

Symptom Clusters and Quality of Life in Older Adult Breast Cancer Survivors

Rachel A. Roiland, MS, RN, and Susan M. Heidrich, PhD, RN

Breast cancer accounts for one in four cancer diagnoses in women in the United States (American Cancer Society [ACS], 2009). Gender and age are the two greatest risk factors for developing the disease, with older women having a higher likelihood of being diagnosed than younger women (ACS, 2009). From 2003–2007, the median age of women diagnosed with breast cancer was 61 and, as of January 2007, about 2.5 million women in the United States had a history of breast cancer (National Cancer Institute, 2010). That number is expected to increase as a large cohort of middle-aged women move into older adulthood and their risk for breast cancer is increased. However, with early detection and improved treatment effectiveness, these women may survive and live for many years after treatment.

As breast cancer survivors age, they can expect to experience a variety of symptoms that may be late effects of cancer, its treatment, the result of normal aging processes, or chronic illnesses (Heidrich, Egan, Hengudomsub, & Randolph, 2006). In breast cancer survivors, those symptoms have been found to negatively affect well-being and have been associated with an increased incidence of depression and anxiety (Kornblith & Ligibel, 2003; Manning-Walsh, 2005a). Similar relationships have been found in other groups of cancer survivors. Mirabeau-Belle et al. (2009) found that fatigue, nausea, vomiting, and sleep disturbance in ovarian cancer survivors were correlated with worse emotional states, lower spirituality scores, increased fear of recurrence, and lower quality of life. Deimling, Bowman, Sterns, Wagner, and Kahana (2006) observed a strong correlation between increased number of symptoms and worry in a sample of breast, colorectal, and prostate cancer survivors; worry was one of the strongest predictors of anxiety and depression.

Effective symptom management may be able to lessen or negate these effects and improve breast cancer survivors' quality of life. How to address the multiple symptoms older adult cancer survivors experience is an important issue. The concept of symptom clusters has emerged as an important topic in oncology research, but the research has not adequately addressed the unique

Purpose/Objectives: To identify symptom clusters in older adult breast cancer survivors (ages 65–97 years) and examine whether symptom clusters are related to demographic, health, and quality-of-life variables.

Design: Factor analysis to identify possible symptom clusters. The resulting clusters then were correlated with quality-of-life measures.

Setting: Phone interviews between the participants and a trained research nurse.

Sample: 192 breast cancer survivors (\bar{X} age = 70).

Methods: This was a secondary data analysis of the baseline measures of demographics, health history, symptom bother, and physical, mental, and existential dimensions of quality of life. Exploratory and confirmatory factor analyses were conducted as well as multiple indicator multiple cause modeling and partial correlation analyses to assess the relationships among clusters and demographic, health history, and quality-of-life measures.

Main Research Variables: Self-reported symptom bother, demographics such as age and education level, health history, and quality of life.

Findings: Seven clinically distinct symptom clusters tapping 36 different symptoms in older adult breast cancer survivors were found. These symptom clusters were significantly related to multiple dimensions of quality of life.

Conclusions: Older adult breast cancer survivors experience multiple concurrent symptoms that appear to cluster. Identifying symptom clusters helps to elucidate possible intersymptom relationships which may lead to the design of more effective symptom management interventions for older adult breast cancer survivors.

Implications for Nursing: Older adult breast cancer survivors should be assessed for a wide variety of symptoms if clinicians hope to identify and understand intersymptom relationships. Such assessment would enable more comprehensive symptom management.

symptom experience of older adult cancer survivors. In addition, a focus on symptom clusters may be important in generally understanding the symptom experience occurring in numerous chronic illnesses or in old age.

