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The Symptom Cluster of Fatigue, Pain, Anxiety, and Depression and the Effect on the Quality of Life of Women Receiving Treatment for Breast Cancer: A Multicenter Study

Winnie K.W. So, PhD, MHA, BN, RN, Gene Marsh, PhD, RN, W.M. Ling, BN, RN, F.Y. Leung, MSc, MBA, BN, RN, Joe C.K. Lo, PDG(HSM), BBA, RN, Maggie Yeung, RN, and George K.H. Li, MBBS, FRCS(Ed), PCSHK, FHKAM(Surg)

Various symptoms are frequently reported by patients with cancer during or after treatment. Fatigue, pain, anxiety, and depression are among the most common (National Institutes of Health, 2004). Most previous literature has examined a single symptom and its effect on patients' functional status and quality of life (QOL). However, patients often experience more than one symptom. The concurrence of related symptoms may have adverse effects on patient outcomes. This study examines the prevalence of fatigue, pain, anxiety, and depression, the relationships among these symptoms, and their effects as well as the effects of other sociodemographic and clinical factors on the QOL of patients with breast cancer undergoing treatment.

Literature Review

Incidence and Survival Rate of Patients With Breast Cancer

Breast cancer is one of the most common cancers worldwide (Breast Health Global Initiative, n.d.). In Hong Kong, breast cancer ranks as the most common cancer and the third leading cause of cancer death in the female population (Hospital Authority: Hong Kong Cancer Registry, 2006b). The incidence rates have increased steadily from 47.7 per 100,000 in 1996 to 72 per 100,000 in 2006 (Hospital Authority: Hong Kong Cancer Registry, 2006a).

The advanced development of cancer treatment increases the survival rate and prolongs lifespan. Overall, the five-year survival rate ranges from 100% (among

Purpose/Objectives: To examine the symptom cluster of fatigue, pain, anxiety, and depression and its effect on the quality of life (QOL) of women receiving chemotherapy or radiotherapy for breast cancer.

Design: Descriptive.

Setting: Oncology outpatient sections of four public hospitals in Hong Kong.

Sample: 215 ethnic Chinese women who were midway through treatment for breast cancer.

Methods: Chinese versions of the Brief Fatigue Inventory, Hospital Anxiety and Depression Scale, Brief Pain Inventory, Functional Assessment of Chronic Illness Therapy for Breast Cancer, and Medical Outcomes Study Social Support Survey were used. Spearman rho correlation and structural equation modeling were used to examine the relationships among the study variables.

Main Research Variables: Breast cancer, fatigue, pain, anxiety, depression, and QOL.

Findings: Most participants reported mild-to-moderate levels of fatigue and pain. Twenty-one percent and 36% of patients might have had an anxiety or depression disorder, respectively. Significant correlations among the four symptoms supported the existence of the symptom cluster. The participants receiving chemotherapy had inadequate social support, experienced higher levels of symptoms, and were more likely to have a poorer QOL.

Conclusions: The findings supported the existence of the symptom cluster that had detrimental effects on QOL.

Implications for Nursing: This study shed light on a contemporary approach of grouping several related symptoms together. The findings enhance nurses' clinical sensitivity when identifying patients in high-risk groups and provide useful information for designing and prioritizing symptom-management strategies to meet patients' needs.

Quick Facts: Hong Kong

Geography: Hong Kong is made up of small islands off the mainland of China covering 1,104 km².

Population: The population in 2008 was 7 million with 98% of Hong Kong's population consisting of Chinese, mainly Cantonese, from mainland China.

Healthcare system priorities and programs: Life expectancy in Hong Kong is 82.5 years (79.4 years for men and 85.5 years for women). Cancer ranked as the leading cause of death in 2007, followed by heart disease and pneumonia. The three most common cancers are lung, colorectal, and breast. Individuals who are diagnosed with cancer can seek medical treatment in the private or public sector. Treatment fees in the public sector range from \$10–\$12 (U.S.) per visit.

Education: The majority of Hong Kong's population has completed a secondary level of education (52%) and 24% of that group received a post-secondary education.

Bibliography

Census and Statistics Department of the Government of Hong Kong. (2009). Education characteristics in Hong Kong. 2006 population by census: Main report. Retrieved May 20, 2009, from <http://www.edb.gov.hk/index.aspx?nodeID=92&langno=1>

Department of Health of the Government of Hong Kong. (2008). *Health facts*. Retrieved May 20, 2009, from http://www.dh.gov.hk/english/statistics/statistics_hs/files/Health_Statistics_pamphlet_2008e.pdf

Hospital Authority: Hong Kong Cancer Registry. (n.d.). Fees and charges for healthcare services. Retrieved May 20, 2009, from http://www.ha.org.hk/visitor/ha_visitor_index.asp?Parent_ID=108&Content_ID=349

Hospital Authority: Hong Kong Cancer Registry. (2006). Leading cancer sites in Hong Kong. Retrieved May 20, 2009, from <http://www3.ha.org.hk/cancereg/eng/stat.asp>

patients with localized disease) to 27% (among patients with distant-stage disease) (American Cancer Society, 2007). However, inevitable damage occurs to healthy cells and tissue when patients receive cancer therapy, leading to side effects or symptoms occurring during or after treatment. Cancer-related symptoms are major stressors in patients during cancer treatment.

Prevalence and Intensity of Fatigue, Pain, Anxiety, and Depression Among Patients With Breast Cancer

Patients with cancer often experience symptoms as a result of the disease and its treatment. Among various symptoms, fatigue, pain, anxiety, and depression are the most prevalent (National Institutes of Health, 2004) affecting patients with breast cancer (de Jong, Courtens, Abu-Saad, & Schouten, 2002; Miaskowski & Dibble, 1995).

Patients with breast cancer usually perceive moderate-to-severe levels of fatigue (Bower et al., 2000) and its severity may be augmented during treatment (de Jong et al., 2002). Previous studies have shown that more than 50% of patients with breast cancer experience pain (Janz

et al., 2007). Anxiety and depression are described as a significant issue for such patients, with prevalence rates ranging from 33% (Zabora, BrintzenhofeSzoc, Curbow, Hooker, & Piantadosi, 2001) to 54% (Gaston-Johansson, Fall-Dickson, Bakos, & Kennedy, 1999).

