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## Research Paper

## The relationship between cancer-related fatigue, quality of life and pain among cancer patients

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## ABSTRACT

**Objectives:** This study aimed to select patients with cancer-related pain to further analyze the relationship between pain severity, fatigue severity, and quality of life.

**Methods:** A cross-sectional study was conducted. A convenience sampling method was used to select 224 patients with cancer-related pain who were undergoing chemotherapy and met the inclusion criteria in two hospitals of two provinces from May to November 2019. All participants were invited to complete a general information questionnaire, the Brief Fatigue Inventory (BFI), the Numerical Rating Scale (NRS) for pain intensity, and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30).

**Results:** In the 24 h before completing the scales, 85 patients (37.9%) had mild pain, 121 (54.0%) had moderate pain, and 18 (8.0%) had severe pain. In addition, 92 (41.1%) patients had mild fatigue, 72 (32.1%) had moderate fatigue, and 60 (26.8%) had severe fatigue. Most patients with mild pain only experienced mild fatigue, and their quality of life was also at a moderate level. Patients with moderate and severe pain mostly had moderate or higher levels of fatigue and a lower quality of life. There was no correlation between fatigue and quality of life in patients with mild pain ( $r = -0.179$ ,  $P = 0.104$ ). There was a correlation between fatigue and quality of life in patients with moderate and severe pain ( $r = -0.537$ ,  $P < 0.01$ ;  $r = -0.509$ ,  $P < 0.05$ ).

**Conclusions:** Patients with moderate and severe pain have more fatigue symptoms and lower quality of life than those with mild pain. Nurses should pay more attention to patients with moderate and severe pain, explore the interaction mechanism between symptoms, and carry out joint symptom intervention to improve the quality of life of patients.

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## What is known?

- A positive correlation between cancer-related pain and cancer-related fatigue was observed.
- Pain affects the patient's normal physical exercise, cognitive rehabilitation, and social interactions, and cancer-related fatigue (CRF) may be more likely to occur.
- Cancer-related pain is not persistent, and the severity of cancer-related pain may vary over time.

## What is new?

- Most patients with mild pain only experienced mild fatigue, and their quality of life was also at a moderate level.
- Patients with moderate and severe pain mostly have moderate or higher levels of fatigue and a lower quality of life, and there is a stronger correlation between symptoms and quality of life.
- The symptoms of patients with moderate and severe pain should be managed differently from those of patients with mild pain.
- Nurses should pay more attention to patients with moderate and severe pain, explore the mechanism of interaction between symptoms and carry out symptomatic joint intervention to improve the quality of life more effectively.

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## 1. Introduction

Pain, fatigue, and distress are common symptoms among cancer patients but are often under-assessed and under-treated [1]. According to the statistics of the WHO, 10 million new cancer patients are diagnosed every year, and there are more than 100 million tumor survivors worldwide. Approximately 60% of these patients have cancer-related pain [2]. In China, approximately 60% of patients receiving antitumor treatment suffer from pain; among these patients, 50% report moderate to severe pain, and 30% report intolerable severe pain. If the pain is not relieved, the patient will feel uncomfortable, and the pain greatly affects their activities, enthusiasm, communication with family and friends, and quality of life (QOL) [3]. Cancer-related fatigue (CRF) is defined as “a physical, emotional, and/or perceived fatigue or tiredness, with a persistent and subjective sense related to cancer or cancer treatments that are disproportionate to recent activities and interferes with usual functioning” [4].

Data show that the incidence of CRF after chemotherapy is 75%–100% [5]. With the extension of the course of the disease and the increase in chemotherapy times, the decline in cardiopulmonary function and activity caused by the tumor itself and treatment and the side effects of chemotherapy are more obvious. Physical fatigue is also more serious than that of mild patients, and the harm to the body and mind of patients is greater [6]. Some studies have shown that non-drug therapies, such as exercise intervention [7] and cognitive behavior management [8], can relieve CRF and improve QOL. It has been reported that pain affects the patient's normal physical exercise, cognitive rehabilitation, and social interactions, and CRF may be more likely to occur.

