C30 can be a useful instrument for the early detection of patients' impaired cognitive function and psychological morbidity. The high psychological distress related to the endocrine disturbances or the impact of NPC itself needs further study. © 2008 Elsevier Inc.

Nasopharyngeal cancer, Psychological distress, Symptom distress, Quality of life, Endocrinopathy.

INTRODUCTION

Nasopharyngeal cancer (NPC) is highly prevalent in Southeast Asia (1). Its annual incidence rate in Taiwan is approximately 5.96 cases per 100,000 persons, making NPC the 9th most prevalent cancer in the country (2). It has been one of the 10 leading causes of cancer death up to 1996, but ranked 14th in the 2 years preceding 2005 (2). However, complications such as mucositis and sequelae such as dry mouth resulting from the main treatment modality of radiotherapy, continue to significantly impact NPC patients (3–6). Because the effectiveness of radiotherapy has been realized in clinical practice, NPC patients have had a better chance at cancer-free life for an extended period. However late complications, including dry mouth and primary hypothyroidism, are usually chronic, progressive, and irreversible (7, 8).

Hypothalamic–pituitary dysfunctions after radiotherapy for NPC are well documented in several studies (9–11), including ours (8, 12–14). Although brain injuries are irreversible, endocrine disturbances are amenable to therapy. Over the past decades, subjective well-being has become recognized as important as biomedical outcome parameters, ushering a growing body of literature concerning health-related quality of life (QoL). However, research focusing on NPC patients' psychological well-being remains sparse, and there has been no study exploring the mental health of NPC patients

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complicated by endocrinopathy, even though patient-centered medical care has already drawn much attention (15).

This study aimed to assess the emotional status, subjective and functional outcome, and their relationship among recurrence-free NPC patients with post-radiotherapy endocrinopathy. It also aimed to investigate predictive factors of QoL.

METHODS AND MATERIALS

Participants

This study was conducted from February 2004 to February 2005 at the outpatient Endocrinology Clinic of the National Taiwan University Hospital. From our previous research, we noted that post-radiotherapy NPC patients could develop hypothalamic–pituitary dysfunction from cranial irradiation (8). Thus patients with complicated physical discomfort such as malaise, constipation, decreased libido, and muscle cramps were referred from the Department of Otolaryngology to the Endocrinology Clinic for further evaluation and management.

Eligible participants were post-radiotherapy, recurrence-free NPC patients who were referred to the Endocrinology Clinic. A total of 43 patients were recruited into this study, including 8 new patients referred during the study period and 35 previous patients before the study was conducted. All of the patients received a total of 7,000 cGy on the primary lesion and an estimated total dose to the hypothalamic-pituitary area of 4,600 to 5,600 cGy. Written informed consent and approval from the Institutional Review Board were obtained before data collection began.

Patients were seen individually at the outpatient clinic and were asked to complete four self-reported questionnaires: The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, version 3.0 (EORTC QLQ-C30 v. 3), the EORTC Head and Neck Cancer Module (EORTC QLQ-H&N35), the Beck Depression Inventory–II (BDI- II), and the Beck Anxiety Inventory (BAI).

A well-trained research assistant recorded the demographic and clinical data, and assisted participants in completing the questionnaires if needed.

Measures

The EORTC QLQ-C30 core questionnaire (16, 17) is a validated and broadly used instrument for a self-assessment of different dimensions of health-related QoL and symptom scores relevant to cancer patients. It is a 30-item questionnaire scored on a four-point scale (1 = not at all, 4 = very much). All scales (five functioning, three symptom, and one global health status/QoL) and single-item measures (five additional symptoms) ranged in a transformed score of 0 to 100. A high score for the functional scale represented a high/healthy level of functioning. A high score for the global health status/QoL represented a high QoL. A high score for the symptom scale/item represented a high level of symptomatology/problems.