Research on symptom clusters has been based on the idea that symptoms are not independent entities but,

instead, interact with each other. Certain symptoms have a tendency to present together or cluster. However, little consensus exists regarding what a symptom cluster is, how to go about identifying and examining symptom clusters analytically, and what the implications are for interventions to improve symptoms. The two most commonly cited definitions are by Dodd, Miaskowski, and Paul (2001) and Kim, McGuire, Tulman, and Barsevick (2005). Dodd et al. (2001) proposed, "When three or more concurrent symptoms (e.g., pain, fatigue, sleep insufficiency) are related to each other, they are called a symptom cluster. The symptoms within a cluster are not required to share the same etiology" (p. 465). Kim et al. (2005) require only two concurrent symptoms to be related to constitute a symptom cluster and add that clusters need to be stable and relatively independent of other clusters. The common element in the definitions is that symptoms occur concurrently and are related to each other in some way. What is meant by related has not been well articulated, but it may be that clustering symptoms relate to each other via a biologic mechanism such as elevated inflammatory processes that result in the presentation of the clustering symptoms (Cleeland et al., 2003). Symptoms also may relate to one another through the degree of burden they inflict on individuals. It may be that symptoms with higher levels of reported burden cluster with each other and interact to exacerbate burden levels. Another possibility is that the ways in which symptoms within a cluster relate vary from cluster to cluster, necessitating examination of those relationships on a cluster-by-cluster basis.

Studies identifying symptom clusters have used different approaches. Some have proposed symptom clusters based on previous empirical research and tested whether the a priori symptom clusters were related statistically (Barsevick, Whitmer, Nail, Beck, & Dudley, 2006; Dodd et al., 2001; Fox & Lyon, 2006, 2007). The most common approach has been to assess symptoms using a symptom inventory, such as the MD Anderson Symptom Inventory or the Edmonton Symptom Assessment Scale, and then identify symptom clusters using factor or cluster analysis (Chen & Lin, 2007; Chow, Fan, Hadi, & Filipczak, 2007; Gleason et al., 2007; Olson et al., 2008; Sarna & Brecht, 1997; Wang, Tsai, Chen, Lin, & Lin, 2008). This last approach may be a better representation of the actual symptom experience because symptoms are assessed systematically.

The impact of symptom clusters on patient outcomes also has been examined. Miaskowski, Dodd, and Lee (2004) proposed that the effects of symptom clusters on patient outcomes are different than the effects of a single symptom. Patients reporting the presence of multiple symptoms or higher distress from multiple symptoms—such as fatigue, pain, sleep insufficiency, and depression—have poorer functional status compared to patients reporting only one symptom or lower symptom

distress scores (Chen & Tseng, 2006; Dodd et al., 2001; Gaston-Johansson, Fall-Dickson, Bakos, & Kennedy, 1999; Given, Given, Sikorskii, & Hadar, 2007). However, whether this difference is a function of the quantity or quality of the clustering symptoms is unknown.

Most research on symptom clusters has been conducted with individuals undergoing treatment for cancer and has focused on treatment-related symptoms. Little symptom cluster research has focused on cancer survivors; particularly older adult cancer survivors who experience multiple concurrent symptoms (Heidrich et al., 2006). In addition, symptom clusters in cancer survivors, particularly older adult survivors, may be chronic as opposed to acute treatment-related symptoms. Chronic symptoms have the potential for long-term impact on quality of life. Identifying possible symptom clusters and their relationship to patient characteristics and outcomes may lead to a better understanding of older adult breast cancer survivors' symptom experiences, which may ultimately lead to better symptom management.

The current study was conducted to address the following gaps in the literature: few symptom cluster studies on cancer survivors, a narrow rather than broad assessment of symptoms, a focus on only acute treatment-related symptoms, and the lack of attention to older adults, who generally experience more symptoms.

The specific aims of this study were to (a) identify symptom clusters in older adult breast cancer survivors and (b) examine whether symptom clusters are related to demographic, health, and quality-of-life variables.

Methods

Design

The current study was a secondary analysis of data from a randomized clinical trial of an individualized symptom management intervention for older adult breast cancer survivors. The parent study tested an eight-week telephone intervention, during which an older adult breast cancer survivor worked with an advanced practice nurse to identify distressing symptoms, identify and discuss beliefs regarding the symptoms, and develop personalized goals and plans for symptom management. Data regarding demographics, health history, quality of life, and number of and distress from symptoms were collected at baseline and were used for this study. The parent study was approved by the Health Sciences Institutional Review Board at the University of Wisconsin–Madison.