Symptom Clusters

Symptoms seldom occur in isolation in patients with cancer (Rutledge & McGuire, 2003). However, the majority of clinical studies have focused on a single symptom (Bostrom, Sandh, Lundberg, & Fridlund, 2004; Connelly & Schmidt, 2004; Stiegelis, Ranchor, & Sanderman, 2004). Although this approach has advanced the understanding of some symptoms, it may not be helpful to healthcare professionals in guiding practice when the patient has several concurrent symptoms.

Dodd et al. (2001) first used the term “symptom clusters” to describe three or more concurrent symptoms that are related to each other. However, the symptoms within the cluster are not required to have the same etiology. Symptom clusters can be used when patients experience fatigue, pain, anxiety, and depression concurrently as a result of cancer or its treatment.

Relationships Among the Symptoms of Fatigue, Pain, Anxiety, and Depression

Empirical evidence has demonstrated a significant association between fatigue and pain, fatigue and psychological disorders, and pain and psychological disorders in a variety of cancer populations (Fox, Lyon, & Farace, 2007; Gaston-Johansson et al., 1999; Hwang, Chang, Rue, & Kasimis, 2003; Reuter et al., 2006). However, most studies have focused on a single symptom or examined an associated symptom. Few studies have examined interactions between fatigue, pain, and psychological disorders together (Fox et al.; Gaston-Johansson et al.). Generalization of the results is limited by the use of small convenience samples and a single clinical setting for data collection. So far, no study has been conducted on a Chinese population.

Factors That Influence Quality of Life Among Patients With Breast Cancer

Numerous studies have examined the QOL and predictors of QOL among patients with breast cancer in western populations. Studies of QOL in a Chinese breast cancer population, however, are limited. Cui et al. (2004) investigated the long-term effects of medical and demographic factors on the QOL of 1,065 Chinese breast cancer survivors and found that recurrence status, time since diagnosis, marital status, income, and education were significantly related to overall QOL. Sun, Wong-Kim, Stearman, and Chow (2005) and

Wong-Kim, Sun, Merighi, and Chow (2005) used qualitative methods to explore QOL in 30 ethnic Chinese patients with breast cancer, including 15 American-born Chinese women and 15 Chinese women not born in the United States. Although family relationships and support were included when describing a good QOL in both groups, more American-born Chinese women used words like independence, freedom, and friendships when describing good QOL. To the best of the authors' knowledge, no research has been conducted investigating the QOL of Chinese women receiving treatment for chemotherapy or radiotherapy. As people from different cultural backgrounds perceive their health and illness differently, cultural beliefs and values should be included when assessing how patients perceive and respond to their illness and symptoms. A need exists to increase knowledge of the symptoms experienced by patients in the context of Chinese culture to help healthcare professionals provide culturally sensitive services.

Effects of the Symptom Cluster on Patient Outcomes

Although nursing research has been carried out to investigate the effects of the symptom cluster on patient outcomes, knowledge obtained in relation to this research still is very limited. Only one study has examined the inter-relationships among the symptoms of fatigue, pain, and depression and their effect on the health status of the breast cancer population (Gaston-Johansson et al., 1999). The findings of this study show that depression ($p < 0.001$) and pain ($p < 0.01$) accounted for 64% (adjusted $R^2 = 0.6$; $F = 15.37$) of the variance in total health status. Fatigue ($p < 0.05$) and depression ($p < 0.001$) accounted for 42% (adjusted $R^2 = 0.36$; $F = 6.46$) of the variance in the perception of health status. However, other sociodemographic and clinical factors that may have affected patient outcomes were not examined.

Purpose

The purpose of this study was to examine the symptom cluster of fatigue, pain, anxiety, and depression and its effect on the QOL of patients with breast cancer receiving chemotherapy or radiotherapy. Specifically, the research sought to answer the following questions.

- What is the prevalence and severity of fatigue, pain, anxiety, and depression?
- Does the symptom cluster of fatigue, pain, anxiety, and depression exist? What is the magnitude of the relationships among these four symptoms?
- What sociodemographic and clinical factors influence QOL?
- To what extent does this symptoms cluster explain participants' QOL?

Conceptual Framework

The **Revised Model for Symptom Management** developed by Dodd et al. (2001) was adopted to guide this study. The model consists of three inter-related dimensions: symptom experience, symptom management strategies, and outcomes. In addition, person, environment, health, and illness are variables influencing all three dimensions (Dodd et al.).

This study focuses on the dimension of symptom experience and outcomes. The researchers modified the model to describe the relationship between experience of the symptom cluster (fatigue, pain, anxiety, and depression) and patients' outcomes (QOL), and the effect of the variables of person (demographics), environment (social support), and health and illness (stage of cancer, comorbidities, types of current treatment, type of surgery received, and time since diagnosis and initial treatment) on outcomes (QOL).

Methods

Setting and Sample

A descriptive design including correlational descriptive and exploratory descriptive components was used in this study. Potential subjects were recruited from the outpatient sections of the departments of clinical oncology or the breast center in the four public hospitals. Eligibility criteria included Chinese women with breast cancer who were aged 18 years or older, had undergone surgery for breast cancer, were midway in their course of chemotherapy or radiotherapy, and were able to communicate in Cantonese. Patients who had a history of a psychiatric disorder, had metastatic brain disease, were diagnosed with stage 0 breast cancer, had a recurrence of breast cancer, or were undergoing palliative care were excluded from the study.

Instruments

Demographic and clinical characteristics: The demographic data form consisted of age, income, marital status, educational level, social support, stage of cancer, comorbidities, duration of illness, type of current treatment, time since initial treatment, and type of surgery received.

Fatigue: The **Brief Fatigue Inventory-Chinese version (BFI-C)** was used to measure the level of fatigue. The BFI-C was developed by Wang et al. (2004) and was translated from the original version of the BFI developed by Mendoza et al. (1999). The tool consists of nine items, including fatigue severity and interference items. An 11-point Likert-type scale ranging from 0 (no fatigue or does not interfere) to 10 (fatigue as bad as you can imagine or completely interferes) was used as a measurement tool. A global fatigue score was obtained

by averaging all the items on the BFI. Good internal consistency and external validity had been demonstrated in a sample of 249 Chinese patients with cancer (Wang et al., 2004). In the current study, the BFI-C was used to measure severity of fatigue in all participants over a one-week period. Cronbach alpha coefficient for the entire scale was 0.94.