The EORTC QLQ-H&N35 is a site-specific module for head-and-neck cancer as a supplement to the EORTC QLQ-C30. Both were translated into Chinese and validated in Taiwan (18). The internal consistency for scales of QLQ-C30 and QLQ-H&N35 as Cronbach's α coefficient ranged from 0.75 to 0.92, except for cognitive functioning (0.51).

Emotional status was measured using the Chinese version of BDI-II (19) and BAI (20, 21). BDI-II is a 21-item, four-point Likert-scored scale (0 = not at all, 3 = always) that assess the presence and severity of affective, cognitive, motivational, vegetative, and psychomotor components of depression in the last 2 weeks. Items in BDI-II include questions on changes in sleep patterns, changes in appetite, tiredness or fatigue, degrees of sadness, feelings of guilt and pessimism, and others. Higher scores indicate more severe depression. The BDI-II has produced reliable and valid results (22–24). The Cronbach's α coefficient was 0.93 in this study.

The BAI is a valid and reliable self-report checklist for anxiety symptoms (25, 26). It consists of 21 items that assess the presence and severity of their anxiety symptoms, both psychological (*e.g.*, feelings of nervousness and fear) and physical (*e.g.*, heart pounding, hands trembling), in the previous week on a four-point scale (0 = not at all, 3 = severely, I can barely stand it). Higher scores indicate more severe anxiety. The Cronbach's α coefficient was 0.91 in this study.

Statistical analysis

The mean scores of the five dimensions of functional scales, symptom scales, and global health/QoL in the QLQ-C30 and symptom scales in QLQ-H&N35 were calculated according to the EORTC Scoring Manual (27). Patients with a BAI score >7 were defined as having anxiety (20). Depression was defined as a BDI-II score >13 (19). The Student *t* test was used for comparison between groups (mean scores).

Pearson's correlation was performed to examine the relationship between the scales, while stepwise multiple linear regression was used to explore predictors of the global QoL and their relationship between emotional status and QoL. All tests were two-tailed, and a 5% significance level was used for statistical significance. The SPSS for Windows, version 12.0 software package (SPSS Inc., Chicago, IL) was used for data processing.

RESULTS

Basic background information of the patients is shown in Table 1. The mean age was 52.0 ± 8.7 years (median, 52.0 years; range, 33–68 years). Of the patients, 17 (39.5%) patients were male. A total of 24 patients (55.8%) were unemployed. The postradiation time varied: <5 years in 15 patients (34.9%), 5–10 and 10–15 years in 9 patients (20.9%), and >15 years in 10 patients (23.2%). The mean time after radiotherapy was 114.4 ± 94.4 months (median, 104.0 months; range, 4–411 months).

Of the 43 patients, 41 (95.4%) had growth hormone deficiency, 27 (62.8%) had hypothyroidism, 12 (27.9%) had adrenal insufficiency, 11 (25.6%) had hypogonadism, and 9 (20.9%) had hyperprolactinemia. Table 2 presents the mean scores for each scale of EORTC QLQ-C30 and QLQ-H&N35. The mean of the total scores of the five functional scales of the EORTC QLQ-C30 was 75.9 ± 20.2, whereas the mean score of the nine symptom scales was 20.6 ± 16.2. The mean score for the global health status/QoL was 52.7 ± 24.2 and the score of symptom distress specific to NPC was 37.1 ± 20.9.

Emotional and cognitive functionings (69.0 ± 28.0 and 70.5 ± 26.2, respectively) were affected significantly, and fatigue (39.0 ± 26.6), insomnia (34.9 ± 33.3), and pain (26.0 ± 28.2) were the main complaints. The mean score of global QoL was low (52.7 ± 24.2). The most distressful symptoms specific to NPC patients were dry mouth (72.1 ± 29.9), sticky saliva (59.7 ± 36.8), and dental problems (48.1 ± 32.8).

