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ORIGINAL ARTICLE

Emotional distress in cancer patients at the beginning of chemotherapy and its relation to quality of life

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Summary

Purpose: *The present study sought to determine the prevalence of emotional distress and evaluate demographic and clinical factors related to anxiety and depression in treatment-naïve cancer patients at the beginning of chemotherapy. Another objective was to explore the associations between emotional distress and quality of life (QoL), an endpoint of great importance in current cancer care.*

Patients and methods: *Adult outpatients with a variety of cancer diagnoses were administered the Hospital Anxiety and Depression Scale (HADS) and the European Organization for Research and Treatment of Cancer (EORTC QLQ-C30) questionnaire prior to the initiation of treatment.*

Results: *A total of 265 patients took part in the study. A sizeable minority of our patients reported intense levels of anxiety (27.2%) and depression (19.6%). Patients without a partner, females, and patients with advanced disease or lower physician-rated performance status (PS) were more likely to experience clinically significant emotional distress. Levels of anxiety and mainly depression were negatively related to all QoL domains.*

Conclusion: *Our results indicate that a significant proportion of Greek cancer patients experience intense anxiety and depression prior to chemotherapy, and confirm the adverse impact of psychological morbidity on patients' QoL. Standardized and timely screening of emotional distress across all phases of cancer will help to effectively identify patients whose symptoms warrant attention. Future studies should continue to develop and evaluate rapid measures for detecting significant emotional distress in cancer patients, and to devise appropriate interventions to treat distress and enhance patients' QoL.*

Key words: cancer, emotional distress, HADS, prevalence, quality of life

Introduction

The onset of cancer is a powerful and traumatic stressor [1]. At the initial phase of the disease - diagnosis or beginning of treatment - a certain amount of emotional distress is considered as a normal reaction against the stressor [2]. In fact, absence of a reactive emotional response to a severe threat is believed to impede adjustment or recovery [3].

Not every patient with cancer experiences emotional distress to the same degree. However, a sizeable minority of patients experience or continue to experience persistent and intense levels of distress [4]. Anxiety and/or depression are the most common mental disorders among whole populations of cancer patients with estimated rates close to 25% of patients with severe and moderate symptomatology, and another 25% with mild symptomatology [4-7]. However, estimates range from a low of 1% to a high of almost 58%, depending on the methodology employed and the cancer populations studied [7-11]. Once emotional distress appears, it can be a long-term and persistent complication, which may last even for 10-20 years after treatment [10,12].

Despite the evidence of how common psychological distress is, it often goes undetected or underdi-

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agnosed [7,11,13,14]. It has been indicated that estimated rates of physicians' failure to detect depression and other psychiatric disorders range from 45% to as high as 90% [15,16]. There are 3 main reasons for this. First, somatic symptoms, especially of depression, are often mistaken for symptoms of cancer and its treatment [7,17]. Second, patients are often hesitant to report affective or emotional complaints to their doctors [4,11,12]. The final reason relates to the fact that doctors are often unskilled in psychosocial aspects of care, and they are reluctant to ask their patients about emotional problems [12,13]. In consequence, patients are denied proper management with adverse effects on QoL, adaptation or even disease course, not to mention the negative impact on the family and the institutional systems [7,17-19]. Moreover, highly distressed patients are less likely to register and assimilate important disease or treatment-related information provided by their doctors [16]. Although the evaluation of emotional functioning has long created a wealth of research, there is still a need for further studies about the prevalence and risk factors of clinically significant emotional distress in outpatients with different cancer types [7,20].

The first objective of this study was to evaluate the prevalence of anxiety and depression in chemotherapy-naïve Greek cancer patients shortly before the start of chemotherapy using a widely used brief screening tool of psychological morbidity. The second objective was to explore demographic and clinical factors associated with anxiety and depression, and thus identify patients at risk. The final objective was to examine the relations between emotional distress and QoL, an endpoint of great importance in current cancer care.