Armstrong proposed a symptom experience model in 2003. According to this theory, symptom experience includes the occurrence frequency, severity, and disturbance of each symptom subjectively perceived by the patient and is characterized by co-occurrence and emotional responsiveness. Different symptoms are interrelated, and one symptom may promote the deterioration of another. Symptoms can produce a series of health outcomes, including the decline of health function, cognitive function, and quality of life [9]. Consequently, there are few in-depth studies on the relationship between pain and CRF. Cancer-related pain is not persistent, and the severity of cancer-related pain may vary over time. When and to what extent cancer-related pain is more closely related to CRF requires further study. It is also unknown how symptoms will lead to changes in the quality of life. According to the symptom experience model, symptoms can produce a series of health outcomes, including quality of life and cognitive decline. Therefore, pain and CRF may affect physical function and QOL. The high energy consumption of cancer cells and treatment measures, such as surgery, radiotherapy, and chemotherapy, easily lead to fatigue, and the effects of these treatments on the QOL of patients with cancer are greater than the effects on pain, nausea, and vomiting [10]. Thus, many studies take QOL as the secondary indicator of CRF assessment [11–13]. Therefore, to better predict the occurrence of CRF and further study the relationship between CRF and cancer-related pain, the study selected patients with cancer-related pain to further analyze the correlation between pain and CRF and QOL.

## 2. Methods

### 2.1. Study design and participants

A cross-sectional study was conducted from May to November 2019. This study report follows the Strengthening the Reporting of Observational Studies in Epidemiology Statement (STROBES)

guidelines. A convenience sampling method was used to select cancer patients experiencing pain who were undergoing chemotherapy in two provinces (one in South China and another in East China). The following inclusion criteria were applied: 1) cancer patients with pain scored based on a Numerical Rating Scale (NRS) [14]; 2) patients voluntarily participated in the study and signed informed consent; 3) patients had basic language understanding abilities, and 4) consciousness was clear, and cognition was normal. The following exclusion criteria were applied: 1) pain was accompanied by other serious physical diseases; 2) patients could not accurately express their ideas; 3) patients had other diseases, such as anemia, kidney function damage, and body infection; and 4) patients were treated with steroids.

### 2.2. Instruments

#### 2.2.1. General information questionnaire

The questionnaire gathered demographic and clinical data, including gender, age, nationality, religious belief, marital status, education level, occupation, residence, personal income level, medical expenses payment method, medical diagnosis, treatment plan, the dosage of opioids, and three levels of analgesic therapy.

#### 2.2.2. The Numerical Rating Scale (NRS) for pain intensity

The NRS for pain intensity is a standard instrument used in chronic pain studies. It is used to assess the most severe pain levels in the past 24 h. The 0–10 NRS uses 11 numbers (0 through 10) to measure pain intensity [15,16]. A score of 0 points indicated no pain, 1–3 points indicated mild pain, 4–6 points indicated moderate pain, and 7–10 points indicated severe pain. Cronbach's  $\alpha$  coefficient for this scale was 0.77–0.82, and the correlation validity is 0.74–0.95 [17]. This study used this scale to assess the most serious pain within 24 h.

#### 2.2.3. Brief Fatigue Inventory (BFI)

The BFI is a questionnaire originally developed in English, and its validity and reliability have been verified. This questionnaire was designed to assess fatigue in cancer patients [18] and consists of 9 items, which are rated using Likert scales ranging from 0 (no fatigue) to 10 (severe fatigue). Average scores for these 9 items are reported as global fatigue scores (GFSs). Scores 1–3, 4–6, and 7–10 are categorized as mild, moderate, and severe, respectively. The higher the score is, the more severe the level of fatigue is. The first three items of the scale assessed the current level of fatigue and the general and worst levels of fatigue in the past 24 h. The last six items assessed the impact of fatigue on different aspects of life. The content included general activities, mood, walking, normal work, relationship with others, and fun in life. The validity of the scale was 0.81–0.92, and the internal consistency was 0.96. The Chinese version of the BFI (BFI-C) has also been shown to have good reliability and validity by different research groups. Wang et al. confirmed the validity of the Chinese version of the BFI [19] and can be used to assess CRF in cancer patients in China. The structural validity of the scale was 0.81–0.91, the Cronbach's  $\alpha$  coefficient was 0.92, and the retest reliability was 0.87 [20]. The scale is simple, easy to understand, and can distinguish the severity of fatigue. However, this scale cannot measure QOL because the BFI and quality of life are evaluated from different perspectives [21]. Therefore, we used the QOL scale to evaluate CRF more comprehensively.