Table 1. Demographic variables and clinical data of the study subjects (n = 43)

Variable	No. (%)
Age (y)	
Mean ± SD	52.0 ± 8.7
Median	52.0
Range	33−68
Gender	
Male	17 (39.5)
Female	26 (60.5)
Education level (yr)	
≤6	13 (30.2)
7−12	14 (32.6)
≥13	16 (37.2)
Occupational status	
Full-time work	16 (37.2)
Part-time work	3 (7.0)
Unemployed	24 (55.8)
Time after radiotherapy (mo)	
Mean ± SD	114.4 ± 94.4
Median	104.0
Range	4−411
Endocrinopathy	
Growth hormone deficiency	41 (95.4%)
Hypothyroidism	27 (62.8%)
Adrenal insufficiency	12 (27.9%)
Hypogonadism	11 (25.6%)
Hyperprolactinemia	9 (20.9%)
Marital status	
Unmarried	5 (11.6)
Married	34 (79.1)
Separated	1 (2.3)
Divorced	1 (2.3)
Widower/widow	2 (4.7)

Abbrevation: SD = standard deviation.

In all, 22 (51.2%) patients had anxiety, 19 (44.2%) had depression, and 13 (30.2%) had both, whereas 14 (32.6%) had neither. Both depression and anxiety were significantly and negatively correlated with functional scales and global health status/QoL (Pearson's correlation coefficient $r = -0.388$ to -0.702), but were significantly and positively correlated with symptom scales (r = 0.321–0.690), except for dyspnea and constipation.

A comparison of total function and symptoms, and global health status/QoL scores between patients with and those without anxiety/depression revealed significant differences. The detailed mean scores for each scale are shown in Table 3. Patients with anxiety demonstrated significantly poor functioning and global health status/QoL except for social functioning. Fatigue, pain, dyspnea, and insomnia were more serious and significantly different as compared with those of nonanxious patients. Depressed patients reported significantly poor functioning in all dimensions and in perceived global health status/QoL. They also presented with symptoms of fatigue, nausea/vomiting, insomnia, and appetite loss, which were statistically different from patients without depression.

There were significantly different scores of total symptom scales between patients with and those without anxiety or depression in terms of detailed mean scores for the H&N35 symptom scales (Table 4). Almost every symptom was scored higher among patients with anxiety, although not statistically significant, except for swallowing problems. However, many problems, including those related to swallowing, speech, social eating, social contact, sexuality, teeth, and feeling ill were scored significantly higher among patients with depression.

Univariate analysis did not reveal any significant relationship in demographic variables (age, sex, marital status, level of education), emotional status (anxiety, depression), and global health status/QoL. However, postradiation time was a relevant variable to QoL (28). Variables used for evaluating their contribution to QoL were the five functioning dimensions: symptom scales, H&N35 symptom scales, postradiation time, BDI-II, and BAI.

Table 2. Mean scores and standard deviation for different scales of EORTC QLQ-C30 and EORTC QLQ-H&N35

EORTC QLQ-C30	Mean ± SD	Median	EORTC QLQ-H&N35	Mean ± S.D.	median
Functional scales	75.9 ± 20.2	79.7	Symptom scales	37.1 ± 20.9	38.2
Physical	81.4 ± 19.2	86.7	Pain	12.6 ± 19.8	8.3
Role	79.1 ± 28.9	83.3	Swallowing	33.1 ± 27.3	25.0
Emotional	69.0 ± 28.0	75.0	Senses problems	26.7 ± 27.5	16.7
Cognitive	70.5 ± 26.2	83.3	Speech problems	33.6 ± 30.3	22.2
Social	77.0 ± 28.0	91.7	Trouble with social eating	30.6 ± 30.2	16.7
Symptom scales	20.6 ± 16.2	16.0	Trouble with social contact	19.8 ± 23.9	6.7
Fatigue	39.0 ± 26.6	33.3	Less sexuality	37.5 ± 37.3	33.3
Nausea/vomiting	4.3 ± 11.0	0	Teeth	48.1 ± 32.8	33.3
Pain	26.0 ± 28.2	16.7	Opening mouth	42.6 ± 39.4	33.3
Dyspnea	17.1 ± 22.3	0	Dry mouth	72.1 ± 29.9	66.7
Insomnia	34.9 ± 33.3	33.3	Sticky saliva	59.7 ± 36.8	66.7
Appetite loss	19.4 ± 31.1	0	Coughing	35.7 ± 35.2	33.3
Constipation	20.2 ± 26.4	0	Felt ill	42.6 ± 29.4	33.3
Diarrhea	9.3 ± 18.3	0			
Financial	15.5 ± 31.2	0			
Global health status/QoL	52.7 ± 24.2	50.0			