Sample

Eligibility criteria for participation in the parent study were: women aged 65 or older, at least one year since breast cancer diagnosis, at least three months post-treatment (except adjuvant hormonal therapies), and no

recurrent or metastatic disease or other cancer diagnosis. A total of 192 participants completed the baseline measurements used for this analysis.

Instruments

Demographic and health history: Participants were asked about their age, education, marital status, living arrangements, ethnicity, and income. Information regarding date of breast cancer diagnosis, past treatments for breast cancer, and dates of treatment also was collected. The number of chronic illnesses was measured with the **Wisconsin Longitudinal Study of Families Form F**. Respondents identified whether they had been told by a healthcare provider that they had any of 20 health problems, and the total number of health issues was computed.

Symptom distress: Symptoms were assessed with the **Symptom Bother Scale-Revised (SB-R)** (Heidrich et al., 2006). The 37-item scale includes symptoms common to old age, chronic conditions common in old age, and late effects of breast cancer and its treatment. Participants were asked to what degree they were bothered by each symptom. The instrument scale ranged from 0 (do not have the symptom) to 5 (extremely bothered). The scale has been found to be reliable and valid in studies with older adults and adults with cancer with reported reliability coefficients (Cronbach alpha) ranging from 0.78–0.89 (Heidrich, 1993, 1994, 1998; Heidrich et al., 2006). In the current study, the total number of symptoms (0–37) and mean symptom distress were calculated. Cronbach alpha was 0.91.

Quality of life: Four instruments were used to measure the physical, emotional, and existential dimensions of quality of life. The **SF-36[®]** is a 36-item scale containing two subscales measuring physical and mental quality of life (Ware & Sherbourne, 1992). These two subscales capture the extent to which physical or mental health problems interfere with different domains of life. Scores are standardized so that higher scores indicate less interference from physical or mental health issues and, therefore, better physical or mental quality of life. The instrument has been found to be reliable and valid in previous studies of older adult patients and patients with breast cancer with reported reliability coefficients ranging from 0.62–0.9 (Schlenk et al., 1998; Ware & Sherbourne, 1992). In the current study, Cronbach alphas were 0.93 and 0.91 for the physical and mental quality-of-life subscales, respectively.

Existential quality of life was measured with two scales: the 14-item **Purpose in Life (PIL)** scale and the 14-item **Positive Relations with Others (PR)** scale, two of Ryff's (1989) psychological well-being scales. The PIL scale measures the degree to which a person's life has meaning, direction, and goals. Purpose in life has been shown to be important in the quality of life and psychological adjustment of breast cancer survivors

(Jim & Anderson, 2007; Manning-Walsh, 2005b; Stanton, Danoff-Burg, & Huggins, 2002; Stanton, Simonelli, Fowler, Maxwell, & Andersen, 2008). The PR scale taps important dimensions of social support, particularly emotional support. Both scales have been used in cross-sectional, longitudinal, and cross-cultural studies and are related to other indices of well-being (i.e., affect balance, life satisfaction, self-esteem, morale, depression, and internal locus of control). For each scale, participants respond to items on a 1 (strongly disagree) to 6 (strongly agree) scale. Higher scores indicate higher levels of purpose in life or more positive relationships with others. In the current study, Cronbach alphas were 0.88 for both scales.

Depressive symptoms were measured using the 10-item version of the **Center for Epidemiologic Studies-Depression (CES-D)** scale (Radloff, 1977). This scale has been tested and validated in a number of studies of older adults (Irwin, Artin, & Oxman, 1999; Kohout, Berkman, Evans, & Cornoni-Huntley, 1993). The respondents answer "yes" (1) or "no" (0) to whether they experienced a given symptom of depression much of

Table 1. Sample Characteristics

Characteristic	\bar{X}	SD	Range
Age (years)	70	5.3	65–97
Education (years)	14	2.61	10–22
Number of chronic illnesses	6	5.93	2–14
Number of symptoms	17	7.6	3–37
Months since diagnosis of breast cancer	39	40.92	12–266

Characteristic	n	%
Race or ethnicity		
Non-Hispanic Caucasian	180	94
African American	8	4
Hispanic	2	1
Native American or Alaskan	1	1
Asian or Pacific Islander	1	1
Married	111	58
Annual family income (\$)		
Less than 25,000	47	24
25,000–54,999	75	39
55,000–84,999	30	16
85,000 or greater	18	9
No response	22	11
Living arrangement		
Living alone	64	33
Living with others	116	60
No response	12	6
Types of cancer treatment^a		
Radiation	135	70
Hormonal therapy	129	67
Lumpectomy	129	67
Mastectomy	75	39
Chemotherapy	72	37

N = 192

^aParticipants may have had more than one type of treatment.

