The Impact of Radiotherapy on Symptoms, Anxiety and QoL in Patients with Cancer

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Abstract. *Aim: To evaluate prospectively disease- and treatment-related symptoms, anxiety and quality of life (QoL), in patients with different types of cancer undergoing external-beam radiotherapy (RT) and examine the relationship among them, at baseline and at the end of the treatment. Patients and Methods: This study included 90 patients with cancer. Patients' QoL was evaluated using the Linear Analog Scale Assessment (LASAs) questionnaire, anxiety was measured with the Spielberger state and trait inventory (STAI), while symptoms were assessed using the MD Anderson Symptom Inventory (MDASI). The assessments were carried-out at baseline and at the end of RT. Results: At baseline, the QoL scores were reduced (7.5±6.5) and MDASI elevated (2.35±1.7). Patients' QoL was correlated with symptoms (r=–0.684, p=0.0005). A correlation was found between STAI-trait with MDASI scores (r=0.214, p=0.046). At the second assessment, there were significant correlations between MDASI and QoL (r=−0.68, p=0.0005). The STAI-trait had a moderate correlation with MDASI score (r=0.43, p=0.0005) and with QoL (r=−0.253, p=0.0017). Conclusion: The present study showed a significant impact of symptoms and high levels of anxiety following RT, which correlated with a compromised QoL. The worsening in patients' perception of their QoL did not seem to lead to a significant reduction in daily activities or treatment tolerance.*

Radiation therapy (RT) is an integral part of cancer management: 30 to 50% of all patients with cancer receive irradiation, either alone or in combination with surgery and chemotherapy (1-4). The aims of cancer treatment are to cure and when there is little or no chance to do so, to prolong and maintain the quality of life (QoL) to a feasible extent (5). All treatment modalities may result in long-term and often in permanent morbidity due to side-effects (4).

The concern regarding symptoms from oncological treatment and the possible adverse effects on patients' behavioural reactions have increased following improvement in the efficacy of oncological treatment (2). The variety of reported symptoms, such as nausea, vomiting, fatigue, skin changes and diarrhoea, may be due to cancer itself or due to the therapy received (5, 6).

Mood disorder may obviously be part of the reaction to the news of a cancer diagnosis, but in many patients it will persist, causing an added burden during treatment and leading to difficulties in providing general management and symptom control (7). The experience of living with cancer from the time of diagnosis and treatment decisions, through treatment itself and survival is fraught with psychological distress (6).

Investigating the impact of cancer treatments on QoL is a two-tailed enterprise in which treatment toxicity is balanced not only against survival duration but also against post-treatment function and well-being (8,9). Treatment strategies are therefore directed not only at increasing the chances of cure, but also at diminishing the impact of treatment on QoL (3). Health-related QoL is a multidimensional construct that reflects the impact of illness and treatment on the physical, psychological, social and functional dimensions of well-being relatively to one's current and future expectations (6, 10, 11).

The present study prospectively evaluated symptoms, anxiety, and QoL in patients with different types of cancer scheduled to undergo external beam RT on an outpatient basis and aimed to examine the relationship among them at two time periods: baseline and at the end of the treatment.

Patients and Methods

The study included 100 consecutive Greek patients with cancer who were referred to the Radiotherapy Department for RT. Patients were eligible to enter the study if they fulfilled the following criteria: presence of histologically-confirmed malignancy, age >18 years,

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ability to communicate effectively with the study personnel, and knowledge of disease diagnosis. All the patients were treated with curative intent and the daily dose of RT was less then 3 Gy.

Exclusion criteria were the following: a history of drug abuse, a diagnosis of psychotic disease, or significant cognitive impairment. Out of 100 patients, 10 (10%) refused to complete treatment or the assessment tools, thus they were excluded from the study. Therefore, 90 patients were finally recruited for the study. Ethical approval was obtained from the Regional Ethical Committee of Aretaieion Hospital (Approval Number: M56, 10-7-2007). Recruitment occurred between January 2007 and August 2007. All patients were informed of the nature of the study and signed an informed consent form.