#### 2.2.4. The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTCQLQ-C30)

This questionnaire assesses 15 areas of QOL with a total of 30 items. There are five functional areas: physical function includes

five items, role function includes two items, emotional function includes four items, cognitive function includes two items, and social function includes two items. There are three symptom areas: fatigue includes three items, nausea and vomiting include two items, and pain includes two items. There are six single items (each as an area): dyspnea, insomnia, appetite loss, constipation, diarrhea, economic difficulties, and general QOL. Items 29 and 30 on the scale were divided into 7 grades. The grades range from “very poor” to “very good” and are assigned scores from 1 to 7 points, respectively. The other items were divided into 4 grades and were reverse scored: “no” (1 point), “a little bit” (2 points), “more” (3 points), and “very many” (4 points). The scores of each field were 0–100 after conversion. The higher the score was, the better the QOL. The score of each item in the Chinese version of the questionnaire is strongly correlated with the score of its field (*R* values were all greater than 0.5). Cronbach’s  $\alpha$  coefficient for this scale ranged from between 0.722 and 0.870, and the test-retest reliability was above 0.7. The confirmatory factor analysis shows that the load value of each topic is above 0.6, and the fit index is above 0.9 [22]. Therefore, the Chinese version of the questionnaire has good reliability and validity and can be used in this study [23].

### 2.3. Data collection

Following standard training, the members of the research group visited patients at the bedside to administer the questionnaire survey after obtaining permission from the head nurse. After obtaining informed consent from the patients and their families, the questionnaire was described to the patients to explain the completion methods and matters needing attention. The investigators read the items and options for patients with disabilities. The questionnaire was completed based on patients’ responses and collected on the spot. A total of 226 questionnaires were distributed. A total of 224 valid questionnaires were obtained. The effective recovery rate was 99.12%. Two questionnaires were considered invalid based on the number of duplicate answers given for the two scales.

### 2.4. Ethical considerations

The protocol for this observational study was prepared by the Declaration of Helsinki and the Ethical Guidelines for Epidemiology Research [24]. Ethical approval was granted by the ethics committee of Fujian Cancer Hospital & Fujian Medical University Cancer Hospital (SQ2018-039-01). All patients were informed of the nature and purpose of the study in writing and orally, and they provided informed consent to participate in the study.

### 2.5. Statistical analysis

All data were entered and checked by two researchers. Continuous variables were described by mean and standard deviation or median and interquartile range, and categorical variables were described by frequency and percentage. The data that did not conform to a normal distribution were analyzed after normal transformation. If normal transformation could not be performed, the correlation between variables were analyzed using Spearman rank correlation analysis. The data were double-checked and then analyzed using SPSS 24.0 (SPSS Inc., Chicago, IL, USA). When  $P < 0.05$ , the difference was considered statistically significant.

## 3. Results

### 3.1. Participants characteristics

Among 224 registered patients, the average age was  $55.74 \pm 14.09$ , ranging from 24 to 85. Among them, 138 (61.6%) were male, and 86 (38.4%) were female. Fifteen patients had pain in two or more locations and two or more natures of pain in five patients. The BMI of the patients was  $21.08 \pm 2.62$ , ranging from 15.43 to 26.91 (Table 1). In this study, the pain sites were divided into the abdomen, chest, shoulder, back, lower limbs, anus, buttocks, hips, neck, waist, head, and joints according to the anatomical position when the pain sites were counted. The income level is classified according to the average income level of residents in the two places (Table 1).