Anxiety and depression: The **Hospital Anxiety and Depression Scale (HADS)**–Cantonese-Chinese version was used to measure levels of anxiety and depression. The HADS–Cantonese-Chinese version was developed by Lam, Pan, Chan, Chan, and Munro (1995) and was translated from the original version of the HADS developed by Zigmond and Snaith (1983). The scale consists of 14 items and two subscales (anxiety and depression) with seven items in each subscale. Each item was scored on a four-point Likert-type scale. Total scores for each subscale were calculated by simple summation of individual item responses in the subscales. A higher score indicated more distress. Consistent with the original version of HADS, the Cantonese-Chinese version has been used for measuring the level of psychological distress in various populations, including general hospital inpatients (Leung, Wing, Kwong, Lo, & Shum, 1999) and older adults (Lam et al.). The results showed that the scale had good internal consistency and external validity with favorable sensitivity and specificity for screening for patients with psychiatric disorders. In the current study, the Cronbach alpha coefficients for the anxiety and depression subscales were 0.805 and 0.726, respectively.

Pain: The **Brief Pain Inventory–Chinese version (BPI-C)** was used to measure the level of pain. Wang, Mendoza, Gao, and Cleeland (1996) developed the BPI-C, which was translated from the original version developed by Cleeland (1989). The tool consists of 11 items, including four pain severity items and seven pain interference items. An 11-point Likert-type scale consisting of 0 (no pain or does not interfere) to 10 (pain as bad as you can imagine or completely interferes) was used as a measurement tool. The average of the four pain severity items represented the patients' overall pain intensity. In the current study, the severity of pain was assessed over the prior week. The reliability and validity of the BPI-C has been demonstrated in a sample of 147 Chinese patients with cancer pain (Wang et al., 1996). In the current study, the Cronbach alpha coefficient for pain severity was 0.868.

Quality of life: The Chinese version of the **Functional Assessment of Cancer Therapy for Breast Cancer (FACT-B)** was used to assess the degree of the QOL of the participants. The FACT-B consists of 36 items divided into five subscales: physical, emotional, social, functional well-being, and breast cancer. Each item was rated on a five-point rating scale consisting of 0 (not at all) to 4 (very much). The total score and the subscale scores for the dimension of well-being were calculated.

Higher scores indicated better functional status. Reliability and validity of the FACT-B were examined in 295 patients with breast cancer (Brady et al., 1997) and the internal consistency of the scale was adequate. In this study, the Cronbach alpha coefficient for the entire scale was 0.727.

Social support: The **Medical Outcomes Study–Social Support Survey–Chinese version (MOS-SSS-C)** was used to examine social support of the participants. The MOS-SSS was developed by Sherbourne and Stewart (1991). Yu, Lee, and Woo (2004) translated the MOS-SSS into the Chinese version. This survey consists of 20 items divided into structural support (one item) and functional support (19 items). The functional support items are categorized into four dimensions: emotional or informational support, tangible support, affectionate support, and positive social interaction. Each item is rated on a five-point rating scale of 1 (none of the time) to 5 (all of the time) to indicate how often the respondent received the support. The individual subscale score was calculated from the summation of all items and the total score is calculated from the mean of the subscale scores. These subscales and total scores were rescaled to a 0–100 scale. A higher score indicated better-perceived social support. Good internal consistency and external validity had been demonstrated in 110 Chinese patients diagnosed with heart failure (Lee, Thompson, & Yu, 2005). In the current study, the Cronbach alpha coefficient for the total scale was 0.92.

Procedure

The study was approved by the ethics committees of the study institutions. Potential subjects were approached by a research nurse midway through their regimen for chemotherapy and the third to sixth week for radiotherapy. Data were collected via face-to-face interviews. The medical records were reviewed by the research nurse for the purpose of recording sociodemographic and clinical variables that may affect QOL.

Training Program for Research Nurses

A training program was conducted for research nurses prior to data collection and included an introduction to the study, a discussion of how to conduct a face-to-face interview using a standardized questionnaire (e.g., contents and rationales of the questionnaire, interviewing skills, how to obtain informed consent, consistent use of the study procedure, data recording), and role play to practice conducting an interview. The performance of the research nurses was assessed and feedback was given to them after practice. Also, building good rapport with the participants was emphasized.

Data Analysis

Descriptive statistics were used to examine all variables. Spearman rho correlation was used to

measure the magnitude of the relationship among the symptoms of fatigue, pain, anxiety, and depression. A p value of 0.05 or less was regarded as statistically significant. Structural equation modeling (SEM) was performed using the Analysis of Moment Structures (AMOS) (Byrne, 2000) to evaluate direct and indirect relationships among the symptoms, QOL, and sociodemographic and clinical characteristics. To determine whether the data fit the model, values of chi-square (χ^2), the minimum discrepancy divided by its degree of freedom (CMIN/DF), comparative fit index (CFI), and root-mean-square error of approximation (RMSEA) were evaluated. An insignificant χ^2 statistic ($p > 0.05$) indicates that the model does not differ significantly from the data and, therefore, a good fit of model is supported. A CMIN/DF value of less than 3, a CFI close to 0.95, and a RMSEA of less than 0.05 indicate good fit. Parameter estimates represent the strength of the path between two variables and are read as standardized regression coefficients (Byrne).

Results

Sample

Two hundred and eighty-six eligible women were approached from the four public hospitals, and 215 participated in the study, a response rate of 75%. Tables 1 and 2 show the sociodemographic and clinical characteristics of the participants.

Prevalence and Severity of Fatigue, Pain, and Anxiety and Depression

The majority of the participants experienced symptoms of fatigue and pain, but at mild-to-moderate levels. Results of the anxiety and depression subscales showed that 21% and 36% of the participants might have anxiety or depression disorder. Table 3 shows the prevalence and severity of fatigue, pain, anxiety, and depression in all participants.