Abbreviations: EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; EORTC QLQ-H&N35 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, Head and Neck Cancer Questionnaire Module; Financial = financial difficulty; QoL = quality of life.

Table 3. Comparison of scores of quality of life dimensions between patients with and those without anxiety or depression

	Anxiety			Depression		
EORTC QLQ-C30	With	Without	*p* Value	With	Without	*p* Value
Functional scales	68.5 ± 18.8	86.5 ± 12.4	0.001	66.2 ± 18.8	86.0 ± 12.3	0.001
Physical	75.2 ± 21.4	90.3 ± 9.6	0.005	75.4 ± 22.8	88.1 ± 11.2	0.036
Role	72.7 ± 29.3	90.0 ± 19.8	0.030	70.2 ± 31.7	89.9 ± 17.2	0.022
Emotional	56.4 ± 25.6	86.3 ± 16.3	<0.001	55.7 ± 25.6	83.0 ± 19.7	<0.001
Cognitive	61.4 ± 30.2	81.7 ± 16.1	0.010	60.5 ± 27.3	79.7 ± 22.5	0.017
Social	73.8 ± 28.7	84.2 ± 21.3	0.198	65.7 ± 30.0	89.1 ± 15.6	0.006
Symptom scales	27.1 ± 15.9	11.4 ± 8.4	<0.001	29.5 ± 15.0	11.4 ± 8.9	<0.001
Fatigue	46.5 ± 26.0	27.8 ± 20.6	0.014	51.5 ± 26.2	26.1 ± 17.6	0.001
Nausea/vomiting	6.1 ± 13.2	0.8 ± 3.7	0.086	7.9 ± 14.0	.00 ± .00	0.025
Pain	36.4 ± 28.5	10.8 ± 14.6	0.001	32.5 ± 26.3	17.4 ± 24.4	0.062
Dyspnea	25.8 ± 25.1	8.3 ± 14.8	0.010	22.8 ± 15.9	13.0 ± 26.1	0.162
Insomnia	48.5 ± 32.1	18.3 ± 27.5	0.002	52.6 ± 33.9	18.8 ± 24.3	0.001
Appetite loss	21.2 ± 28.3	13.3 ± 29.4	0.381	29.8 ± 33.1	7.3 ± 20.0	0.015
Constipation	21.2 ± 30.1	16.7 ± 20.2	0.573	26.3 ± 30.6	13.0 ± 19.4	0.096
Diarrhea	13.6 ± 22.2	5.0 ± 12.2	0.124	15.8 ± 23.2	4.4 ± 11.5	0.061
Financial	24.2 ± 35.9	1.7 ± 7.5	0.008	26.3 ± 37.8	2.9 ± 9.6	0.016
Global health status/QoL	47.4 ± 26.8	61.3 ± 15.8	0.050	39.9 ± 22.0	65.6 ± 16.9	<0.001

Data presented as mean ± standard deviation.

Abbreviations: EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; Financial = financial difficulties; QoL = quality of life.

A series of stepwise linear regression analyses was performed, which demonstrated that physical distress symptoms of QLQ-C30 and physical functioning were the significant predictors of QoL (Table 5). Physical distress symptoms accounted for 52% of the variance in the final model, and physical functioning explained an additional 10.7% (F = 31.31, $p < 0.001$).