Note. Because of rounding, not all percentages total 100.

the time during the past week. Higher scores indicate more depressive symptoms. The short version, using a cutoff score of 4 for clinical depression, has a sensitivity of 97%, specificity of 84%, and positive predictive value of 85% in older adults. In this study, Cronbach alpha was 0.65. The lower reliability may be from the dichotomous response scale.

Data Analysis

To identify symptom clusters, symptom bother scores for each of the 37 symptoms from the baseline SB-R were analyzed using exploratory and confirmatory factor analysis. Exploratory factor analysis was conducted first with maximum likelihood as the estimator and quartimin (oblique) rotation. Symptoms were retained if the symptom had a factor loading greater than or equal to 0.2 on any of the factors. Generally, the cutoff criteria for factor loadings is from 0.3–0.4 but, given the exploratory nature of this study, 0.2 was used to include the largest number of symptoms in the analysis so as to better represent the symptom experience of the study participants. The factor structure was then tested using a confirmatory factor analysis. In the confirmatory factor analysis, each symptom was assigned to the factor on which it had the highest loading in the exploratory factor analysis. Three fit indices were used to determine the adequacy of the model's fit with the data. For the chi-square to degrees of freedom ratio (χ^2/df), a ratio less than or equal to 3 indicates a good fit for the data (Bollen, 1989). For the Comparative Fit Index (CFI) and the Tucker Lewis Index (TLI), 0.95 or greater indicates good fit (Hu & Bentler, 1999). Both the exploratory and confirmatory factor analyses were completed using the statistical package Mplus®, version 5.

To examine relationships among clusters and demographic and health history variables, multiple indicator multiple cause (MIMIC) structural equation models were used. A MIMIC model allows for the regression of latent variables, such as factors (in this case, the symptom clusters), on to grouping variables that can be either continuous or categorical (Woods, Oltmanns, & Turkheimer, 2009). The MIMIC model analyses were completed using Mplus, version 5.

Relationships among factors and quality-of-life variables were examined by first calculating symptom cluster scale scores by averaging the individual symptom SB-R ratings for the clusters that were identified in the confirmatory factor analysis. The scale scores were then correlated with quality-of-life variables to identify possible significant relationships. This analysis was conducted using the statistical program SPSS®, version 16.0.

Results

Demographic and Clinical Characteristics

Most participants were Caucasian, married, and had a mean age of 70 years. The average time since diagnosis was less than five years, and mean time since last treatment was 34.8 months. Participants reported an average of six chronic conditions with arthritis and rheumatism (74%), high cholesterol (59%), and high blood pressure (57%) being the most prevalent (see Table 1).

Symptom Frequency and Bother

Participants reported an average of 17 symptoms (SD = 7.6). The frequency and mean bother scores for each of the 37 symptoms are shown in Table 2. The five most frequently reported symptoms were stiffness,

