

Original Article

The Relationship Between Cancer-Related Fatigue and Patient Satisfaction with Quality of Life in Cancer

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Abstract

Fatigue affects a majority of patients undergoing cancer-related therapies. We conducted a study of 954 adult cancer patients presenting for treatment at our hospital between April 2001 and November 2004 to quantify the relationship between fatigue and patient satisfaction with quality of life (QoL). Fatigue was measured using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire fatigue subscale. Patient satisfaction with QoL was measured using the Ferrans and Powers Quality of Life Index (QLI). The relationship between fatigue and QLI was evaluated using univariate and multivariate linear regression after controlling for the effects of clinical and demographic factors. Of the 954 patients, 579 were females and 375 males, with a median age at presentation of 56 years (range 20–90 years). Sixty-six percent had failed prior treatment. The most common cancers were breast (26%), colorectal (19%), and lung (16%) cancers. After controlling for the effects of age and prior treatment history, every 10-unit increase in fatigue was statistically significantly associated with 1.5-, 0.22-, 0.77-, 0.27-, and 0.85-unit declines in QLI health and physical, social and economic, psychological and spiritual, family, and global function scores, respectively. Consequently, a 30-point increase in fatigue score correlates with a 4.5-point decline in QLI health functioning—a clinically significant decline. In our study, we found that fatigue is strongly associated with patient satisfaction with QoL independent of the effects of age and prior treatment history. J Pain Symptom Manage 2007;34:40–47. © 2007 U.S. Cancer Pain Relief Committee. Published by Elsevier Inc. All rights reserved.

Key Words

Fatigue, quality of life, cancer

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Introduction

Fatigue is the most frequently reported symptom in cancer patients.^{1–6} An estimated 60%–96% of cancer patients undergoing treatment experience fatigue, including 60%–93% of patients on radiotherapy and 80%–96% of patients on chemotherapy.^{3,7} There is no commonly agreed upon definition of fatigue, and one of the most accepted ones is that provided by the National Comprehensive Cancer

Network, which defines cancer-related fatigue (fatigue) as a common, persistent, and subjective sense of tiredness related to cancer or to treatment for cancer that interferes with usual functioning.³

Quality of life (QoL) is a significant concern for cancer patients, and its disruption is often associated with symptoms such as fatigue, insomnia, and psychological distress.⁸⁻¹² Several studies have demonstrated the adverse impacts of fatigue on physical, emotional, economic, and social aspects of cancer patients' lives.^{8,13-18} In a study of 1,957 breast cancer survivors, fatigue, measured by the RAND 36-Item Health Survey, was found to be significantly associated with high levels of depression, pain, and sleep disturbance.¹³ In a study conducted in a group of cancer patients undergoing radiotherapy, fatigue, measured by the Multidimensional Fatigue Inventory (MFI-20), was associated with poor QoL. This association was considerably lower before treatment than at post-treatment or follow-up assessment, suggesting that fatigue becomes most important when treatment has ended.¹⁶ In a study of 60 patients with uterine cancer treated at a university hospital in Sweden, fatigue, measured by MFI-20 and the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ-C30) fatigue subscale, was found to be significantly associated with global QoL.⁸ In a study conducted in 54 patients receiving adjuvant chemotherapy for breast cancer, fatigue, measured by the Fatigue Scale from the Profile of Mood States and Fatigue Symptom Inventory, showed strong significant correlations with emotional upset, muscle weakness, pain, numbness, sleep problems, problems with concentration, and heartburn before the start of chemotherapy.¹⁵ In a study of 61 women with breast cancer who had completed adjuvant chemotherapy, fatigue was significantly associated with poorer sleep quality, more menopausal symptoms, and presence of a psychiatric disorder.¹⁴ In another study conducted in 171 outpatients with advanced lung cancer, fatigue was found to interfere with at least one daily life activity in more than half the patients. Fatigue predominantly interfered with physical activities such as walking and work.¹⁷