Procedure and measurements. Eligible patients were asked to participate in the study on the day of the first outpatient appointment for treatment. All patients were interviewed by a member of the team in order to elicit their background medical history, including demographic data. Evaluation was completed with a brief interview. Those who agreed to participate were asked to complete three measures (Linear Analog Self-Assessment (LASA), M.D. Anderson Symptom Inventory (MDASI) and Spielberger State and Trait Inventory (STAI)) questionnaires at baseline and when the therapy was completed. A clinician-rated instrument focusing on performance status measured patients' overall physical functioning, as defined by the Eastern Cooperative Oncology Group (ECOG) (0=optimum performance status, 4=worst performance status) (12). Patients with an ECOG score of 0 or 1 were categorized as having 'good' performance status, and those with a score of 2 or 3 were categorized as having 'moderate to poor' performance status. All side-effects (leukopenia, blood toxicity, anorexia, nausea, skin desquamation, erythema, diarrhoea, polyuria) were coded from the Common Toxicity Criteria (CTC; grades range from 1=mild to 5=death) (12).

Measures. Participants were asked to complete the following self-reported scales at two time points: at the beginning of RT and the day after the completion of RT.

The MDASI is a brief measure of the severity and impact of cancer-related symptoms (13). It consists of 15 core symptom items. Each symptom is rated on an 11-point scale (0-10), in order to indicate the presence and severity of the symptom (0='not present' and 10= 'as bad as you can imagine' in the previous 24 h). It also includes six interference symptoms regarding the function of a patient's life in the previous 24 h. The interference items are also measured on scales from 0 to 10, (0='did not interfere' and 10= 'interfered completely') (13). The questionnaire has been validated in a sample of Greek patients with cancer, showing satisfactory psychometric properties (11).

The STAI (14) was used to identify the probable causes of anxiety. It comprises of two self-report scales for the measurement of two distinct anxiety concepts: state and trait anxiety. State (current or situational) anxiety is considered a transitory emotional state, while trait anxiety (general) is related to relatively stable individual characteristics in proneness to anxiety. Each scale contains 20 statements regarding how respondents feel at a particular moment in time (state-anxiety) and about how they generally feel (trait-anxiety) (14). A cut-off of 40/41 was employed, because each scale of the questionnaire has 20 statements (15). The Greek version of STAI was used in the current study (16, 17).

The LASA is a self-report questionnaire consisting of three visual analogue scales to assess the continuum of selected energy, daily function and QoL, graded from 0 ('as bad as it can be') to 10 ('as good as it can be') (18, 19).

Table I. *Information on patients' sociodemographic and clinical characteristics*.

Variable	Value	
Age, mean±standard deviation (min-max): 61.17±13.77 (18-87)		
	N	Percentage
Male	41	45.6
Female	49	54.4
Education		
Primary	27	30
High school-university	63	70
Family status		
Married	73	81.1
Single/divorced	17	18.9
Cancer diagnosis		
Breast	29	32.2
Urogenital	27	30
Lung	16	17.8
Gastrointestinal	18	20
Metastasis		
No	80	88.9
Yes	10	11.1
Relapse		
No	74	82.2
Yes	16	17.8
Chemotherapy		
Yes	45	50
No	45	50
Homotherapy		
Yes	52	57.8
No	38	42.2
Surgery		
Yes	28	31.1
No	62	68.9

Statistical analysis. Basic descriptive statistics were computed for sociodemographic variables, means, standard deviations, and ranges for all scale variables measured in the study (STAI, MDASI, LASA).

Spearman's rank correlation coefficient and *t*-tests or analysis of variance were calculated, in order to examine the univariate associations between anxiety, symptom distress, energy, daily functions, and QoL at baseline, as well as at the end of RT. The association of the quantitative variables with RT was calculated with *t*-test or analysis of variance.

All statistical analysis was performed using IBM SPSS version 15.0 for Windows, Chicago, USA.

Results

Descriptive analysis. Out of 90 patients, 41 (45.5%) were male and 49 (54.5%) were female. The average age was 61.17 years (range=19-89 years). Information on patients' sociodemographic and clinical characteristics is shown in Table I.