Patients and methods

This single-center, cross-sectional study was conducted at the Division of Oncology, Department of Medicine of the University of Patras Medical School (Rion, Greece) over a period of 2 years. Adult chemotherapy-naïve outpatients with a confirmed diagnosis of solid malignancy scheduled to commence chemotherapy with an Eastern Cooperative Oncology Group (ECOG) PS of 0 or 1 were approached shortly before their initial course of treatment and were invited to take part in the study. We approached chemotherapy-naïve patients so as to eliminate the potential effects of any prior treatment on patients' responses at study entry. Patients with brain metastases were excluded, as were those with pre-existing major neurologic or psychiatric problems. Also excluded were non-Greek patients and those who had a history of drug abuse. All eligible patients gave written informed consent before study entry according to our institutional guidelines.

A total of 265 patients who consented to participate were administered the questionnaires prior to the initial chemotherapy course in an office set aside especially for the purpose by a researcher who offered assistance when needed, and checked the answers for omissions. Sociodemographic data were elicited from patients and disease-related information was obtained from the treating physicians or from the hospital charts. The demographic and clinical characteristics of study participants are presented in Table 1.

Instruments

Psychological distress was assessed using the HADS [21], an internationally acceptable instrument for rating psychological morbidity in cancer patients [10,22]. The HADS consists of 14 items, 7 for anxiety (HADS-A) and 7 for depression (HADS-D). All items are based solely on the psychological symptoms of mood and anxiety disorders to the exclusion of somatic

Table 1. Demographic and clinical patient characteristics

Characteristic	*No. of patients*	*%*
All patients	265	100
Age, years		
Mean ± SD	58.1±11.4	
Educational level, years		
Mean ± SD	8.5±3.9	
Sex		
Male	110	41.5
Female	155	58.5
Marital status		
Married	220	83
Without partner (single, divorced, widowed)	45	17
Cancer diagnosis		
Breast	89	33.6
Colorectal	55	20.8
Lung (SCLC and NSCLC)	47	17.7
Genitourinary	32	12.1
Other	42	15.8
ECOG PS		
0	206	77.7
1	59	22.3
Disease		
Limited	140 (52.8)	52.8
Advanced	125 (47.2)	47.2

ECOG: Eastern Cooperative Oncology Group, PS: performance status, SCLC: small cell lung carcinoma, NSCLC: non small cell lung carcinoma, SD: standard deviation

symptoms. Each subscale is scored from 0 to 21. In accordance with Zigmond and Snaith, scores of 0-7 represent a noncase of anxiety and depression, 8-10 a doubtful or borderline case, and 11-21 a definite case. Cronbach's alphas were 0.90 for HADS-A and 0.88 for HADS-D.

Patient's QoL was obtained from the Greek version of the EORTC QLQ-C30 questionnaire [23]. This consists of 30 items, relating to 5 functional scales (physical, role, cognitive, emotional, and social function), 3 symptom scales (fatigue, pain, nausea and vomiting), a number of single-item symptom measures (constipation, dyspnea, insomnia, loss of appetite, diarrhea, financial impact of the disease), and a global health status/QoL scale. In accordance with the procedures recommended by the EORTC, raw scores were linearly transformed to values between 0 and 100. For the functional and global QoL scales, higher values indicate a better level of function. For the symptom/single-item scales, higher scores reflect more symptoms.

Statistical analysis

Data were analyzed using SPSS for Windows (version 11.0; SPSS Inc., Chicago, IL). Descriptive statistics were generated for all variables. Pearson correlation coefficients were calculated for possible relationships among continuous measures, and x^2 tests were used to evaluate associations among categorical variables. The one-way analysis of variance (ANOVA) was applied to compare means of continuous variables for 2 or more groups. All tests were two-tailed and statistical significance was set at $p < 0.05$.