To predict depression, the five functioning dimensions and global health status/QoL variables were entered into the regression analysis. We found that the model explained 53.7% of the variance (F = 23.59, $p < 0.001$). Emotional functioning ($p = 0.001$) and social functioning ($p = 0.003$) were the significant predictors. For predicting anxiety, the model explained 58.1% of the variance (F = 35.64, $p < 0.001$). Emotional functioning and physical functioning were the significant predictors of anxiety (Table 6).

DISCUSSION

The present study investigates the QoL of post-radiotherapy NPC patients complicated with endocrinopathy, and its relationship with emotional status. The results demonstrate that emotional and cognitive functionings are significantly affected over other measures of function. The low mean

Table 4. Comparison of EORTC H&N-35 scores between patients with and without anxiety or depression

	Anxiety			Depression		
EORTC H&N-35	With	Without	*p* Value	With	Without	*p* Value
Symptom scales	41.18 ± 18.70	29.10 ± 16.17	0.041	44.66 ± 18.80	28.77 ± 15.18	0.007
Pain	9.85 ± 15.57	11.25 ± 13.59	0.759	11.84 ± 14.52	9.42 ± 14.72	0.596
Swallowing	39.02 ± 24.04	23.33 ± 25.16	0.045	42.11 ± 28.39	22.83 ± 19.50	0.013
Senses problems	28.03 ± 23.22	21.67 ± 27.63	0.422	30.70 ± 25.62	20.29 ± 24.60	0.188
Speech problems	34.34 ± 28.26	29.44 ± 30.00	0.589	42.69 ± 32.56	23.19 ± 22.45	0.034
Trouble with social eating	36.51 ± 30.45	20.83 ± 24.56	0.078	42.59 ± 34.29	18.12 ± 17.16	0.011
Trouble with social contact	22.86 ± 21.35	12.67 ± 18.59	0.112	29.63 ± 23.46	8.70 ± 11.62	0.002
Less sexuality	44.44 ± 37.76	25.93 ± 32.95	0.114	52.94 ± 40.50	22.72 ± 26.99	0.013
Teeth	54.55 ± 31.78	38.33 ± 31.11	0.103	57.89 ± 33.04	37.68 ± 28.96	0.041
Opening mouth	45.45 ± 40.56	36.67 ± 37.31	0.471	52.63 ± 42.04	31.88 ± 34.05	0.085
Dry mouth	77.27 ± 27.96	65.00 ± 31.48	0.188	75.44 ± 29.06	68.12 ± 30.94	0.437
Sticky saliva	63.64 ± 35.50	53.33 ± 38.08	0.370	66.67 ± 40.06	52.17 ± 33.07	0.206
Coughing	40.91 ± 36.99	26.67 ± 29.81	0.180	33.33 ± 33.33	34.78 ± 35.50	0.893
Felt ill	46.97 ± 30.27	35.00 ± 25.31	0.174	57.89 ± 29.06	27.54 ± 19.21	<0.001

Data are presented as mean ± standard deviation.

Abbreviations: EORTC QLQ-H&N35 = The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, Head and Neck Cancer Questionnaire Module.

Table 5. Multiple linear regression analysis of functioning, symptoms, and post-radiation time to global health status/quality of life

	Model	β-coefficient	SE	p Value	Adj. R^2
1	(Constant)	76.748	4.182	<0.001	
	Symptom scales*	−1.113	0.176	<0.001	0.520
2	(Constant)	27.543	15.204	0.079	
	Symptom scales*	−0.752	0.189	<0.001	
	Physical functioning	0.514	0.154	0.002	0.627

Abbreviations: Adj. = adjusted; EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; SE = standard error.
* Subscale of EORTC QLQ-C30.