Relationships Among Fatigue, Pain, Anxiety, and Depression

Significant correlations were reported among the symptoms of fatigue, pain, anxiety, and depression, which ranged from 0.248–0.627 ($r_{\text{fatigue-pain}} = 0.465$, $r_{\text{fatigue-anxiety}} = 0.467$, $r_{\text{fatigue-depression}} = 0.529$, $r_{\text{pain-anxiety}} = 0.294$, $r_{\text{pain-depression}} = 0.248$, $r_{\text{anxiety-depression}} = 0.627$; all $p < 0.01$).

Figure 1 shows the full model of sociodemographic and clinical characteristics, symptoms, and QOL in women with breast cancer undergoing chemotherapy or radiotherapy. All possible relationships between variables were included in the full model.

The fit of the original model was poor ($\chi^2 = 298.948$ [55, $N = 215$], $p < 0.001$, CMIN/DF = 5.435, CFI = 0.689,

RMSEA = 0.141). Three major modifications were performed to improve the fit: nonsignificant paths were removed from the model, a direct path between monthly household income and social support was added, and all sociodemographic or clinical characteristics were removed except characteristics that significantly predicted the four symptoms and QOL. After modification, the final model demonstrated a good fit, $\chi^2 = 17.596$, $p = 0.285$, CMIN/DF = 1.173, CFI = 0.995, RMSEA = 0.028 (see Figure 2).

Factors That Influenced Quality of Life

Results of squared multiple correlation (SMC) showed that the factors of fatigue, pain, anxiety, and depression, together with the covariates of social support and type of treatment, explained 66% of the variance associated with QOL. Participants who had experienced a higher level

Table 1. Participants' Demographic Characteristics

Characteristic	$\bar{X}$	SD	Range
Age (years)	51.65	10.36	29–84
Social support	76.01	15.27	26.32–100
Emotional and informational support	74.78	16.09	22.50–100
Tangible support	76.57	18.98	20–100
Affectionate support	80.97	15.17	40–100
Positive social interaction	74.67	17.71	20–100

Characteristic	n	%
Marital status		
Single, divorced, or widowed	50	23
Cohabitation or married	165	77
Educational level		
No formal education or primary school (grades 1–6)	76	35
Secondary (grades 7–12)	108	50
University	31	15
Occupation		
Employed	48	23
Not employed	160	77
Monthly household income (Hong Kong \$)^a		
Less than 5,000	39	18
5,001–10,000	47	22
10,001–30,000	100	47
30,001–50,000	20	9
More than 50,000	9	4
Religion (i.e., Catholic, Christian, Buddhist, or ancestor worship)		
Yes	112	52
No	103	48
Clinical site		
1	12	6
2	71	33
3	60	28
4	72	33

$N = 215$

^a\$1 in U.S. currency equals about \$7.80 in Hong Kong currency.

Note. Because of incomplete data, not all values total 215.

Table 2. Participants' Clinical Characteristics

Characteristic	$\bar{X}$	SD	Range
Time since breast cancer diagnosis (months)	5.53	2.99	2–19
Time since initial treatment started (weeks)	16.92	8.49	3–63
Time since current treatment started (weeks)	8.36	5.61	2–29
Comorbidity (Charlson Index)	2.13	0.46	2–6

Characteristic	n	%
Stage of cancer		
I	33	15
II	112	52
III	69	32
IV	1	1
Current treatment		
Chemotherapy	128	60
Radiotherapy	87	40

N = 215

of fatigue, pain, anxiety and depression, inadequate social support, and were undergoing chemotherapy were more likely to have poorer QOL than participants who had lesser symptoms, adequate social support, and were receiving radiotherapy. Monthly household income and type of surgery predicted QOL through an indirect pathway by its association with social support, depression, and pain. Participants with lower incomes and who had undergone mastectomy were prone to have poorer QOL if they had inadequate social support and higher levels of depression.

Discussion

Prevalence and Severity of Fatigue, Pain, Anxiety, and Depression

In the current study, the prevalence of severe fatigue and pain were lower than previous studies (de Jong et al., 2002; Miaskowski & Dibble, 1995). Possible reasons include the different types of treatment patients received, the period of data collection, and the length of the postsurgical period. In general, patients with breast cancer receive radiation treatment five days per week for four to six consecutive weeks. Lower levels of fatigue in the group of patients receiving radiotherapy might have affected the overall mean score of fatigue among all participants. Also, patients receiving chemotherapy for breast cancer usually receive four to eight courses, and each course of treatment is received once every three weeks. The responses at the time of data collection might not have been at the peak level of symptom experience, which may have caused underestimation of the severity of fatigue experienced by participants.

Miaskowski and Dibble (1995) examined the prevalence and cause of pain among 97 outpatients with breast cancer. The majority reported that pain was caused by postsurgical neuropathic syndrome and bone metastases. In this study, data were collected midway through chemotherapy and radiation treatment. The length of the postsurgical period and the various types of pain experienced by participants during the period of data collection may have affected the reported pain levels.

Results on the anxiety and depression subscales showed that 21% (n = 44) had anxiety and 36% (n = 77) might have been at risk for depression. These results indicate that breast cancer and its related treatment may have had greater negative effects on the psychological well-being of the participants. Also, psychological disorders may reduce the efficacy of chemotherapy by altering neuronal and hormonal secretion during stress (Su et al., 2005).

