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Prevalence and Associated Factors of Cancer-Related Fatigue Among Cancer Patients in Eastern China

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Key Words. Cancer-related fatigue • Prevalence • Associated factors

Abstract

Background. Cancer-related fatigue (CRF) is a subjective and distressing symptom, and its associated factors in developing countries remain ambiguous. The goal of this study was to determine the prevalence of and factors associated with CRF among cancer patients in China.

Methods. This study was designed as a cross-sectional study to determine the prevalence of and factors associated with CRF among cancer patients in eastern China, regardless of their diagnoses. Data were collected by using a questionnaire survey (including demographic information and brief fatigue inventory) after informed written consent was obtained. A chi-square test was used to analyze the correlations between single categorical factors and CRF, and multiple logistic regression analysis was used to evaluate the associations of potential risk factors with the presence of CRF.

Results. Out of a total population of 1,938 cancer patients, 1,749 had completed the study questionnaire; 52.07% (n = 904) reported clinically significant fatigue (score ≥4 on Brief Fatigue Inventory). Four hundred twenty-seven (48.47%) patients younger than age 58 years (the median age) and 475 (55.69%) patients age 58 years or older reported clinically significant fatigue. In multivariate analysis, higher sleep quality ($p < .01$) was negatively associated with CRF, whereas never engaging in physical exercise ($p < .01$) and higher clinical stage of cancer ($p < .01$) were positively associated factors that could increase the odds of CRF.

Conclusion. The results of this study suggest that effective management of the two changeable contributing factors of CRF may reduce CRF and thus could be used as references for CRF management. ***The Oncologist*** 2016;21:1349–1354

Implications for Practice: The two modifiable factors of cancer-related fatigue (CRF)—sleep disturbance and physical exercise—should be specifically assessed and managed to mitigate CRF.

Introduction

The occurrence of cancer has increased recently, and developing countries account for approximately 57% of cancer cases worldwide [1]. With the continued development of cancer diagnostic and therapeutic technologies, patient survival duration has been significantly extended. However, improvements in the quality of life of cancer patients have fallen short of expectations because of cancer-related fatigue (CRF), one of the most common cancer-related symptoms [2]. CRF can also be a barrier to cancer survivors' return to work, thus imposing an enormous burden on society [3]. Therefore, it is necessary to identify and minimize the factors contributing to CRF.

CRF is a subjective and distressing symptom experienced by nearly all cancer patients [4, 5]; it does not result from activity or exertion and is not relieved by sleep or rest [6]. Spichiger et al. [7] examined 103 hospitalized patients with advanced cancer and found that younger patients and patients with lower functional status, depression, or anemia experienced greater fatigue. In addition, CRF is also correlated with a high body mass index [8, 9] and white blood cell count [8], increased limb volume [8], low levels of physical activity [8–11], higher tumor grade [9, 12–15], and sleep disturbances [12, 14]. Because significant discrepancies exist among these studies (e.g., some studies show associations between sociodemographic data and fatigue [7, 12], whereas others indicate the opposite [9, 13]) and because most of this research (except for two studies) has been conducted in developed countries, the factors associated with CRF in developing countries remain ambiguous. Therefore, additional relevant research is warranted.

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The purpose of this study was to examine the prevalence of and factors contributing to CRF among cancer patients in China and to provide a basis for future CRF management.

Materials and Methods

Ethical Considerations

Ethical clearance was obtained from the Research Ethics Committee of the School of Nursing, Fudan University, Shanghai, China. Participants were explicitly informed that the data produced in the survey would be confidential, would not affect their treatment, and would be used only for academic research purposes. Written informed consent was obtained from all participants, who were informed that participation was voluntary and that they could withdraw at any time during the survey.