While the above studies suggest an inverse association between fatigue and QoL in

cancer, several methodological features of these studies limit the conclusions that can be drawn about the impact of fatigue on patient QoL. The above studies have predominantly evaluated the relationship between fatigue and QoL using univariate correlation coefficients without accounting for the clinical and demographic factors that might influence QoL. Most studies have used a variety of QoL assessment tools that primarily measure the activities of daily living,^{8,13,19} and, to our knowledge, there is no study that has evaluated the relationship between fatigue and patient satisfaction with QoL. A QoL tool that takes into account patient satisfaction or dissatisfaction with the areas of life that are valuable to the patient is important considering the fact that different people have different values, which causes aspects of life to vary in their impact on QoL. Finally, a small sample size^{8,14,15,19} in some of the above studies makes it difficult to detect small to modest associations between fatigue and QoL.

The present study was conducted to evaluate and address each of the major limitations in prior research. This study evaluates the quantitative relationship between fatigue and patient satisfaction with QoL using standardized assessment tools in a large heterogeneous sample of 954 cancer patients after controlling for the clinical and demographic predictors of QoL.

Methods

Study Population and Procedures

The study cohort was made up of a consecutive series of 954 patients who presented and were later treated at the Cancer Treatment Centers of America® at Midwestern Regional Medical Center between April 2001 and November 2004. Patients were contacted for participation in the quality of life study at their first visit to the hospital. The inclusion criteria for participation in this investigation were a histological diagnosis of a neoplastic disease and the ability to read English. Patients with any tumor type and stage of the disease were eligible for the study. Patients were excluded if they were unable or unwilling to give informed consent or were unable to understand or cooperate with the study conditions. A trained clinical coordinator described the study and

determined eligibility after patients signed in at the clinic. As part of the consent process, patients were assured that refusal to participate in the study would not affect their future care in any way. Eligible patients were presented with the questionnaires at their initial visit and returned their completed questionnaires to the clinical coordinator within 24 hours. Patients filled in the questionnaires before they had the opportunity to undergo therapy. The study was approved by the Institutional Review Board at Midwestern Regional Medical Center.

Assessment of Fatigue and Patient Satisfaction with QoL

Fatigue was assessed using the fatigue subscale of the EORTC QLQ-C30. The QLQ-C30 incorporates five functional scales (physical, role, cognition, emotional, and social), nine symptom scales (fatigue, pain, nausea/vomiting, dyspnea, insomnia, loss of appetite, constipation, diarrhea, and financial problems), and a global health status/QoL scale. The fatigue subscale in the QLQ-C30 is represented by the following three items: "During the past week: 'Did you need to rest?,' 'Have you felt weak?,' and 'Were you tired?,'" Each item is answered on a four-point scale of "Not at all," "A little," "Quite a bit," and "Very much." The raw scores were transformed into a total score ranging from 0 to 100 as instructed in the EORTC QLQ-C30 scoring manual. Lower fatigue scores indicate lower fatigue, while higher scores indicate worse fatigue. The QLQ-C30 is valid, reliable, and sensitive²⁰⁻²² and is one of the most commonly used QoL questionnaires in cancer research. The fatigue scale of the QLQ-C30 provides a useful approach to assessing this important symptom.²³

Patient satisfaction with QoL was assessed using the Ferrans and Powers Quality of Life Index (QLI). The QLI measures global QoL as well as the QoL in four major subscales: health and physical, social and economic, psychological and spiritual, and family. Each subscale includes questions on patient satisfaction as well as personal importance of the domain. Each question on satisfaction with a particular aspect of life is later followed by a question on the importance of that aspect of life. For example, the question "How satisfied are you with your health?" under the satisfaction section

of the questionnaire is accompanied by the question "How important to you is your health?" under the importance section of the questionnaire. Ratings are made on a 1-6 scale ranging from very dissatisfied/unimportant to very satisfied/important. Patient satisfaction with various areas of life is calculated and interpreted in view of their perceived importance. This weighting adjusts for the influence of individual values and thus produces a more accurate reflection of QoL. All scores range from 0 to 30, with higher scores indicating a better QoL. This questionnaire is valid, reliable, and sensitive and has been used in many studies involving cancer patients.²⁴⁻²⁷