The findings of the study show the importance of assessing the psychological well-being of this patient population. In Chinese culture, patients may not express their emotions openly because of the importance placed on the virtues of tolerance and maintaining interpersonal relationships in harmony (Bond, 1991). Therefore, incorporating the measurement of psychological disorders into nursing assessment procedures is vital. Once psycho-

Table 3. Prevalence and Severity of Fatigue, Pain, and Psychological Distress

Symptom	n	%	$\bar{X}$	SD	SE	Range
Fatigue			3.04 ^a	2.22	0.15	0–9.33
None	26	12				
Mild to moderate	111	52				
Severe	78	36				
Pain			2.01 ^b	1.74	0.12	0–8
None	50	23				
Mild to moderate	137	64				
Severe	28	13				
Anxiety			4.73 ^c	3.73	0.25	0–19
Normal	171	79				
Mild to moderate	41	19				
Severe	3	2				
Depression			6.11 ^d	4.06	0.28	0–18
Normal	138	64				
Mild to moderate	72	33				
Severe	5	3				

N = 215

^a Global fatigue score

^b Pain intensity score

^c Anxiety subscale score

^d Depression subscale score

SE—standard error

Note. Fatigue prevalence scales had a range of 0 (no fatigue) to 10 (severe fatigue); pain had a range of 0 (no pain) to 10 (severe pain); anxiety had a range of 0 (normal) to 15 or higher (severe anxiety disorder); and depression had a range of 0 (normal) to 15 or higher (severe depression disorder).

logical symptoms are detected, patients can be promptly referred to the clinical psychiatrist or psychologist for additional examination and receive effective symptom-relieving strategies from healthcare professionals.

Relationships Among Fatigue, Pain, Anxiety, and Depression

Significant associations were found between fatigue, pain, anxiety, and depression. Although weak correlations were reported between anxiety and pain and depression and pain, the low magnitude of the pain scores may have mitigated the effect of the strength of associations.

Results of the final model provided a better fit of the direct and indirect relationships among the symptoms of fatigue, pain, anxiety, and depression, which supported the existence of the symptom cluster. The interpretation of the SEM model suggests that the physical symptoms influence the psychological symptoms directly and indirectly. Pain and fatigue had direct and indirect effects on psychological symptoms. As in previous studies, posi-

tive relationships among these symptoms were found in the breast cancer population (Bennett, Goldstein, Lloyd, Davenport, & Hickie, 2004; Haghighat, Akbari, Holakouei, Rahimi, & Montazeri, 2003; Miaskowski & Dibble, 1995). However, no literature explored how one symptom could influence the other through its relationship to a third symptom. Results of the study generated new knowledge of the inter-relationships between physical and psychological symptoms that could be incorporated into symptom assessment and management.

Factors That Influenced Quality of Life

Among all the sociodemographic and clinical factors, only the type of current treatment and social support were significantly associated with QOL. These two factors reflect factors reported in other studies (Janz et al., 2005; Osborne, Ostir, Du, Peek, & Goodwin, 2005). Poorer QOL among participants undergoing chemotherapy may be the result of more severe treatment side effects and poorer self-esteem because treatment side ef-

fects often involve changes in physical appearance. Social support was directly and indirectly associated with QOL. The findings were consistent with previous studies claiming that social support may influence symptom perceptions and be associated with the QOL of patients with cancer (Baider et al., 2003; Moyer & Salovey, 1999; Sammarco, 2001).

Monthly household income and the type of surgery received had an indirect effect on the QOL of the study participants. Poorer QOL was influenced by lower incomes and having undergone mastectomy. Results of the study are consistent with previous research (Ganz, 2004; Luo, Pang, & He, 2005). The economic conditions may affect the adequacy of tangible support that is associated with QOL. Disfigurement of the body after mastectomy may have an adverse effect on emotional well-being. Additional research is needed to examine the effects of the two factors on the QOL of study participants.

Although marital status and educational levels were found to be two factors that influenced the QOL of patients with

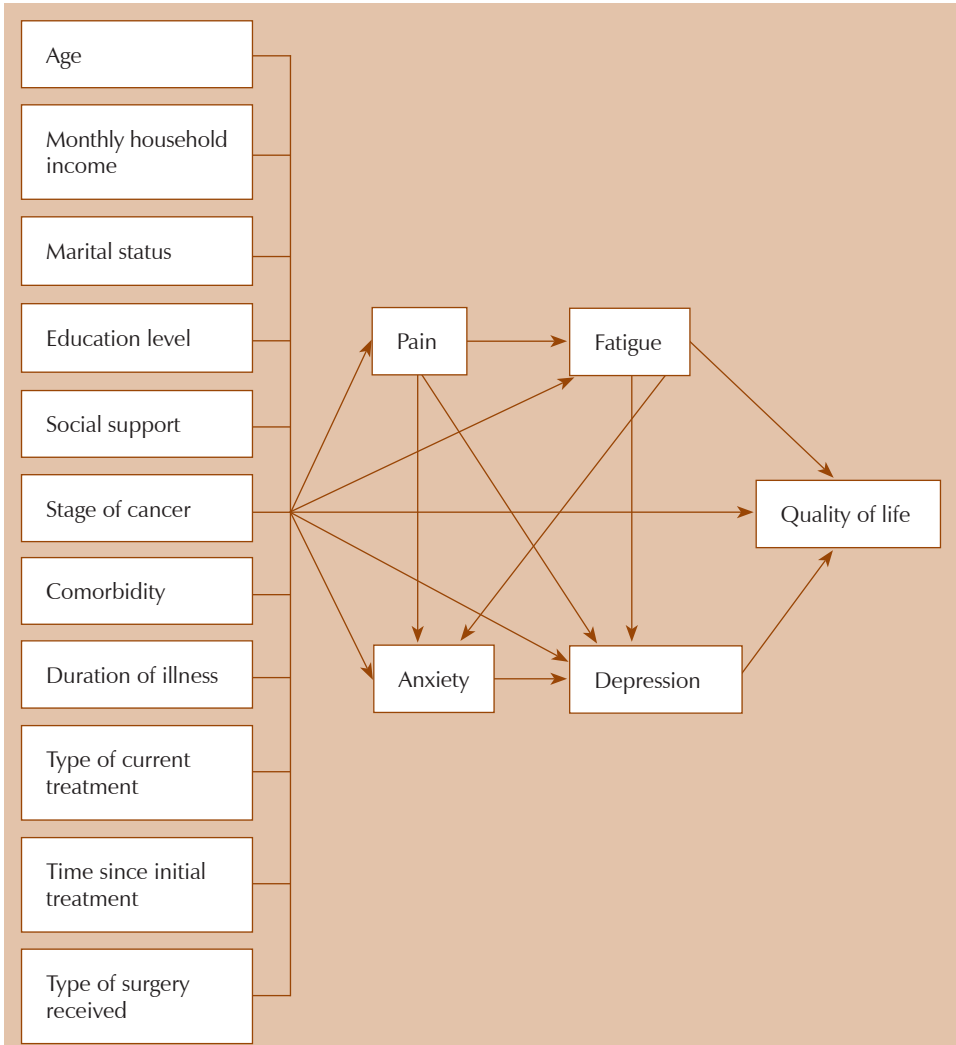


Figure 1. Full Model of Sociodemographic and Clinical Characteristics, Symptoms, and Quality of Life in Study Participants