Table II. *Relationships between Linear Analog Scale Assessment (LASA) measures and MD Anderson Symptom Inventory (MDASI) components, and Spielberger State and Trait scores.*

		MDASI		Spielberger	
LASA		Symptoms	Interference	State	Trait
Baseline (pre-treatment period)					
Energy	r	–0.612	–0.490	–0.056	–0.160
	p-Value	<0.0005	<0.0005	NS	NS
Daily function	r	–0.608	–0.545	–0.084	–0.160
	p-Value	<0.0005	<0.0005	NS	NS
QoL	r	–0.560	–0.490	–0.021	–0.130
	p-Value	<0.0005	<0.0005	NS	NS
End of RT					
Energy	r	–0.690	–0.602	0.022	–0.298
	p-Value	<0.0005	<0.0005	NS	0.005
Daily function	r	–0.629	–0.632	0.005	–0.284
	p-Value	<0.0005	<0.0005	NS	0.007
QoL	r	–0.684	–0.667	0.015	–0.253
	p-Value	<0.0005	<0.0005	NS	0.017

NS: Not significant . QoL: Quality of Life .

A total of 84% of the patients at the two assessed times (baseline and at the end of radiotherapy treatment) had ECOG scores of 0-1, while 15% of the patient had an ECOG score of 2-3.

After the completion of the RT many side-effects were reported, such as skin desquamation and moderate erythema in 76.7% of the patients. Moreover, anorexia was apparent in 20% of the patients, nausea in 20% and 37.8% of the patients had diarrhoea. Furthermore, 12.2% of the patients exhibited polyuria, dysuria and nocturia. Leucopenia and blood toxicity was observed in 12.2%, but no packed cell transfusion was required. All adverse effect grades were between 1 and 2 (mild to moderate). Means for the MDASI symptom scores at baseline and after RT were 1.67 (±1.6) and 2.35 (±1.7), respectively.

Mean energy, daily function and QoL scores were 6.8 (±1.8), 6.8 (±2.2), and 7.5 (±6.5) respectively, and at the second measurement were 5.6 (±1.6), 5.7 (±1.9), and 6.7 (±1.8) respectively. STAI questionnaire for state had a mean score of 51.4 (±6.5) and for trait of 45.1 (±6.5) at baseline, while at the second measurement, the mean scores were 53.09 (±6.6) and 47.0(±5.6), respectively.

Univariate analysis. Table II shows the relationships between the assessed measurements at baseline. Our findings revealed a high statistically significant negative association between distressing symptoms, energy (r=–0.61, p=0.0005), QoL (r=–0.56, p=0.0005), and daily function (r=–0.60, p=0.0005).

QoL had a statistically significant negative correlation with performance status (r=–0.55, p=0.01).

For the second measurement (Table II), the distressing symptoms of the MDASI were strongly correlated with anxiety and QoL components. More specifically, a high statistically significant negative association was found between distressing symptoms and energy (r=–0.69, p=0.0005), as well as with QoL (r=–0.68, p=0.0005), and daily function (r=–0.62, p=0.0005). As far as the Spielberger trait is concerned, a moderate correlation was found with distressing symptoms (r=0.43, p=0.0005) and a low but statistically significant negative correlation with energy (r=–0.29, p=0.005), QoL (r=–0.25, p=0.002), and daily function (r=–0.28, p=0.007).

After the end of RT, the most common side-effects were dermatic, upper and lower gastrointestinal–such nausea, vomiting and diarrhoea– and urogenital, such as dysuria and polyuria (data not shown).

Discussion

Radiotherapy is a long-lasting treatment given for patients who have frequently not recovered from the optimal psychological and physical conditions from other treatments (3, 8). Additionally, a cluster of symptoms can be an additional source of emotional and physical distress, leading to changes in a patient's QoL (5, 7, 20).

In the current study, we prospectively evaluated performance status, disease- and treatment-related symptoms, anxiety and QoL in patients with different types of cancer undergoing external-beam RT.

QoL, energy and daily function were lower at the end of the treatment than at the baseline. Furthermore, QoL in particular appeared to be the most negatively affected at the end of the treatment, in comparison to energy and daily function. It seemed that although RT could provide a long life expectancy, it might also worsen the patient's quality of life and well-being. The results appeared to coincide with previous findings, which also identified lower QoL, physical well-being and functional status after RT (4, 8, 10, 21-24). On the other hand, some studies reported that patients who received external beam RT had no significant changes in daily activities during the treatment course (8, 21).