Results

Prevalence of anxiety and depression

The first part of our analysis was concerned with the rates of emotional distress. For the anxiety subscale (HADS-A), 141 (53.2%) patients were noncases, 52 (19.6%) were borderline cases and 72 (27.2%) were definite cases. For the depression subscale (HADS-D), the corresponding figures were 176 (66.4%), 37 (14%) and 52 (19.6%), respectively.

Univariate associations between emotional distress, demographic and clinical characteristics

We next examined how patients' emotional distress varied with demographic and clinical characteristics. Univariate analyses failed to achieve statistical significance for age, educational level or cancer diagnosis. There were, however, significant effects for gender, marital status, disease extent and clinician-rated PS (Table 2). That is, female patients experienced significantly higher anxiety and depression than males, and were more likely to be probable cases of both anxiety and depression. Married patients reported lower levels of anxiety and depression compared with those who were single, divorced or widowed, and were less likely to be probable cases of anxiety and depression. Patients with advanced disease tended to be more depressed than their counterparts who had limited disease, and were also more likely to score above cutoff levels on the HADS-D subscale. Also, patients with a low PS described more symptoms of depression and were more likely to be probable cases than were those with a good PS.

Table 2. Mean scores and percentage of anxiety and depression cases (score ≥11) by demographic and clinical characteristics

	HADS-A			*HADS-D*			*HADS-A cases*		*HADS-D cases*	
Characteristic	*Mean*	*SD*	*p-value*	*Mean*	*SD*	*p-value*	*Percentage*	*p-value*	*Percentage*	*p-value*
Gender										
Male	6.4	4.1	0.000	6.1	4.0	0.011	16.4	0.001	13.6	0.039
Female	9.0	4.9		7.6	4.8		34.8		24.0	
Marital status										
Married	7.7	4.7	0.044	6.7	4.4	0.016	24.0	0.009	17.2	0.026
Without partner	9.2	5.1		8.5	5.1		43.2		31.8	
Disease										
Limited	7.5	4.7	0.10	6.2	4.4	0.005	23.0	0.095	13.6	0.009
Advanced	8.4	4.8		7.8	4.6		32.0		26.4	
ECOG PS										
0	7.7	4.8	0.12	6.5	4.5	0.001	25.7	0.32	15.5	0.002
1	8.8	4.7		8.8	4.2		32.2		33.9	

HADS-A: Hospital Anxiety and Depression Scale-Anxiety, HADS-D: Hospital Anxiety and Depression Scale-Depression, SD: standard deviation, ECOG: Eastern Cooperative Oncology Group, PS: performance status

Relationships between emotional distress and QoL

The final stage of our analysis used Pearson correlations and tested for all possible relationships between emotional distress and QoL. As can be seen in Table 3, HADS-A and HADS-D correlated negatively with the QLQ-C30 function scales and the global/health status scale, and positively with all the symptom scales. Overall, HADS-D was significantly more highly associated than HADS-A with the majority of QoL domains.

Discussion

The findings of the current observational study corroborate previous evidence that in the aggregate a sizeable minority of new cancer outpatients experience intense levels of anxiety (27.2%) and depression (19.6%) at the beginning of chemotherapy. The rates of symptomatology observed are in general comparable to those reported in previous research of outpatients with several cancer types [24], and furthermore, support the finding that anxiety is more frequently manifested in cancer patients than depression [22].

With respect to the identification of patients at risk, marked effects were noted for gender, marital status, disease extent and clinician-rated PS. Female patients were more prone to experiencing significantly higher levels of anxiety and depression than were male patients. This finding is in line with recent articles [11,20,22], and an explanation may be that women have generally been found to be more susceptible than men to psychiatric disorders, particularly when confronted with stressful life events [25]. In accordance with earlier studies, we also found that married patients experienced significantly less emotional distress than those without a partner [11,18]. This is possibly attributable to the fact that marriage exerts a health-protective effect on its members by means of increased material resources, psychosocial support and control of health-damaging behaviors [26]. Confirming earlier studies, patients who had advanced disease and a lower PS were more likely to be depressed than those with limited disease and a higher PS [20,27-29]. The final finding emerging from this study was that anxiety and mainly depression were significantly associated with all QoL dimensions, adding further evidence on the deleterious impact of psychological morbidity on cancer patients' QoL [6,7,30,31].