Data Analysis and Statistical Methods

All data were analyzed using SPSS Version 11.5 (SPSS Inc., Chicago, IL). Means, medians, and standard deviations of all QLI subscales were calculated. The relationship between the QLQ-C30 fatigue subscale and patient satisfaction with QoL was evaluated using univariate and multivariate linear regression. The primary independent variable was the QLQ-C30 fatigue subscale. The primary outcome variable was the QLI. Since the QLI had four functioning subscales and one global subscale, each one of those subscales was treated as an outcome variable in separate analyses. The following demographic and clinical variables were evaluated, using univariate regression analysis, for their association with QLI: age at first presentation to our hospital (current age), gender, prior treatment history, and stage of tumor at diagnosis. The prior treatment history variable categorized the patients into those who had received definitive cancer treatment elsewhere before coming to our institution and those who were newly diagnosed. Stage at diagnosis was categorized into two groups: Stages I and II (early disease) and Stages III and IV (late disease). The current age was used as a continuous variable. Multivariate linear regression analyses were then performed to evaluate the joint predictive significance of fatigue and those clinical and demographic factors that were shown to be significant on univariate analyses. A test was considered to be statistically significant if the *P*-value was less than or equal to 0.05.

Results

Patient Characteristics

Of the 954 patients, 579 were females and 375 males, with a median current age of 56 years (range 20–90 years). Sixty-six percent had failed prior treatment before coming to our hospital. The most common cancers were breast (26%), colorectal (19%), and lung (16%) cancers. At the time of this analysis, 588 patients were alive and 366 had expired. Table 1 describes the baseline characteristics of our patient cohort in greater detail. Table 2 describes the means, medians, and standard deviations of the QLI subscales. The health and functioning subscale had the lowest mean score of 15.8, while the highest mean score of 24.2 was recorded for the family functioning. The mean, median, and standard deviation for the QLQ-C30 fatigue subscale were 45.5, 33.3, and 28.4, respectively.

Univariate Regression Analysis

Table 3 describes the results of univariate linear regression analysis using the QLQ-C30 fatigue subscale as the independent variable and QLI subscales as the dependent variables. The change in QLI scores for every 10-unit increase in fatigue scores, along with the respective 95% confidence intervals, is shown. We found that every 10-unit increase in fatigue was statistically significantly associated with

Table 2
Baseline QLI Scores of the 954 Cancer Patients

Subscale	Mean	Median	Standard Deviation
Health and Functioning	15.8	16.1	6.8
Social and Economic	21.2	21.8	4.2
Psychological/Spiritual	20.6	21.7	6.3
Family	24.2	25.2	5.3
Global	19.4	19.7	4.7

1.6-, 0.25-, 0.84-, 0.29-, and 0.90-unit decreases in QLI health and physical, social and economic, psychological and spiritual, family, and global function scores, respectively. Also, fatigue accounted for 43%, 2.8%, 14.5%, 2.3%, and 29.4% of the total variance in QLI health and physical, social and economic, psychological and spiritual, family, and global function scores, respectively. Table 4 describes the change in QLI scores for every 10-year increase in current age. We found that every 10-year increase in current age was statistically significantly associated with 0.75-, 0.63-, 0.95-, and 0.67-unit increases in QLI health and physical, social and economic, psychological and spiritual, and global function scores, respectively. Table 5 describes the differences in QLI scores between newly diagnosed patients and those who had failed definitive treatment elsewhere before coming to our hospital. As expected, all mean QLI subscale scores were significantly higher (better) among newly diagnosed patients. Similar comparisons were made for gender, and no significant differences in QLI scores were observed except for the family subscale (Table 6). Similar analysis involving stage at diagnosis revealed no significant associations except for the family subscale (Table 6).