Table 6. Multiple linear regression analysis of functioning dimensions and global health status/quality of life to emotional status

		BDI-II			
	Model	β-coefficient	SE	p Value	Adj. R^2
1	(Constant)	34.390	3.991	<0.001	
	Emotional functioning	−0.290	0.053	<0.001	0.429
2	(Constant)	40.980	4.167	<0.001	
	Emotional functioning	−0.199	0.056	0.001	
	Social functioning	−0.168	0.054	0.003	0.537

		BAI			
	Model	β-coefficient	SE	p Value	Adj. R^2
1	(Constant)	27.775	3.399	<0.001	
	Emotional functioning	−0.252	0.045	<0.001	0.435
2	(Constant)	41.923	4.717	<0.001	
	Emotional functioning	−0.219	0.039	<0.001	
	Physical functioning	−0.200	0.052	<0.001	0.581

Abbreviations: Adj. = adjusted; BAI = Beck Anxiety Inventory; BDI-II = Beck Depression Inventory−II; SE = standard error.

scores of emotional functioning are similar to those of previous studies (29, 30).

In this study, the median time point for the assessment of QoL after radiotherapy is 8.67 years, which was 5.9 years and 3.4 years in the studies by Huguenin and Cengiz, respectively (29, 30). This indicates that a lack of emotional well-being is a complication of radiotherapy that is long lasting and probably not easy to overcome.

Our subjects' cognitive functioning scores were relatively lower than those in the studies by Huguenin *et al*. (29), Cengiz *et al*. (30), and Chie *et al*. (18). The latter was conducted at the Department of Otolaryngology of the National Taiwan University Hospital, where the subjects did not have endocrinopathy. Memory impairment, intellectual deficits, and other cognitive problems in NPC patients after radiotherapy have been documented by previous researchers (9–11). From these studies, the median time for neuropsychologic dysfunction relating to temporal lobe radio-necrosis was about 5 years, whereas that for endocrine dysfunction was 8 years. In this study, the median time after radiotherapy was 8.67 years. Therefore, profound cognitive function impairment was highly correlated with cranial irradiation.

As to global health status/QoL, the mean scores were also remarkably lower (52.7 ± 24.2) as compared with previous studies that had similar irradiation dosages for NPC (18, 29, 30). Because our patients' cases were complicated by endocrine problems although these patients had been receiving hormonal therapy, the debilitating situation might explain their lower scores of emotional and cognitive functioning, as well as the global health status/QoL. The most severe symptoms were fatigue, insomnia, and pain, and the distressful symptoms specific to NPC patients were dry mouth and sticky saliva. These presentations were consistent with earlier studies (4, 5, 18, 29, 30).

From the BAI and BDI assessment, one third of patients had neither anxiety nor depression. Several studies using BDI to screen depression among cancer patients showed that the prevalence of depression was approximately 15% to 20% (24, 31–33). In the study by Fowler *et al*., 29% of gynecologic cancer patients showed significant anxiety using the BAI assessment (34). Compared with these, the higher percentage of depression and anxiety in our results indicate that our subjects' endocrinopathy probably contributed to their emotional status. Although our subjects received appropriate adrenal, thyroid, and gonadal hormone replacement therapy, 41 patients (95.4%) with growth hormone deficiency were reluctant to take growth hormone supplement because of the high cost of the treatment regimen and the inconvenience in terms of daily injection.

Physiologic effects of growth hormone deficiency in adults and the benefits of growth hormone replacement are well documented (35). As to the psychological impact, which includes decreased energy, increased tiredness, irritability, pain, depression, social isolation, and impaired QoL, these are demonstrated from many studies (36–39). Possible mechanisms by which growth hormone may improve QoL at the neural and somatic sites are being proposed and are still under investigation (36). Moreover, there is neuropsychological evidence that growth hormone deficiency is associated with cognitive impairment in adults and treatment with growth hormone can improve cognitive function (40–42). Therefore, growth hormone deficiency in our subjects may play an important role in psychological morbidity, impaired QoL, and cognitive function.