Table 2. Symptom Occurrence and Bother

Symptom	n	Occurrence (%)	\bar{X} Bother	SD
Stiffness	169	88	2.11	1.26
Pain	163	85	2.34	1.31
Joint pain	157	82	2.27	1.46
Aching	154	80	1.97	1.39
Fatigue	150	78	1.93	1.33
Waking too often	132	69	1.62	1.42
Dry skin	129	67	1.38	1.3
Difficulty falling asleep	119	62	1.47	1.45
Memory problems	115	60	1.28	1.31
Weight gain or loss	112	58	1.55	1.57
Weakness	104	54	1.28	1.46
Decreased sex drive	104	54	1.03	1.29
Shortness of breath	100	52	1.1	1.29
Hot flashes	100	52	1.29	1.52
Vaginal dryness	96	50	1.04	1.29
Swelling in hands and feet	92	48	1.08	1.32
Waking too early	90	47	1.1	1.42
Increased urination	90	47	0.96	1.24
Numbness or tingling in hands, arms, or legs	90	47	1.09	1.35
Irritated eyes	86	45	0.99	1.24
Feeling anxious	86	45	0.94	1.18
Balance problem	83	43	0.96	1.28
Itching	81	42	0.99	1.37
Hair thinning or loss	79	41	1.02	1.48
Incontinence	79	41	0.95	1.32
Headaches	79	41	0.75	1.1
Dry mouth	77	40	0.9	1.33
Trouble concentrating	73	38	0.73	1.1
Constipation	67	35	0.83	1.33
Thirst	67	35	0.65	1.04
Depression	58	30	0.67	1.17
Nightmares or disturbing dreams	58	30	0.52	0.93
Mood swings	54	28	0.53	0.97
Dizziness	50	26	0.51	0.99
Changes in smell or taste	48	25	0.47	0.96
Lymphedema	33	17	0.44	1.11
Vaginal discharge	25	13	0.2	0.61

N = 192

pain, joint pain, aching, and fatigue. Mean symptom bother scores ranged from 2.3 for pain to 0.2 for vaginal discharge. The five most bothersome symptoms reported by participants were pain, joint pain, stiffness, aching, and fatigue.

Exploratory Factor Analysis

Results from the exploratory factor analysis indicated a seven-factor solution was the most acceptable. The fit indices for this model were $\chi^2/df = 1.62$, $p = 0.001$, CFI = 0.9, and TLI = 0.85. The CFI and TLI were below the "good fit" values, but the solution warranted additional examination because the factors were clinically interpretable. Only one symptom (vaginal discharge) was dropped because of factor loadings less than 0.2.

Confirmatory Factory Analysis

The seven-factor solution from the exploratory factor analysis was tested with confirmatory factor analysis using a maximum likelihood estimation and quartimin (oblique) rotation. Results are reported in Table 3. The fit indices were $\chi^2/df = 1.82$, $p = 0.001$, CFI = 0.821, and TLI = 0.803. Overall, the indices indicate an adequate fit of the model to the data. The seven factors were labeled musculoskeletal, neurocognitive, dryness, urinary, circulatory, sleep, and hormonal symptoms.

All standardized factor loadings were significant in this model, indicating that the items were appropriately assigned to the factors and were sufficient indicators of the latent variable underlying each cluster. In addition, the R^2 was greater than 0.2 for 32 of 36 symptoms, indicating the item is a reliable indicator of the factor. Four symptoms had an R^2 less than 0.2 (vaginal dryness, hot flashes, decreased sex drive, and shortness of breath), but were retained because at least 50% of the sample reported having these symptoms.

Symptom cluster scale scores were computed by averaging the SB-R bother mean scores for each item loading on the cluster. The two most bothersome clusters were the musculoskeletal and sleep clusters, with mean bother scores of 1.98 and 1.4, respectively.

Table 3. Confirmatory Factor Analysis Loadings, Factor Alphas, and Mean Symptom Bother Scores