**Table 1**  
Demographic characteristics of participants ( *n* = 224 ).

Characteristics	<i>n</i>	%
Type of cancer		
Colorectal cancer	58	25.9
Lung cancer	51	22.8
Bladder cancer	3	1.3
Prostate cancer	3	1.3
Liver cancer	13	5.8
Pancreatic cancer	10	4.5
Gastric cancer	52	23.2
Nasopharyngeal carcinoma	3	1.3
Lymphoma	5	2.2
Breast cancer	2	0.9
Esophageal cancer	3	1.3
Others	21	9.4
Marital status		
Married	213	95.1
Non marital	11	4.9
Educational level		
Junior college or above	26	11.6
Senior high school, technical secondary school	40	17.9
Junior middle school	70	31.3
Primary school and below	88	39.3
Monthly income (RMB)		
< 3,000	129	57.6
3,000–8,000	84	37.5
> 8,000	11	4.9
Pain site		
Head and neck	11	4.9
Chest, shoulder and back	35	15.6
Waist and abdomen	148	66.1
Lower limbs, anus, buttocks and joints	30	13.4
Nature of pain		
Nociceptive pain	175	78.1
Neuropathic pain	22	9.8
Mixed pain	27	12.1
Three levels of analgesic therapy		
First level	10	4.5
Second level	48	21.4
Third level	166	74.1
Stage		
I or II	18	8.0
III	84	37.5
IV	122	54.5
BMI		
Low	41	18.3
Normal	170	75.9
High	13	5.8
Smoking history		
Yes	69	30.8
No	155	69.2
Alcoholism history		
Yes	35	15.6
No	189	84.4

### 3.2. QOL, BFI scores, and pain index

In terms of the most serious pain in the past 24 h, 85 patients (37.9%) had mild pain, 121 (54.0%) had moderate pain, and 18 (8.0%) had severe pain (Table 2). Regarding the overall level of fatigue, different degrees of CRF were observed. A total of 92 (41.1%) had mild fatigue, 72 (32.1%) had moderate fatigue, and 60 (26.8%) had severe fatigue. Regarding the BFI-1\_ Fatigue right now ratings, there were 31 patients without fatigue, 185 with mild fatigue, and 8 with moderate fatigue. In the past 24 h, 11 patients (4.9%) had no fatigue, 72 (32.1%) had mild fatigue, 92 (41.1%) had moderate fatigue, and 49 (21.9%) had severe fatigue (Table 2).

### 3.3. Correlations between pain-related indicators and CRF items among cancer-related pain patients

The overall BFI score and QOL score did not conform to a normal distribution, so a normal transformation was carried out. Finally, the overall BFI score was normalized. The overall QOL score and pain digital score could not undergo normal transformation. Therefore, the pain was divided into mild, moderate, and severe pain groups according to the scoring criteria of the pain scale. The fatigue and quality of life scores of patients with mild pain were 2.67 (1.89, 3.78) and 50.00 (33.33, 66.67), respectively. The fatigue and quality of life scores of patients with moderate pain were 5.11 (2.64, 6.56) and 41.67 (16.67, 52.08), respectively. The fatigue and quality of life scores of patients with severe pain were 4.67(3.50, 5.94) and 33.33 (29.17, 50.00), respectively. There was a correlation between pain and fatigue ( $r = 0.296, P < 0.01$ ), and there was also a correlation between pain and quality of life ( $r = -0.141, P < 0.01$ ). There was no correlation between fatigue and quality of life in patients with mild pain ( $r = -0.179, P = 0.104$ ). There was a correlation between fatigue and quality of life in patients with moderate and severe pain ( $r = -0.537, P < 0.01$ ;  $r = -0.509, P < 0.05$ ).