The results showed that there were statistically significant correlations between distressing symptoms and QoL, energy and daily functions as high or scores of symptoms showed a decrease in QoL and low functional ability at baseline, consistent with previous findings (25-27). Furthermore, there was an association between anxiety and distressing symptoms at baseline. The sources of anxiety are multiple and differ between individuals. Fears related to the disease and its outcome are common and might result in expressing anxiety (24). This gives weight to the argument for the screening and detection of psychopathological comorbidity in patients with cancer (25, 26).

The present study showed a significant impact of symptoms after RT on patients' QoL and a significant association between patients' anxiety and their QoL. The severity of symptoms following RT correlated with a compromised QoL and levels of anxiety. Symptom complications such as fatigue, sleeplessness, pain, and diarrhoea following RT were significantly associated with a poor QoL and high levels of anxiety. Contrary to our findings, in recent studies, it was reported that symptoms were increased at the end of RT, but there was no relationship between them and QoL nor performance status (8, 25).

Adverse physical symptoms impose restrictions on functional status and contribute to a decrease in daily activities of patients with cancer (3, 20, 23, 28). The symptoms of pain and fatigue were found to be associated with a greater number of concurrent symptoms, such as fever, dyspnoea, trouble sleeping, nausea, appetite loss, weight loss, and functional impairment (29). Patients who experienced symptoms reported a poorer physical well-being and functional status in the study periods compared with the pre-treatment period, results that our present findings concur with (8).

On the other hand, in other studies, the worsening in QoL perception did not lead to any significant reduction in daily activities or treatment tolerance. It might be hypothesized that psychological and physical adaptation to treatment-related changes is the result of a complex of reciprocally influencing factors such as age or information about side-effects (21).

Furthermore, anxiety was greatest when patients had the worst performance status. Anxiety was also related to bodily pain. Psychological symptoms had a greater effect on patients' QoL and distress than disease status, but were less frequently treated (6). Psychological problems present issues beyond merely poor QoL. Frick *et al.*'s study found that there was a weakly-positive correlation between anxiety and QoL (25), a result that our study agrees with.

There are number of limitations to this study. The first is that it was a comparatively small sample and, therefore, we cannot draw firm conclusions from our findings. Therefore, one important suggestion as to future research in this area is to collect data from larger samples. The second drawback is that many of the patients had already received another treatment, such as hormone therapy, chemotherapy and surgery, prior to entry into the study. It is possible that some of the changes that were detected after RT were simply due to delayed effects of these other treatments. In order to minimize this risk, patients were only included in the study if they had completed chemotherapy at least one month before starting RT. Although it would have been preferable only to study patients in whom RT was the sole treatment, this would not have been very practical given the current vogue for combined therapies.

In conclusion, symptom complications after RT were significantly associated with a poor QoL and high levels of anxiety. Enhanced understanding of the common symptoms, psychological concerns and QoL of patients with serious illness can help improve the clinical care of these patients (30). By this way, it is possible that we may be able to combat treatment toxicities (*e.g.* fatigue, nausea, pain and other symptoms) and enhance QoL more effectively. We believe that any effort aiming to improve QoL and to treat symptoms in patients with cancer may be a direct way to lessen patient suffering. The implication of this study is that cancer patients receiving RT have highest risk of decline regarding their QoL and express high levels of anxiety. Therefore, it may be a rational approach to assess QoL, symptoms and anxiety periodically, so as to be able to intervene any decline in any dimension of QoL, as soon as possible. In this sense, this study identifies various clinical features associated with improvement in QoL and symptoms during RT. In addition, it makes a recommendation toward regular monitoring of QoL, symptoms and anxiety in patients with cancer. Management of symptoms requires a team approach. Understanding the factors influencing patients' well-being enables healthcare professionals to tailor interventions more effectively towards the relief of physical symptoms and distress (22, 29). Because the side-effects of treatment will continue after treatment, a longer follow-up with nutritional assessment, symptom control with medication, antidepressive/anxiolytic medications should be given to patients with cancer (2, 20, 23). Psychotherapeutic interventions are required to help these patients to anticipate a better future (25). Meanwhile, thorough pre-treatment information may enable patients to cope better with subjective toxicity, as symptoms and their anxiety may be better tolerated when they are anticipated.

Our findings needed to be validated in a randomized trial to effectively address the issues of heterogeneity across

groups. Future studies are required to better elucidate the associations of symptoms, anxiety and QoL in a homogenous sample of patients in RT units.

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