Factor and Item	Standardized Loadings*	Standard Error	Factor Alpha	\bar{X} Bother	SD
Musculoskeletal	–	–	0.89	1.98	1.1
Aching	1.18	0.08	–	–	–
Stiffness	0.99	0.08	–	–	–
Pain	0.97	0.08	–	–	–
Joint pain	1.05	0.09	–	–	–
Weakness	1.13	0.09	–	–	–
Fatigue	0.95	0.09	–	–	–
Neurocognitive	–	–	0.81	0.87	0.94
Balance problem	0.88	0.09	–	–	–
Dizziness	0.58	0.07	–	–	–
Memory problems	1.03	0.08	–	–	–
Trouble concentrating	0.9	0.07	–	–	–
Dryness	–	–	0.69	1.09	0.85
Dry skin	0.77	0.1	–	–	–
Itching	0.87	0.1	–	–	–
Dry mouth	0.82	0.1	–	–	–
Thirst	0.59	0.08	–	–	–
Shortness of breath	0.55	0.1	–	–	–
Urinary	–	–	0.98	0.98	0.84
Incontinence	1.06	0.1	–	–	–
Increased urination	0.95	0.09	–	–	–
Decreased sex drive	0.23	0.1	–	–	–
Irritated eyes	0.41	0.01	–	–	–
Circulatory	–	–	0.69	0.82	0.8
Swelling in hands and feet	0.9	0.09	–	–	–
Changes in smell and taste	0.45	0.07	–	–	–
Hair thinning or loss	0.72	0.12	–	–	–
Constipation	0.62	0.1	–	–	–
Lymphedema	0.52	0.09	–	–	–
Numbness in hands and feet	0.76	0.1	–	–	–
Sleep	–	–	0.8	1.4	0.96
Waking too often	1.34	0.09	–	–	–
Waking too early	1.14	0.09	–	–	–
Difficulty falling asleep	0.84	0.1	–	–	–
Vaginal discharge	0.17	0.05	–	–	–
Hormonal	–	–	0.88	0.89	0.76
Mood swings	0.82	0.06	–	–	–
Depression	0.97	0.07	–	–	–
Feeling anxious	0.83	0.08	–	–	–
Nightmares	0.47	0.07	–	–	–
Hot flashes	0.5	0.11	–	–	–
Headaches	0.5	0.08	–	–	–
Vaginal dryness	0.35	0.1	–	–	–

* $p < 0.001$

Relationship of Symptom Clusters to Demographic, Health History, and Quality of Life

MIMIC models were used to test whether any demographic or clinical variables (i.e., past cancer treatments) were significantly related to any of the symptom cluster scale scores. For demographic variables, the only significant relationship was between years of education and the circulatory cluster ($\gamma = 0.002$, $p = 0.006$). For health history, the number of chronic illnesses was significantly related to all seven symptom clusters: musculoskeletal

($\gamma = 0.23, p = 0.0001$), neurocognitive ($\gamma = 0.17, p = 0.0001$), dryness ($\gamma = 0.14, p = 0.0001$), urinary ($\gamma = 0.18, p = 0.0001$), circulatory ($\gamma = 0.215, p = 0.0001$), sleep ($\gamma = 0.15, p = 0.0001$) and hormonal ($\gamma = 0.11, p = 0.0001$). Having had a mastectomy was significantly related to the hormonal cluster ($\gamma = 0.74, p = 0.021$), and past lumpectomy (but not radiation) was significantly related to the neurocognitive cluster ($\gamma = 0.528, p = 0.042$).

Relationship Between Symptom Clusters and Quality of Life

Partial correlations were computed between the symptom cluster scale scores and the quality-of-life measurements, controlling for number of medications, age, years of education, family income, and number of chronic conditions. As shown in Table 4, higher levels of depression and poorer mental quality of life were significantly related to higher symptom bother from all seven symptom clusters. Worse physical quality of life was associated with higher symptom bother from all but the hormonal symptoms. Less purpose in life was associated with higher symptom bother for all but the sleep symptoms, and less positive relations were associated with higher symptom bother from all but the musculoskeletal and sleep symptoms.

Discussion

Seven clinically distinct symptom clusters tapping 36 different symptoms in older adult breast cancer survivors were found, and the symptom clusters were significantly related to multiple dimensions of quality of life. The finding of clinically distinct symptom clusters may indicate that a biologic mechanism is linking the symptoms within a cluster together and distinguishing the clusters from each other. Uncovering biologic mechanisms is one of the goals of symptom cluster research because such mechanisms suggest that treatment for one symptom may be efficacious in treating all symptoms in the cluster (Miaskowski & Aouizerat, 2007). The Sickness Behavior Model has been proposed to explain a biologic mechanism for the symptoms observed in individuals with cancer or who are undergoing treatment for cancer (Cleland et al., 2003). The model suggests that the presence of cancerous tumors leads to increased production of pro-inflammatory cytokines, such as interleukin-1 and interleukin-6. In animal models, increased production of these cytokines has been associated with fever, pain, somnolence, and

decreased activity. Increased levels of these pro-inflammatory cytokines also have been found to be related to changes in measurements of depression and quality of life in patients with cancer who had not yet started treatment (Rich, 2007). Whether the Sickness Behavior Model can explain the numerous and often chronic symptoms experienced by older adult cancer survivors is unclear.