## 4. Discussion

This study evaluated fatigue in patients with cancer-related

pain. Approximately 60% of the patients demonstrated moderate to severe fatigue. The conclusion was similar to those obtained in another study [6]. Our study used the BFI, which had been used worldwide at the time the intervention was implemented. The validity of the Cancer Fatigue Scale, an alternative tool for measuring fatigue that is available in Japanese, has been verified [19]. However, we chose the BFI because it allows a multidimensional assessment of fatigue. The BFI results showed that moderate or severe CRF was found in a high proportion of patients (58.9%). In the past 24 h, the average fatigue index was at the middle level. This finding indicated that the experience of cancer-related pain in most patients resulted in moderate to severe fatigue. On the BFI subscale, most of the items displayed the moderate fatigue. This finding is slightly different from another study [25]. The explanation is that during the investigation, the investigators were all professional nurses in the ward, and they obtained the data through conversation. In addition, the investigators also provided information support and humanistic care to the patients, which could have helped the patients achieve temporary relief from their physical discomfort. Therefore, this finding also shows the importance of humanistic care, information support, and social concern from nurses during treatment.

Regarding the impact on different aspects of life, BFI-4\_General ability displayed the highest score. The BFI-8\_Relations with other people obtained the second-highest score. BFI-7\_Normal work and BFI-9\_Fun in life were the least affected scores. These findings show that fatigue has a considerable influence on the general activities and social activities of patients. A possible explanation is that patients do not need to participate in work and entertainment activities during hospitalization most of the time; therefore, fatigue had a relatively small impact on the fun of work and life. The patients were mainly engaged in general daily activities, such as eating, dressing, and toileting. Therefore, the effect of fatigue from cancer-related pain was mainly reflected in daily activities. Body pain and fatigue affected the daily activities of patients to a certain extent. In addition, the disease also caused great changes in the patient's lifestyle. The complications caused by the treatment also made the patient unable to engage in normal social activities,

**Table 2**  
Scores on pain index, QOL and BFI among cancer patients (n = 224 ).

Item	Range	Mean ± SD	Median ( P <sub>25</sub> , P <sub>75</sub> )
Cancer-related fatigue			
BFI-1_Fatigue right now	0–10	4.85 ± 2.67	4.00 (3.00, 7.00)
During past 24 h			
BFI-2_Usual level of fatigue	0–10	4.74 ± 2.46	4.00 (3.00, 7.00)
BFI-3_Worst level of fatigue	0–10	4.94 ± 2.69	5.00 (3.00, 8.00)
BFI-4A_General ability	0–10	5.15 ± 2.81	4.00 (3.00, 6.00)
BFI-4B_Mood	0–10	4.39 ± 2.70	3.00 (2.00, 6.00)
BFI-4C_Walking ability	0–10	4.06 ± 3.05	4.00 (1.00, 6.00)
BFI-4D_Normal work	0–10	3.99 ± 3.10	5.00 (2.00, 8.00)
BFI-4E_Relations with others	0–10	4.88 ± 3.45	4.00 (0.00, 5.00)
BFI-4F_Fun in life	0–10	3.23 ± 3.04	4.00 (1.00, 7.00)
Average score of BFI	0–10	4.10 ± 2.24	3.78 (2.33, 6.11)
NRS score	0–10	4.14 ± 1.64	4.00 (3.00, 5.00)
EORTCQLQ-C30			
Physical function	0–100	56.94 ± 31.20	66.67 (33.33, 80.00)
Role function	0–100	54.65 ± 31.68	66.67 (33.33, 66.67)
Emotional function	0–100	74.02 ± 24.36	75.00 (66.67, 100.00)
Cognitive function	0–100	68.84 ± 23.71	66.67 (50.00, 83.33)
Social function	0–100	49.55 ± 29.25	50.00 (33.33, 66.67)
Nausea and vomiting	0–100	74.17 ± 31.34	83.33 (66.67, 100.00)
Fatigue	0–100	24.43 ± 42.18	33.33 (0.00, 50.00)
Pain	0–100	38.14 ± 31.22	33.33 (0.00, 66.67)
Average score of EORTC QLQ-C30	0–100	42.56 ± 23.21	41.67 (25.00, 58.33)