Study Design and Sampling Frame

This study used a cross-sectional design. Convenience sampling of cancer patients from general hospitals in Shanghai, Suzhou, Wuxi, and Nantong was conducted simultaneously from October 2013 to June 2014. The inclusion criteria included the following: (a) a pathology- or cytology-based diagnosis, regardless of cancer type and treatment; (b) age ≥18 years; (c) no cognitive impairment; and (d) a willingness to participate, as specified by the written consent form. The sample size was calculated on the basis of results from a pilot investigation by using estimation methods for a cross-sectional survey (i.e., $n = t_\alpha^2\,[P(1-P)/\delta^2]$, where n is sample size, t_α is the confidence level of the study findings, P is the estimating prevalence, and δ is the maximal likely error that can be tolerated. The occurrence rate of clinically significant fatigue was 24% [16], and the two-tailed α level was set at 0.05; the admissible error δ was set at 0.1π; therefore, $n = 1.96^2(0.24[1-0.24])/(0.1\times 0.24)^2 = 1{,}266$. Considering a 20% nonresponse rate, a minimum of 1,583 patients were required for the study.

Data Collection

Data were collected by using a questionnaire survey after informed written consent was obtained. The researchers instructed patients on how to fill out the questionnaire, and the patients then did so accordingly.

The questionnaire consisted of the following two parts.

Demographic information

Personal characteristics (including age, gender, ethnicity, educational level, religion, marital status, household income per capita, medical insurance, sleep quality, awareness of disease, and physical activity) and disease-related information (including disease diagnosis, diagnosis time, clinical stage, and current treatment) were collected in this part. The personal characteristics were supplied by the patients themselves, and the disease information was obtained from medical records. Sleep quality in the past month and awareness of disease were self-reported (very bad/bad/good/very good and unknown/partially acquainted/entirely acquainted, respectively). Aerobic exercise, resistance exercise/muscle strengthening, and stretching exercise were considered as the forms of physical activity, and the intensity, duration, and frequency of the exercise were assessed by the patients' self-report.

Brief Fatigue Inventory

The Brief Fatigue Inventory (BFI) was initially developed by Mendoza et al. [17], and the instrument used in this study was the Chinese version [18]. It includes nine items, with the first three assessing the "now," "usual," and "worst" levels of fatigue during the past 24 hours. Fatigue severity was evaluated by using an integer scale of 0 (no fatigue) to 10 (fatigue as bad as you can imagine), which was recommended by National Comprehensive Cancer Network (NCCN) guidelines for screening and re-evaluation of cancer related fatigue, with the cutoff score for clinically significant fatigue being 4 [2]. The internal consistency reliabilities (Cronbach α) of the first three items in the Chinese version is 0.92 [18]. The remaining six items assess the extent to which fatigue has interfered with daily life during the past 24 hours in terms of general activity, mood, walking ability, normal work, relationships with other people, and enjoyment of life. The internal consistency reliabilities (Cronbach α) of the remaining six items in the Chinese version is 0.90 [18]. This study primarily explored fatigue severity using the first three items of the BFI.

Statistical Analysis

The data were analyzed by using SAS software, version 9.3 (SAS Institute, Inc., Cary, NC, http://www.sas.com). The prevalence of CRF was estimated for the overall population and for each age and sex group. Multiple logistic regression models were developed with CRF as the dichotomous dependent variable and relevant predictors as covariates. If the p value was $<.10$ in univariate models, these possible predictors were included in multiple logistic regression models. All probabilities quoted were two-sided and were considered statistically significant at $p < .05$.

Results

Patient Characteristics

In this study, 1,938 patients participated in the survey, 1,749 effective questionnaires were collected, and 189 questionnaires were not included because the key clinical data (such as pathological or cytological data for diagnosis) were missing in the medical records of these patients. Of all participants, 99.54% were of the Han nationality. The distributions of sociodemographic and disease characteristics of the participants are shown in Table 1.