Emotional distress has recently been recognized as the 6th vital sign in cancer care, which should be closely monitored and treated along with the other 5 vital signs, namely temperature, respiration, heart rate, blood pressure, and pain [32]. Many of the patients in the current study experienced intense levels of anxiety and depression shortly before the initiation of chemotherapy. As noted earlier, once emotional distress appears, unless properly treated, it can be a long-term complication, which, beyond its detrimental effects on QoL, may also hamper treatment adherence, impede

Table 3. Correlations between emotional distress and QoL domains

EORTC QLQ-C30	*HADS-A*	*EORTC QLQ-C30*	*HADS-D*
Physical function	−0.37***	Physical function	−0.55***
Role function	−0.25***	Role function	−0.43***
Cognitive function	−0.43***	Cognitive function	−0.43***
Emotional function	−0.74***	Emotional function	−0.62***
Social function	−0.48***	Social function	−0.64***
Fatigue	0.38***	Fatigue	0.54***
Nausea/vomiting	0.18**	Nausea/vomiting	0.20**
Pain	0.23***	Pain	0.33***
Dyspnea	0.26***	Dyspnea	0.30***
Sleep disturbance	0.33***	Sleep disturbance	0.34***
Appetite loss	0.20**	Appetite loss	0.41***
Constipation	0.17**	Constipation	0.26***
Diarrhea	0.18**	Diarrhea	0.13*
Financial impact	0.19**	Financial impact	0.17**
Global health status/QoL	−0.48***	Global health status/QoL	−0.68***

QoL: quality of life, EORTC: European Organization for Research and Treatment of Cancer, HADS-A: Hospital Anxiety and Depression Scale-Anxiety, HADS-D: Hospital Anxiety and Depression Scale-Depression
*$p \leq 0.05$, **$p \leq 0.01$, ***$p \leq 0.001$

recovery and increase mortality [7,17,18]. The implication of our findings is that routine and timely screening of emotional distress throughout the course of disease is mandatory, because it will contribute to identifying as quickly as possible those patients for whom pharmaceutical management and/or psychological intervention may be most warranted and salutary.

However, our results must be set in the context of one methodological consideration relating to the use of HADS. The HADS is a screening rating scale and not a diagnostic instrument of distress. Perhaps, a standardized psychiatric clinical interview, such as the Structured Clinical Interview (SCID) according to the Statistical Manual of Mental Disorders (DSM-IV) [33], might have produced lower prevalence rates of clinically significant distress, although this would require considerably more time and resources in a busy oncology clinic. Nonetheless, our experience with HADS has been positive over the years, and it has now become the screening tool of choice in our center. As cancer care is increasingly administered on an outpatient basis, further studies should test and validate new rapid instruments of emotional distress in the Greek setting, one of those being the National Comprehensive Cancer Network (NCCN) Distress Thermometer, which has recently been introduced into the armamentarium of clinical cancer research and practice with really promising results [34-36]. Finally, it would be helpful if future studies use common cut-off scores of severity of distress within the same scales to allow meaningful comparisons among them [20].

In summary, the results of this study indicate that quite a few outpatients with a variety of cancer diagnoses experience clinically significant distress levels at the beginning of chemotherapy. Risk factors for increased distress were being female, having no partner, and having advanced disease or low PS. Levels of anxiety and mainly depression were negatively correlated with QoL. Standardized screening of emotional distress will help to effectively identify patients whose symptoms warrant attention. Future studies should continue to develop and evaluate measures for detecting significant emotional distress in cancer patients, and to devise appropriate multicomponent interventions to treat distress and enhance patients' QoL.

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