A major issue is whether the symptom clusters identified in older adult breast cancer survivors are from the individual's past cancer and cancer treatment or attributable to normal aging and age-related chronic health issues. In this study, significant relationships were noted between mastectomy and the hormonal cluster and lumpectomy and the neurocognitive cluster, whereas number of chronic conditions was significantly related to all seven symptom clusters. The explanations for those relationships are unclear, but it would be informative to compare symptom clusters in cancer and noncancer groups over time to see whether clusters change from treatment through survivorship or differ by diagnosis. Such an examination might provide a clearer explanation for relationships between past treatment and current symptoms in older adult cancer survivors. Future studies also should examine the possible mechanisms underlying symptom clusters to better understand how and when symptoms interact.

Age was significantly related to two clusters (neurocognitive and dryness), even with the restricted age range in the sample. This underscores the importance of taking age into account in research on symptoms since so many symptoms are age-related. Ignoring the influence of age can lead to erroneous causal inferences (i.e., that a symptom cluster is related to the underlying diagnosis [in this case, breast cancer] rather than the aging process or other unknown age-related health issues). On the other hand, the number of chronic conditions was significantly related to all of the clusters, underscoring the importance of taking comorbidities into account in studies of older adults to avoid erroneous conclusions about, for example, the effects of aging.

Table 4. Partial Correlations Among Symptom Clusters and QOL Measures

Symptom Cluster	CES-D	Physical QOL	Mental QOL	PIL	PR
Musculoskeletal	0.43**	-0.71**	-0.33**	-0.19**	-0.03
Neurocognitive	0.48**	-0.14**	-0.54**	-0.41**	-0.29**
Dryness	0.39**	-0.45**	-0.45**	-0.37**	-0.28**
Urinary	0.32**	-0.32**	-0.29**	-0.22**	-0.16*
Circulatory	0.46**	-0.55**	-0.47**	-0.33**	-0.19**
Sleep	0.39**	-0.33**	-0.21**	-0.12	-0.09
Hormonal	0.54**	-0.12	-0.72**	-0.54**	-0.45**

* $p < 0.05$; ** $p < 0.01$

CES-D—Center for Epidemiologic Studies—Depression; PIL—Purpose in Life scale; PR—Positive Relations With Others scale; QOL—quality of life

Note. Correlations calculated using the scale scores from the symptoms clusters; correlations adjusted for number of medications, age, years of education, family income, and number of chronic conditions.

The results of this study provide additional evidence for the relationship between symptom experience and quality of life. In this study, the musculoskeletal cluster and physical quality of life were highly correlated. This relationship makes intuitive sense given that the symptoms in this cluster (aching, weakness, joint pain, stiffness, pain, and fatigue) would make it difficult to be physically active or carry out physical activities of daily living. Another particularly strong relationship was observed between the hormonal cluster (mood swings, depression, anxiety, nightmares, hot flashes, headache, weight gain or loss, and vaginal dryness) and mental quality of life. This finding is consistent with other studies that found hot flashes to be more distressing and severe in breast cancer survivors compared to women with no cancer history (Carpenter, Johnson, Wagner, & Andrykowski, 2002). Hot flashes also have been related to greater sleep disturbance and interference with activities of daily living, as well as poorer quality of life (Carpenter et al., 2002; Gupta et al., 2006; Rand et al., 2010). A study by Schultz, Klein, Beck, Stava, and Sellin (2005) found significant relationships between menopausal symptoms such as hot flashes and painful intercourse (a possible indication of vaginal dryness) and unhappiness, fatigue, and difficulty concentrating. However, for the current study, some measurement overlap may have occurred given that the symptom of depression loaded on the hormonal cluster and the mental quality-of-life subscale taps depressed mood.