Multivariate Regression Analysis

Table 7 describes the results of multivariate linear regression analysis using the QLQ-C30 fatigue subscale as the independent variable and QLI subscales as the dependent variables after controlling for the effects of current age and prior treatment history, the two variables found significant upon univariate analysis. We found that every 10-unit increase in fatigue was statistically significantly associated with 1.5-, 0.22-, 0.77-, 0.27-, and 0.85-unit declines in QLI health and physical, social and economic, psychological and spiritual, family,

Table 1
Baseline Characteristics of the 954 Cancer Patients

Characteristic	Categories	n	%
Current age (years)	Mean	55.7	
	Median	56	
	Range	20–90	
Gender	Male	375	39.3
	Female	579	60.7
Tumor site	Breast	251	26.3
	Colorectal	177	18.6
	Lung	156	16.4
	Pancreas	55	5.8
	Prostate	43	4.5
	Other	272	28.5
Tumor stage at diagnosis	Stage I	89	9.3
	Stage II	181	19.0
	Stage III	194	20.3
	Stage IV	291	30.5
	Unknown	199	20.9
Treatment history	No treatment history or newly diagnosed	322	33.8
	Prior treatment history	632	66.2

Table 3
Impact of 10-Unit Increase in Fatigue Score on Patient Satisfaction with QoL

QLI Subscale	Change in QoL Score	Standard Error	95% Confidence Interval	P-Value
Health and Physical Function	-1.6	0.06	-1.7 to -1.5	<0.001
Social and Economic Function	-0.25	0.05	-0.34 to 0.02	<0.001
Psychological and Spiritual Function	-0.84	0.07	-0.97 to -0.71	<0.001
Family Function	-0.29	0.06	-0.4 to -0.2	<0.001
Global Function	-0.90	0.05	-0.9 to -0.8	<0.001

and global function scores, respectively. It was interesting to see that current age and prior treatment history also retained their statistical significance in all multivariate models.

Discussion

Fatigue affects a majority of patients undergoing cancer-related therapies. The wide range of its prevalence reported in the literature can be attributed to the differences in patient selection, lack of clear symptom definition, and variation in fatigue measurement techniques. Nevertheless, fatigue continues to be a significant problem in patients with cancer and has a deleterious effect on QoL. While several studies have reported the adverse impact of fatigue on patients' QoL, no study in the literature has systematically quantified this impact using standardized fatigue and QoL questionnaires. The current study takes the research in the above area to the next step by providing parameter estimates of the impact of fatigue on patient satisfaction with QoL. We believe that this information will be useful to treating oncologists and other professionals involved in the care of cancer patients to effectively evaluate and monitor fatigue-related QoL changes.

In the present study, we found that fatigue is a strong predictor of patient satisfaction with QoL independent of the effects of age and prior treatment history. Fatigue was most

strongly related to the health and functioning subscale of the QLI. Extrapolating the data from Table 6, a 30-point increase in QLQ-C30 fatigue score, a large clinically significant increase,²⁸ is associated with a 4.5-point decline in patient satisfaction with QLI health and functioning, again a clinically significant change. Similarly, a 30-point increase in QLQ-C30 fatigue score is associated with a 2.3-point decline in patient satisfaction with psychological and spiritual functioning, again a significant change.

Using QLI to measure patient satisfaction with QoL has several advantages over the QoL tools that measure activities of daily living. QLI is a statement from the patients on how they characterize the effects, good or bad, of their medical condition on their well-being. The QLI asks the patients how satisfied they are with their life in the face of a life-threatening disease. This view of QoL assumes that only the patient can provide an objective evaluation of the impact of the treatment of a life-threatening disease on his or her well-being. Consequently, from the point of view of the patient, the data on the impact of disease and its treatment are different from the data on patients' physical function, and can provide valuable information regarding the impact of fatigue on patient QoL.

Our study has several strengths, including a large sample size of 954. There were no missing data on the fatigue subscale of QLQ-C30 and all subscales of QLI for the entire study

Table 4
Impact of 10-Year Increase in Current Age on Patient Satisfaction with QoL

QLI Subscale	Change in QoL Score	Standard Error	95% Confidence Interval	P-Value
Health and Physical Function	0.75	0.20	0.35 to 1.15	<0.001
Social and Economic Function	0.63	0.12	0.39 to 0.87	<0.001
Psychological and Spiritual Function	0.95	0.18	0.59 to 1.31	<0.001
Family Function	0.18	0.16	-0.13 to 0.49	0.26
Global Function	0.67	0.14	0.40 to 0.95	<0.001