Note: BFI = the Brief Fatigue Inventory. NRS = the Numerical Rating Scale. EORTC QLQ-C30 = the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire .The score of the quality of life of the patients has been converted from the rough score to the standard score.

resulting in fatigue and affecting their relationships with others. Regarding QOL, the scores for the role, society, and physical function were lower, which was related to the effect of CRF on general activity abilities and social activity. However, the emotional function score was higher, which may have been related to the reduced influence of CRF on life pleasure and emotion. Therefore, the QOL results are consistent with those with CRF and similar to other study results [26]. These data also suggest that nurses should pay attention to the daily life care of patients with cancer-related pain and fatigue and help patients improve their self-care ability and maintain good interpersonal relationships through communication with their families to minimize the impact of complications on the body.

The results of correlation analysis showed that patients with moderate and severe pain had more severe fatigue and worse quality of life than patients with mild pain. The results of this study are similar to the other study [27]. If the pain of patients is not effectively alleviated, it will seriously affect the treatment compliance and the overall physical and mental condition of patients, resulting in the shortening of the survival period of patients and the reduction of their quality of life [28]. Most patients with mild pain only experienced mild fatigue, and their quality of life was moderate. However, patients with moderate and severe fatigue mostly have moderate or above fatigue and lower quality of life. This suggests that the symptoms of patients with moderate and severe pain should be managed differently from those of patients with mild pain. The 2020 National Comprehensive Cancer Network (NCCN) cancer-related pain guidelines also pointed out that when mild cancer-related pain occurs, nonopioids and adjuvant therapies should first be considered. Opioids should be used when moderate or severe cancer-related pain occurs [4]. Additionally, the clinical practice guidelines for cancer-related fatigue in 2021 also pointed out that mild fatigue does not require special treatment and only needs auxiliary treatment. Only when moderate or severe fatigue occurs are further evaluation and drug and non-drug interventions needed [29]. Therefore, nurses should pay attention to patients with moderate and severe pain during their work. We paid attention to whether there was moderate or severe cancer-related fatigue, explored the mechanism of interaction between symptoms, and carried out symptomatic joint intervention to improve the quality of life more effectively.

## 5. Limitations

No sensitive physiological indicators of pain or CRF were collected in this study. Therefore, we aimed to further introduce psychological and social predictors of patients with cancer-related pain to predict CRF more comprehensively in the future. In addition, the sample size was not large and was limited to two hospitals. In future studies, we should consider expanding the collection scope of the sample size and appropriately increasing the sample size. Third, the interaction between symptoms in this study was limited to pain and cancer-related fatigue. There is no further in-depth analysis of the characteristics of other symptoms of patients with cancer-related pain and the interaction mechanism between various symptoms. In future studies, the correlation between multiple symptoms should be examined to lay a foundation for formulating a more comprehensive and accurate intervention plan.

## 6. Conclusion

Most patients with cancer-related pain experience moderate to severe fatigue. In addition, their QOL is at a moderate level. The pain had a considerable influence on the general physical function and

social activities of patients. Most patients with mild pain only experienced mild fatigue, and their quality of life was moderate. However, patients with moderate and severe fatigue mostly have moderate or higher levels of fatigue and a lower quality of life. The symptoms of patients with moderate and severe pain should be managed differently from those of patients with mild pain. Nurses should pay attention to patients with moderate and severe pain in their work and explore the mechanism of interaction between symptoms and carry out symptomatic joint intervention to improve the quality of life more effectively.

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## Data availability statement

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

## CRediT authorship contribution statement

**Dun Liu:** Conceptualization, Software, Writing- original draft.-  
**Jin-Sen Weng:** Investigation, Methodology, Validation. **Xi Ke:** Project administration, Writing- reviewing and editing. **Xian-Yi Wu:** Supervision, Resources. **Si-Ting Huang:** Investigation, Data curation.

## Declaration of competing interest

The authors have declared no conflict of interest.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijnss.2022.12.006>.

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