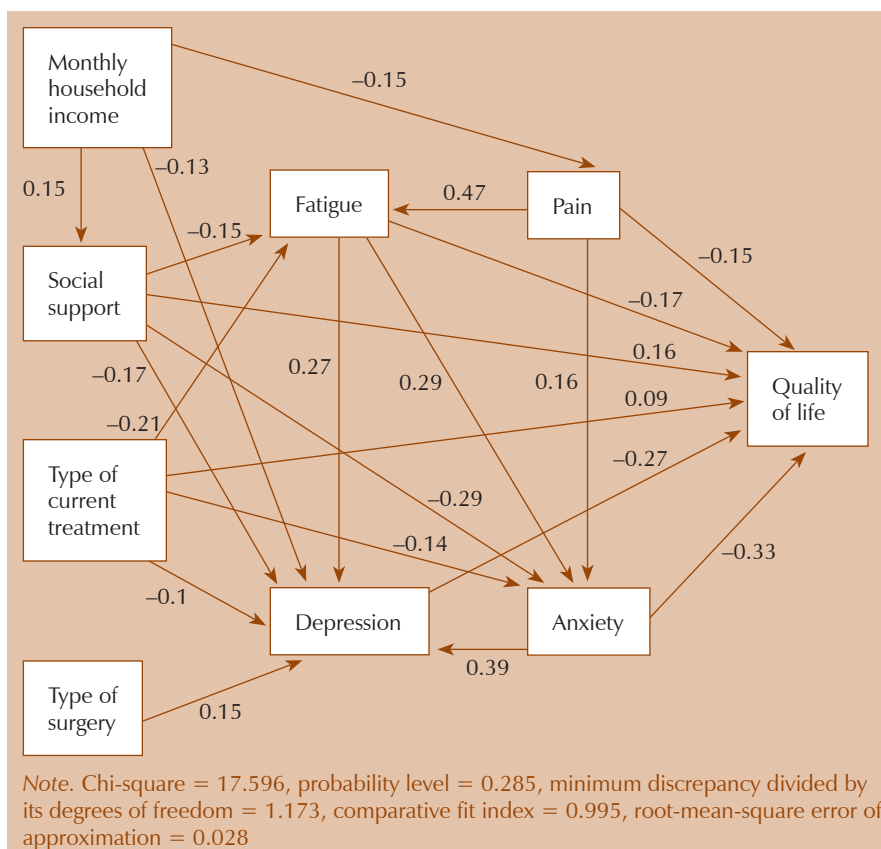


Figure 2. Path Diagram of the Final Model

cancer in other studies (Cui et al., 2004), the factors were excluded from the final model of the current study. Possible reasons may be related to the cultural beliefs and values of this Chinese population. In fact, the family is viewed as the basic structural and functional unit in Chinese culture. Therefore, family beliefs may affect perceptions of health and behavior in maintaining well-being. In a study to explore the QOL of Chinese women with breast cancer, Wong-Kim et al. (2005) found that the immediate family was a source of primary support and an important factor when assessing QOL. Family members played a significant role in a patient's decision-making process. Participants who were single identified their extended family and friends as their primary support system. Therefore, adequate social support from family members may be more important in maintaining the QOL of the participants than other factors, such as marital status and education. Research is needed to better understand how Chinese cultural norms influence the QOL of Chinese patients with breast cancer.

Extent to Which Fatigue, Pain, Anxiety, and Depression Explain Quality of Life

The factors of fatigue, pain, anxiety, and depression, together with covariates of social support and type of treatment, explained 66% of the variance associated

with QOL. Previous research also supported the association of the symptoms of fatigue, pain, and psychological distress with QOL (Lehto, Ojanen, & Kellokumpu-Lehtinen, 2005; Schreier & Williams, 2004; Yen et al., 2006). However, the studies only examined the effect of a single symptom on QOL. The clinical significance of the results of the current study is that healthcare professionals should increase their awareness of the adverse effects of multiple symptoms on QOL.

Limitations

The cross-sectional design of this study provided information about the symptom levels of the participants at only one point in time. The pattern, consistency, and intensity of the symptoms over time were not evaluated. The structured questionnaire consisted of several validated instruments and took the participants 20–30 minutes to complete, which may have created a burden for some participants. Items on the FACT-B include emotional impact and treatment side-effects, the two items in the symptom cluster. Therefore, the results of the study should be interpreted with caution, bearing in mind the presence of these confounding factors.

Implications for Nursing

Results of the study have several implications. The prevalence of severe pain was low, which may have affected pain in the symptom cluster. In future studies, more severely ill patients or patients receiving chemotherapy exclusively could be recruited to examine the existence of the symptom cluster and its effect on QOL when pain is more prominent among the study participants. The findings revealed that the three symptoms and covariates explained 66% of the variance in QOL. The remaining 34% of variance indicated the existence of unexplored factors, such as other symptom distresses and type of chemotherapy agents. The unexplored factors should be included in future research. Because fatigue, pain, anxiety, and depression are the most prevalent symptoms in the cancer population, testing whether the findings of the study can be generalized to wider populations is important.

This study identified specific factors that contributed to QOL. The results should enhance nurses' clinical

sensitivity in identifying patients in high-risk groups. Additional support should be provided to this vulnerable group of patients according to their needs (i.e., provision of education, introduction to peer support group, collaboration with other disciplines for providing better social support, and provision of a hotline service for responding to patients' queries). The coexistence of fatigue, pain, anxiety, and depression provides an insight into the importance of assessing a cluster of symptoms rather than focusing on a single one. Because fatigue, pain, anxiety, and depression are the most prevalent symptoms in patients with cancer, a quick screening for the symptoms should be incorporated into nursing assessment procedures. Any evaluation of the effectiveness of symptom management strategies also should examine the effects on multiple symptoms.