Prevalence of Cancer-Related Fatigue

Of 1,749 patients, 904 (52.07%) experienced clinically significant fatigue (≥4). Four hundred fifty-seven female patients (52.71%), 446 male patients (50.57%), 427 patients younger than age 58 years (the median age) (48.47%), and 475 patients aged ≥58 years (55.69%) reported clinically significant fatigue (Table 2).

Factors Associated With CRF Prevalence

Table 2 shows the univariate and multivariate associations of cancer-related fatigue in the study population. In univariate analysis, increasing age, lower awareness of disease, poor sleep quality, the absence of physical exercise, and higher

Table 1. Sociodemographic characteristics of the participants

Variables	Value, *n* (%)
Age, mean ± SD (median), yr	56.86 ± 13.15 (58)
Gender	
Male	882 (50.43)
Female	867 (49.57)
Education level	
No formal education[a]	177 (10.12)
Elementary school	402 (22.98)
Junior high school	581 (33.22)
Senior high school/technical secondary school	327 (18.70)
Junior college	133 (7.60)
University	129 (7.38)
Religion	
Yes	401 (22.93)
No	1,348 (77.07)
Marital status	
Single, never married	55 (3.14)
Married/cohabitating	1,614 (92.28)
Divorced	24 (1.37)
Widowed	56 (3.20)
Household income per capita	
<500 RMB/month	120 (6.86)
500–1,000 RMB/month	272 (15.55)
1,000–2,000 RMB/month	562 (32.13)
>2,000 RMB/month	795 (45.45)
Medical payments	
Self-pay	171 (9.78)
At public expense	30 (1.72)
Medical insurance	1,188 (67.92)
Rural endowment insurance	360 (20.58)
Diagnosis	
Lung cancer	325 (18.58)
Colorectal cancer	271 (15.49)
Gastric cancer	247 (14.13)
Breast cancer	244 (13.95)
Gynecological cancer	146 (8.35)
Head and neck cancer	118 (6.75)
Esophageal cancer	102 (5.83)
Other	296 (16.92)

Unless otherwise noted, values are the number (percentage) of patients.
[a]These patients filled out the questionnaire with the help of their families.
Abbreviation: RMB, renminbi.

clinical stage of cancer were significantly associated with a higher prevalence of cancer-related fatigue ($p < .05$). Other factors, such as gender, education level, religion, marital status, household income per capita, medical payments, and current treatment modalities, were not significantly associated with the prevalence of cancer-related fatigue. In multivariate analysis, low sleep quality ($p < .01$), never performing physical exercise ($p < .01$), and higher clinical stage ($p < .01$) were significantly associated with an increasing prevalence of cancer-related fatigue.

Discussion

In this survey, 52.07% of 1,749 cancer patients experienced clinically significant fatigue. Disease- or treatment-specific factors and sociodemographic factors were included in the unconditional logistic regression analysis, yet only sleep quality, physical exercise, and clinical stage of cancer were correlated with CRF. Meanwhile, other factors, such as awareness of one's disease, household income per capita, medical payments, current treatment modalities, and marital status, showed no correlation with CRF.

Among all cancer patients, 30%–75% experience sleep/wake disturbances [19], which can clearly aggravate CRF [20]. In this survey, sleep quality showed a significant association with clinically significant fatigue, in accord with previous research [12, 14]. In addition, good or very good sleep quality can alleviate CRF to some extent, whereas there was no significant difference between bad and very bad sleep quality. Therefore, sufficient attention should be paid to the management of sleep/wake disturbances.

Haas [21] reported that physical activity levels were associated with CRF, and lower levels of physical activity lead to CRF [8–11]. In this study, no particular exercise frequency was found to exacerbate CRF when compared with other frequencies of physical exercise. However, there was no statistically significant difference among the five exercise frequencies, except between two to three times per week and six to seven times per week (odds ratio, 1.77; 95% confidence interval, 1.26–2.50). In this survey, the most common mode of physical exercise reported by the participants was home-based walking at a tolerated speed without any exercise prescription, and the exercise duration, intensity, and frequency were all reported by the patients themselves with no professional supervision, which may partially explain this result. The optimal frequency and intensity of exercise should be discussed with medical professionals [22].