Patients with the complication of endocrinopathy have to be closely followed to monitor their physical condition and to examine their endocrine parameters, aside from hormonal therapy. Whether their frequent hospital visits reinforce their sick roles and affect their psychological well-being needs more exploration. A study by Chawla *et al*. regarding the temporal assessment of QoL in head-and-neck cancer patients receiving radiotherapy revealed that BDI scores increased during weeks 3 to 4 and were improved but not restored to pretreatment levels at 3 months post-radiotherapy (43). In this study, we did not assess our subjects at multiple time points, and the postradiation time did not contribute to the QoL as a result of the rejection by the regression model.

There was a strong association between emotional status and role functions and symptoms. Patients with anxiety or

depression demonstrated poorer functioning, especially emotional and cognitive functioning, global QoL, and more serious symptoms. As expected, depressive cases manifested more impaired social function. The significant symptoms reported also fitted the symptomatology of anxiety or depression. As to the relationship between QoL and emotional status, regression analysis revealed that impaired social functioning could explain depression in addition to the contribution of emotional functioning measured by EORTC QLQ-C30. Poorer physical functioning also accounted for anxiety, along with emotional functioning.

These results indicate the strong predictive power of emotional functioning in EORTC QLQ-C30 for psychological morbidity, which is consistent with the findings of Mystakidou *et al*. (44). However, our results highlight the predictive power of social functioning in depression and physical functioning in anxiety.

With regard to QoL, we focused on the global QoL because we were more interested in the dimensions that affected the patients' overall perception of QoL. Multiple regression analysis demonstrated stressful symptoms and physical functioning significantly predicted global QoL. This result was not compatible with a study conducted in Switzerland (29), in which NPC patients reported the highest morbidity on the H&N module although there was no great impact on global QoL. However, that study included only 12 NPC cases, and no further analysis was performed to verify the conclusions. As compared to the general population, the study conducted in Finland indicated that global QoL judgments were likely to be based on emotional status (45).

In the current study, we found that physical distress played a much more important role in the perception of QoL. These distressful symptoms might hamper physical functioning and lead to dissatisfaction with the QoL. However, the symptoms included in the EORTC QLQ-C30, but not in the H&N35 module, were strongly associated with global QoL. Although we closely examined the salient symptoms (*i.e*., fatigue, insomnia, pain), we thought these actually inferred several psychological components. Therefore, careful management of side effects after radiotherapy is important and masked depression and anxiety needs more careful attention from the clinician for early detection.

The limitation of this study is the specific recruitment of patients with endocrinologic complications. As such, our results only represent the QoL in a more serious or chronic group and cannot be generalized to all post-radiotherapy NPC patients.

Based on our findings here, several issues need to be explored. First, should sophisticated neuropsychological tests be used to verify the nature and magnitude of cognitive impairment after screening by EORTC QLQ-C30? Second, is the cognitive impairment solely due to late temporal lobe necrosis after irradiation or related to growth hormone deficiency? Third, does growth hormone replacement have beneficial effects to some or all cognitive functions and negative emotions?

Furthermore, the endocrinopathies that occur after radiotherapy should be considered a potential surrogate that could be helpful in the identification of patients who might be at risk for emotional distress. Early recognition is crucial and other surrogates should be sought. Routine application of the EORTC QLQ-C30 at multiple time points is suggested to help clinicians provide timely and effective therapy. Further large scale, sequential, and prospective investigations into the interrelationship among emotions, brain functioning, and endocrine markers are also highly recommended to elucidate the impact of irradiation.

CONCLUSIONS

In conclusion, NPC patients with post-radiotherapy endocrinopathy demonstrate impaired cognitive function and obvious negative emotions that are strongly associated with functional status, physical distress, and QoL. The different dimensions of EORTC QLQ-C30 seem to mirror depression or anxiety as measured by BDI or BAI, making it a potentially useful instrument for the early identification of patients at risk for difficulties and compromised QoL.

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