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Winnie K.W. So, PhD, MHA, BN, RN, is an assistant professor in the Department of Nursing Studies at the University of Hong Kong SAR; Gene Marsh, PhD, RN, is an associate professor in the College of Nursing at the University of Colorado Health Science Center in Denver; W.M. Ling, BN, RN, is a nurse specialist in the Department of Clinical Oncology at the Pamela Youde Nethersole Eastern Hospital in Hong Kong SAR; F.Y. Leung, MSc, MBA, BN, RN, is the departmental operation manager of the Infection Control Unit and Joe C.K. Lo, PDG(HSM), BBA, RN, is the departmental operation manager of the Oncology Department, both at Princess Margaret Hospital in Hong Kong SAR; Maggie Yeung, RN, is a registered nurse in the Department of Clinical Oncology at Tuen Mun Hospital in Hong Kong SAR; and George K.H. Li, MBBS, FRCS(Ed), PCSHK, FHKAM(Surg), is an associate consultant in the Department of Surgery at Queen Mary Hospital in Hong Kong SAR. Funding for this research was received from the University of Hong Kong and the University of Colorado. So can be reached at wkwo@hku.hk, with copy to editor at ONF.Editor@ons.org. (Submitted February 2008. Accepted for publication September 23, 2008.)

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References

- American Cancer Society. (2007). *Breast cancer facts and figures, 2007–2008*. Atlanta, GA: Author.
- Baider, L., Andritsch, E., Uziely, B., Ever-Hadani, P., Goldzweig, G., Hofmann, G., et al. (2003). Do different cultural settings affect the psychological distress of women with breast cancer? A randomized study. *European Journal of Cancer Care*, 12(3), 263–273.
- Bennett, B., Goldstein, D., Lloyd, A., Davenport, T., & Hickie, I. (2004). Fatigue and psychological distress—Exploring the relationship in women treated for breast cancer. *European Journal of Cancer Care*, 40(11), 1689–1695.
- Bond, M.H. (1991). *Beyond the Chinese face: Insights from psychology*. Hong Kong: Oxford University Press.
- Bostrom, B., Sandh, M., Lundberg, D., & Fridlund, B. (2004). Cancer patients' experiences of care related to pain management before and after palliative care referral. *European Journal of Cancer Care*, 13(3), 238–245.
- Bower, J.E., Ganz, P.A., Desmond, K.A., Rowland, J.H., Meyerowitz, B.E., & Belin, T.R. (2000). Fatigue in breast cancer survivors: Occurrence, correlates, and impact on quality of life. *Journal of Clinical Oncology*, 18(4), 743–753.
- Brady, M.J., Cella, D.F., Mo, F., Bonomi, A.E., Tulskey, D.S., Lloyd, S.R., et al. (1997). Reliability and validity of the functional assessment of cancer therapy—Breast quality-of-life instrument. *Journal of Clinical Oncology*, 15(3), 974–986.
- Breast Health Global Initiative. (n.d.). About the Breast Health Global Initiative and its mission. Retrieved June 28, 2007, from <http://www.paho.org/English/AD/DPC/NC/pcc-bhgi-about.htm>
- Byrne, B.M. (2000). *Structural equation modeling with AMOS: Basic concepts, applications, and programming*. Mahwah, NJ: Lawrence Erlbaum Associates.
- Cleeland, C.S. (1989). Measurement of pain by subjective report. In C.R. Chapman & J.D. Loeser (Eds.), *Advances in pain research and therapy: Issues in pain measurement* (vol. 12, pp. 391–403). New York: Raven Press.
- Connelly, S.T., & Schmidt, B.L. (2004). Evaluation of pain in patients with oral squamous cell carcinoma. *Journal of Pain*, 5(9), 505–510.
- Cui, Y., Shu, X.O., Gao, Y., Cai, H., Wen, W., Ruan, Z.X., et al. (2004). The long-term impact of medical and sociodemographic factors on the quality of life of breast cancer survivors among Chinese women. *Breast Cancer Research and Treatment*, 87(2), 135–147.
- de Jong, N., Courtens, A.M., Abu-Saad, H.H., & Schouten, H.C. (2002). Fatigue in patients with breast cancer receiving adjuvant chemotherapy: A review of the literature. *Cancer Nursing*, 25(4), 283–299.
- Dodd, M., Janson, S., Facione, N., Faucett, J., Froelicher, E.S., Humphreys, J., et al. (2001). Advancing the science of symptom management. *Journal of Advanced Nursing*, 33(5), 668–676.
- Fox, S.W., Lyon, D., & Farace, E. (2007). Symptom clusters in patients with high-grade glioma. *Journal of Nursing Scholarship*, 39(1), 61–67.
- Ganz, P.A. (2004). Quality of life at the end of primary treatment of breast cancer: First results from the moving beyond cancer randomized trial. *Journal of the National Cancer Institute*, 96(5), 376–387.
- Gaston-Johansson, F., Fall-Dickson, J.M., Bakos, A.B., & Kennedy, M.J. (1999). Fatigue, pain, and depression in preautotransplant breast cancer patients. *Cancer Practice*, 7(5), 240–247.
- Haghighat, S., Akbari, M.E., Holakouei, K., Rahimi, A., & Montazeri, A. (2003). Factors predicting fatigue in breast cancer patients. *Supportive Care in Cancer*, 11(8), 533–538.
- Hospital Authority: Hong Kong Cancer Registry. (2006a). Annual figures by site, age group, and sex. Retrieved May 20, 2009, from http://www3.ha.org.hk/cancereg/e_b1.asp
- Hospital Authority: Hong Kong Cancer Registry. (2006b). Leading cancer site in Hong Kong in 2006. Retrieved May 20, 2009, from <http://www3.ha.org.hk/cancereg/eng/stat.asp>
- Hwang, S.S., Chang, V.T., Rue, M., & Kasimis, B. (2003). Multidimensional independent predictors of cancer-related fatigue. *Journal of Pain and Symptom Management*, 26(1), 604–614.
- Janz, N.K., Mujahid, M., Chung, L.K., Lantz, P.M., Hawley, S.T., Morrow, M., et al. (2007). Symptom experience and quality of life of women following breast cancer treatment. *Journal of Women's Health*, 16(9), 1348–1361.
- Janz, N.K., Mujahid, M., Lantz, P.M., Fagerlin, A., Salem, B., Morrow, M., et al. (2005). Population-based study of the relationship of treatment and sociodemographics on quality of life for early stage breast cancer. *Quality of Life Research*, 14(6), 1467–1479.
- Lam, C.L.K., Pan, P., Chan, A.W.T., Chan, S., & Munro, C. (1995). Can the Hospital Anxiety and Depression (HAD) scale be used on Chinese elderly in general practice? *Family Practice*, 12(2), 149–154.
- Lee, D.T.F., Thompson, D.R., & Yu, D.S.F. (2005). Reliability and validity of the Medical Outcomes Study Social Support Survey