Other dimensions of quality of life also were found to have significant relationships with several of the symptom clusters. Purpose in life was significantly related to all of the clusters except for the sleep cluster. Previously, purpose in life in men and women older than age 85 has been shown to be negatively affected by musculoskeletal symptoms, and older adults reporting low levels of purpose in life experienced earlier death compared to individuals with high levels of purpose in life (Boyle, Barnes, Buchman, & Bennett, 2009; Hedberg, Gustafson, & Brulin, 2010). Positive relationships also were significantly correlated with the majority of the symptom clusters; a finding consistent with Manning-Walsh (2005b) who found that positive relations were negatively related to symptom distress in breast cancer survivors. Purpose in life and positive relationships with others have been found to be important components of quality of life in old age in the general population (Borg, Hallberg, & Blomqvist, 2006; Bowling, Banister, Sutton, Evans, & Windsor, 2002; Low & Molzahn, 2007). The significant relationships among symptom clusters and quality-of-life measures observed in the current study illustrate the far-reaching effects symptoms can have on multiple dimensions of breast cancer survivors' quality of life and emphasizes the importance of adequate symptom management in this population.

Limitations

The first limitation to this study is that the cross-sectional design precludes the ability to determine causal relationships. For instance, it may be that the symptom clusters influenced quality of life or it may be that quality of life influenced either the experience or reporting of different symptoms, or the relationships may be reciprocal. On the other hand, previous cancer treatments, such as mastectomy and lumpectomy, have been related to some current symptom clusters. Because this study was cross-sectional, the authors also could not address the temporal nature of how symptoms are experienced (i.e., symptoms often wax and wane over time). Future studies should incorporate a longitudinal design to better understand those issues.

A second limitation is that the sample for this study included only women who had been diagnosed and treated for breast cancer. Participants primarily were Caucasian and somewhat highly educated. The results of this study may not be generalizable to men, different racial and ethnic groups, or to survivors with other types of cancers. On the other hand, the women in this study were diverse in terms of socioeconomic status and rural versus urban communities. In addition, they were similar to older women in the general population in terms of their overall health status.

A final limitation is the use of self-report data that can be associated with monomethod bias and attenuated correlations. Future studies of symptom clusters would benefit from the addition of biophysical measures, particularly if underlying biologic mechanisms of symptom clusters are to be determined.

Conclusions

Seven symptom clusters were identified and were found to be significantly related to multiple dimensions of quality of life in older adult breast cancer survivors. Older adult breast cancer survivors experience multiple symptoms concurrently and should be screened for a wide variety of symptoms if clinicians hope to provide comprehensive symptom management. Identifying symptom clusters may help to elucidate intersymptom relationships, which may lead to the design of more effective interventions that can target symptoms known to be related to one another. This may result in greater improvements in patient outcomes, such as quality of life.

Implications for Nursing Practice

Thorough symptom assessment should be routine for breast cancer survivors if clinicians hope to provide comprehensive symptom management. Given the number of symptoms identified by participants in this study (an average of 17), symptom assessments should be

comprehensive, including symptoms common to old age as well as symptoms common in breast cancer survivors, since these symptoms may interact and, thereby, cause greater burden to the individual. The assessments should be incorporated into the care provided by nurses and physicians in oncology and primary care to ensure that changes in symptom occurrence, burden, and severity are identified and interventions are developed. In addition, communication between primary care providers and oncology specialists in caring for older cancer survivors is essential to being able to assess the etiology of symptoms that can be ambiguous in older adult cancer survivors. A yearly assessment of symptoms and educating patients to report any new, worrisome symptoms would be im-

portant in determining whether a change in symptoms is from aging, chronic health problems, or a new or recurrent cancer. Developing more effective and efficient symptom management may lead to better quality of life for breast cancer survivors.

Rachel A. Roiland, MS, RN, is a dissertator and the John A. Hartford Building Academic Geriatric Capacity scholar and Susan M. Heidrich, PhD, RN, is a professor emerita in the School of Nursing, both at the University of Wisconsin–Madison. This study was supported by an award (#R01AG022914) from the National Institute on Aging and the Office of Cancer Survivorship, National Cancer Institute. Roiland can be reached at raroiland@wisc.edu, with copy to editor at ONFEditor@ons.org. (Submitted October 2010. Accepted for publication November 12, 2010).

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