The preceding two factors were modifiable factors associated with CRF; a less controllable factor, clinical stage, also significantly influenced CRF. In addition, a higher clinical stage correlated with a greater level of CRF.

Kim et al. [23] found that employment and low income were also associated with fatigue; however, in this study, this association was not statistically significant. Furthermore, there was no association between educational level or marital status and CRF.

Our findings were based on a relatively large study sample, and many possible influencing factors were included in the statistical analysis, such as sociodemographic factors and disease- and treatment-specific factors. However, in the chemotherapy regimen analysis, the result was not very clear because of the small sample size for each treatment; the result should be confirmed by increasing the sample size in future studies. The inclusion criteria might cause selection bias because only patients who were willing to participate were included. Thus, the results of this study may not universally apply to all cancer patients during this period. In this study, we used BFI as a screening tool, an

Table 2. Univariate analyses of risk factors of cancer-related fatigue

Variable	Nonfatigued (*n*)	Fatigued[a] (*n*)	Univariate		Multivariate	
			OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age						
<58 yr	454	427	**0.75 (0.62–0.90)**	**<.01**	0.87 (0.70–1.09)	.23
≥58 yr	378	475	Ref		Ref	—
Gender						
Female	410	457	Ref		Ref	—
Male	436	446	0.92 (0.76–1.11)	.37	0.94 (0.75–1.17)	.58
Educational level						
University	58	71	Ref		—	—
Junior college	64	69	0.88 (0.54–1.43)	.61	—	—
Senior high school/technical secondary school	165	162	0.80 (0.53–1.21)	.29	—	—
Junior high school	297	284	0.78 (0.53–1.15)	.21	—	—
Elementary school	187	215	0.94 (0.63–1.40)	.76	—	—
No formal education	75	102	1.11 (0.70–1.76)	.65	—	—
Religion						
Yes	190	211	Ref		—	—
No	656	692	0.95 (0.76–1.19)	.65	—	—
Marital status						
Widowed	25	31	Ref		—	—
Single, never married	27	28	0.84 (0.40–1.77)	.64	—	—
Married/cohabitation	781	833	0.86 (0.50–1.47)	.58	—	—
Divorced	13	11	0.68 (0.26–1.78)	.44	—	—
Household income per capita						
>2,000 RMB/month	373	422	Ref		—	—
1,000–2,000 RMB/month	271	291	0.95 (0.77–1.18)	.64	—	—
500–1,000 RMB/month	146	126	0.76 (0.58–1.01)	.16	—	—
< 500 RMB/month	56	64	1.01 (0.69–1.48)	.96	—	—
Medical payments						
Rural endowment insurance	167	193	Ref		—	—
Self-pay	90	81	0.78 (0.54–1.12)	.18	—	—
At public expense	12	18	1.30 (0.61–2.77)	.50	—	—
Medical insurance	577	611	0.92 (0.72–1.16)	.47	—	—
Awareness of disease						
Unknown	24	35	Ref		Ref	—
Partially acquainted	331	455	0.94 (0.55–1.62)	.83	0.93 (0.50–1.73)	.82
Entirely acquainted	491	413	**0.58 (0.34–0.99)**	**.04**	0.72 (0.38–1.33)	.29
Sleep quality in recent month						
Very bad	12	52	Ref		Ref	—
Bad	145	380	0.61 (0.31–1.17)	.13	**0.33 (0.14–0.76)**	**<.01**
Good	514	410	**0.18 (0.10–0.35)**	**<.01**	**0.11 (0.05–0.25)**	**<.01**
Very good	173	61	**0.08 (0.04–0.16)**	**<.01**	**0.05 (0.02–0.13)**	**<.01**
Physical exercise						
>7 times/wk	19	9	Ref		Ref	—
6–7 times/wk	183	104	1.20 (0.52–2.75)	.67	1.45 (0.59–3.55)	.41
4–5 times/wk	72	47	1.38 (0.58–3.30)	.47	1.51 (0.59–3.87)	.39
2–3 times/wk	125	126	2.13 (0.93–4.88)	.07	1.85 (0.76–4.52)	.18
1 time/wk	141	108	1.61 (0.70–3.71)	.26	1.69 (0.69–4.14)	.25
Never	304	509	**3.53 (1.58–7.91)**	**<.01**	**3.09 (1.30–7.34)**	**.01**