Table 5
Differences in QLI Scores Between Newly Diagnosed and Previously Treated Patients

QLI Subscale	Difference in QoL Score	Standard Error	95% Confidence Interval	PValue
Health and Physical Function	4.0	0.50	3.1 to 4.9	<0.001
Social and Economic Function	0.89	0.3	0.32 to 1.4	0.002
Psychological and Spiritual Function	2.7	0.42	1.9 to 3.5	<0.001
Family Function	0.91	0.36	0.2 to 1.6	0.012
Global Function	2.5	0.31	1.9 to 3.1	<0.001

sample. Our study sample consisted of a variety of different tumors at different stages of the disease process, thereby providing a large heterogeneous study population. Fatigue and patient satisfaction with QoL were assessed using validated questionnaires.

Several limitations of this study require careful acknowledgment. The patient cohort was limited to only those patients who were English speakers. This study sample, therefore, is not broadly representative of cancer patients in general. A majority of our patients had advanced-stage disease and had failed primary treatment elsewhere before coming to our hospital. As a result, generalizability of the study findings to cancer patients with early-stage disease might be questionable. However, we have no reasons to believe that patients with early-stage disease will have different findings. Since the fatigue subscale of the QLQ-C30 only contains a few items with a limited number of possible responses, it can be argued that the fatigue subscale might not provide an in-depth evaluation of fatigue. This limitation was minimized by including a large number of patients in our study, which makes it possible to detect quite modest changes in fatigue scores. The

temporal relationship between fatigue and QoL cannot be evaluated from this study because both were assessed at the same time. A longitudinal analysis would provide more definitive information about the impact of fatigue on patient QoL. Finally, the use of the terms “decline” and “increase” while describing the association between fatigue and QoL is not meant to refer to changes over time since this study was cross-sectional in nature but is meant to indicate the differences in scores across patients. Indeed, it remains unclear whether similar relationships between fatigue and QoL would be observed if changes over time in each of these variables were examined.

Despite these limitations, our study demonstrates a strong association between fatigue and patient satisfaction with QoL in a large heterogeneous sample of cancer patients. Future research should use a longitudinal study design to further investigate whether the association between fatigue and QoL is sustained across the entire spectrum of cancer diagnosis and treatment. Specific treatment interventions targeting fatigue and aiming to improve patient QoL could then be evaluated.

Table 6
Differences in QLI Scores Across Gender and Stage at Diagnosis

QLI Subscale	Difference in QoL Score	Standard Error	95% Confidence Interval	PValue
Gender (females as referent category)				
Health and Physical Function	0.86	0.45	0.02 to 1.8	0.06
Social and Economic Function	-0.03	0.28	-0.58 to 0.51	0.9
Psychological and Spiritual Function	0.80	0.41	-0.01 to 1.6	0.06
Family Function	0.89	0.35	0.2 to 1.6	0.01
Global Function	0.63	0.31	0.02 to 1.25	0.043
Stage at diagnosis (late stage as referent category)				
Health and Physical Function	1.0	0.52	-0.02 to 2.03	0.06
Social and Economic Function	-0.41	0.32	-1.04 to 0.22	0.2
Psychological and Spiritual Function	-0.42	0.48	-1.36 to 0.51	0.37
Family Function	-1.15	0.40	-1.94 to -0.36	0.004
Global Function	0.02	0.36	-0.69 to 0.73	0.95

Table 7
Impact of 10-Unit Increase in Fatigue Score on Patient Satisfaction with QoL after Controlling
for the Effects of Current Age and Prior Treatment History

QLI Subscale	Change in QoL Score	Standard Error	95% Confidence Interval	PValue
Health and Physical Function	-1.5	0.06	-1.6 to -1.4	<0.001
Social and Economic Function	-0.22	0.05	-0.31 to -0.13	<0.001
Psychological and Spiritual Function	-0.77	0.07	-0.90 to -0.64	<0.001
Family Function	-0.27	0.06	-0.38 to -0.15	<0.001
Global Function	-0.85	0.04	-0.93 to -0.76	<0.001

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