- (Chinese version). *Journal of the American Geriatrics Society*, 53(5), 920–921.
- Lehto, U.S., Ojanen, M., & Kellokumpu-Lehtinen, P. (2005). Predictors of quality of life in newly diagnosed melanoma and breast cancer patients. *Annals of Oncology*, 16(5), 805–816.
- Leung, C.M., Wing, Y.K., Kwong, P.K., Lo, A., & Shum, K. (1999). Validation of the Chinese-Cantonese version of the Hospital Anxiety and Depression Scale and comparison with the Hamilton Rating Scale of Depression. *Acta Psychiatrica Scandinavica*, 100(6), 456–461.
- Luo, Y., Pang, D., & He, X. (2005). Analysis of factors influencing living quality of patients with breast cancer. *Chinese Nursing Research*, 19(8A), 1426–1429.
- Mendoza, T.R., Wang, X.S., Cleeland, C.S., Morrissey, M., Johnson, B.A., Wendt, J.K., et al. (1999). The rapid assessment of fatigue severity in cancer patients: Use of the Brief Fatigue Inventory. *Cancer*, 85(5), 1186–1196.
- Miaskowski, C., & Dibble, S.L. (1995). The problem of pain in outpatients with breast cancer. *Oncology Nursing Forum*, 22(5), 791–797.
- Moyer, A., & Salovey, P. (1999). Predictors of social support and psychological distress in women with breast cancer. *Journal of Health Psychology*, 4(2), 177–191.
- National Institutes of Health. (2004). State-of-the-Science Conference Statement on symptom management in cancer: Pain, depression, and fatigue. *Journal of the National Cancer Institute. Monographs*, 32, 9–16.
- Osborne, C., Ostir, G.V., Du, X., Peek, M.K., & Goodwin, J.S. (2005). The influence of marital status on the stage at diagnosis, treatment, and survival of older women with breast cancer. *Breast Cancer Research and Treatment*, 93(1), 41–47.
- Reuter, K., Classen, C.C., Roscoe, J.A., Morrow, G.R., Kirshner, J.J., Rosenbluth, R., et al. (2006). Association of coping style, pain, age, and depression with fatigue in women with primary breast cancer. *Psycho-Oncology*, 15(9), 772–779.
- Rutledge, D.M., & McGuire, C. (2003). Evidence-based symptom management. In C.H. Yarbro, M.H. Frogge, & M. Goodman (Eds.), *Cancer symptom management* (3rd ed.). Sudbury, MA: Jones and Bartlett.
- Sammarco, A. (2001). Perceived social support, uncertainty, and quality of life of younger breast cancer survivors. *Cancer Nursing*, 24(3), 212–219.
- Schreier, A.M., & Williams, S.A. (2004). Anxiety and quality of life of women who receive radiation or chemotherapy for breast cancer. *Oncology Nursing Forum*, 31(1), 127–130.
- Sherbourne, C.D., & Stewart, A.L. (1991). The MOS Social Support Survey. *Social Science and Medicine*, 32(6), 705–714.
- Stiegelis, H.E., Ranchor, A.V., & Sanderman, R. (2004). Psychological functioning in cancer patients treated with radiotherapy. *Patient Education and Counseling*, 52(2), 131–141.
- Su, F., Ouyang, N., Zhu, P., Ouyang, N., Jia, W., Gong, C., et al. (2005). Psychological stress induces chemoresistance in breast cancer by upregulating *mdr1*. *Biochemical and Biophysical Research Communications*, 329(3), 888–897.
- Sun, A., Wong-Kim, E., Stearman, S., & Chow, E.A. (2005). Quality of life in Chinese patients with breast cancer. *Cancer*, 104(12, Suppl.), 2952–2954.
- Wang, X.S., Hao, X.S., Wang, Y., Guo, H., Jiang, Y.Q., Mendoza, T.R., et al. (2004). Validation study of the Chinese version of the Brief Fatigue Inventory (BFI-C). *Journal of Pain and Symptom Management*, 27(4), 322–332.
- Wang, X.S., Mendoza, T.R., Gao, S., & Cleeland, C.S. (1996). The Chinese version of Brief Pain Inventory (BPI-C): Its development and use in a study of cancer pain. *Pain*, 67(2–3), 407–416.
- Wong-Kim, E., Sun, A., Merighi, J.R., & Chow, E.A. (2005). Understanding quality-of-life issues in Chinese women with breast cancer: A qualitative investigation. *Cancer Control*, 12(Suppl. 2), 6–12.
- Yen, J.Y., Ko, C.H., Yen, C.F., Yang, M.J., Wu, C.Y., Juan, C.H., et al. (2006). Quality of life, depression, and stress in breast cancer women outpatients receiving active therapy in Taiwan. *Psychiatry and Clinical Neurosciences*, 60(2), 147–153.
- Yu, D.F., Lee, D.T., & Woo, J. (2004). Issues and challenges of instrument translation. *Western Journal of Nursing Research*, 26(3), 307–320.
- Zabora, J., BrintzenhofeSzoc, K., Curbow, B., Hooker, C., & Piantadosi, S. (2001). The prevalence of psychological distress by cancer site. *Psycho-Oncology*, 10(1), 19–28.
- Zigmond, A.S., & Snaith, R.P. (1983). The Hospital Anxiety and Depression Scale. *Acta Psychiatrica Scandinavica*, 67(6), 361–370.