(continued)

Table 2. (continued)

Variable	Nonfatigued (*n*)	Fatigued[a] (*n*)	Univariate OR (95% CI)	Univariate *p* value	Multivariate OR (95% CI)	Multivariate *p* value
Clinical stage						
IV	328	444	Ref		Ref	—
III	161	175	**0.80 (0.62–1.04)**	**<.01**	0.87 (0.66–1.15)	.34
II	161	165	**0.76 (0.58–0.98)**	**.04**	0.83 (0.62–1.10	.20
I	137	74	**0.40 (0.29–0.55)**	**<.01**	**0.33 (0.23–0.47)**	**<.01**
Current treatment modalities						
Chemotherapy and radiotherapy	15	15	Ref		—	—
None	208	278	1.34 (0.64–2.80)	.44	—	—
Surgery	6	6	1.00 (0.26–3.82)	1.00	—	—
Chemotherapy	318	306	0.96 (0.46–2.00)	.92	—	—
Radiotherapy	61	68	1.12 (0.50–2.47)	.79	—	—
Traditional Chinese medicine	176	165	0.94 (0.44–1.98)	.87	—	—
Endocrine therapy	20	28	1.40 (0.56–3.50)	.47	—	—

Values presented in bold are statistically significant at $p < .05$.
[a]The cutoff score for the nonfatigued and fatigued scores using the integer scale of 0 to 10 ("current fatigue" item in the Brief Fatigue Inventory) is 4.
Abbreviations: —, no data; CI, confidence interval; OR, odds ratio; Ref, reference; RMB, renminbi.

instrument that may not be as accurate as criteria based on the International Classification of Diseases, 10th revision. We assessed sleep quality, exercise, and awareness mainly on the basis of the patients' self-report. In addition to these factors included in our study, other cancer-related symptoms (e.g., pain [24], depression and anxiety [25], and nausea [10]) and objective markers (e.g., increased total white cell count [26], lower sodium [27], lower hemoglobin [<10 g/dL] [27], and higher levels of C-reactive protein [28]) were significantly correlated with CRF. However, the current study did not include these factors, which can be further explored in future studies.

Conclusion

Two negatively associated factors (sleep quality and physical exercise) and one positively associated factor (higher clinical stage of cancer) were determined to be factors influencing CRF prevalence. The results of this study suggest that effective management of the two modifiable contributing factors of CRF (sleep disturbance and physical exercise) may be conducive to CRF management.

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Data analysis and interpretation: Li Tian, Lu Lin, Ke J. Chen, Yan Hu
Manuscript writing: Li Tian, Lu Lin, Yan Hu
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Disclosures

The authors indicated no financial relationships.

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For Further Reading:

Elisabeth C.W. Neefjes, Maurice J.D.L. van der Vorst et al. Aiming for a Better Understanding and Management of Cancer-Related Fatigue. ***The Oncologist*** 2013;18:1135–1143.

Implications for Practice:

Cancer-related fatigue (CRF) is a common problem in patients with cancer and has a major impact on quality of life. The causes of CRF are multifactorial and not fully understood. To get a better insight into the underlying mechanisms and the potential treatment possibilities of CRF, we provide an overview of currently available literature on this subject. Because current treatment options other than antitumor therapy for some of the patients are scarce and only directed at symptoms, further investigation of CRF is warranted to develop rational treatment options.