Original Article

Longitudinal Examination of Symptom Profiles Among Breast Cancer Survivors

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Nancy E. Avis, PhD, Beverly Levine, PhD, Sarah A. Marshall, MPH, and Edward H. Ip, PhD

Department of Social Sciences and Health Policy (N.E.A., B.L., E.H.I.), Wake Forest School of Medicine; and Department of Biostatistical Sciences (S.A.M., E.H.I.), Wake Forest School of Medicine, Winston-Salem, North Carolina, USA

Abstract

Context. Identification of cancer patients with similar symptom profiles may facilitate targeted symptom management.

Objectives. To identify subgroups of breast cancer survivors based on differential experience of symptoms, examine change in subgroup membership over time, and identify relevant characteristics and quality of life (QOL) among subgroups.

Methods. Secondary analyses of data from 653 breast cancer survivors recruited within eight months of diagnosis who completed questionnaires at five time points. Hidden Markov modeling was used to 1) formulate symptom profiles based on prevalence and severity of eight symptoms commonly associated with breast cancer and 2) estimate probabilities of changing subgroup membership over 18 months of follow-up. Ordinal repeated measures were used to 3) identify patient characteristics related to subgroup membership and 4) evaluate the relationship between symptom subgroup and QOL.

Results. A seven-subgroup model provided the best fit: 1) low symptom burden, 2) mild fatigue, 3) mild fatigue and mild pain, 4) moderate fatigue and moderate pain, 5) moderate fatigue and moderate psychological, 6) moderate fatigue, mild pain, mild psychological, and 7) high symptom burden. Seventy percent of survivors remained in the same subgroup over time. In multivariable analyses, chemotherapy and greater illness intrusiveness were significantly related to greater symptom burden, while not being married or partnered, no difficulty paying for basics, and greater social support were protective. Higher symptom burden was associated with lower QOL. Survivors who reported psychological symptoms had significantly lower QOL than did survivors with pain symptoms.

Conclusion. Cancer survivors can be differentiated by their symptom profiles.   J Pain Symptom Manage 2017;53:703−710. © 2016 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.

Key Words

Breast cancer, hidden Markov model, symptoms, quality of life, longitudinal

Introduction

Breast cancer patients commonly experience symptoms such as pain, depression, and fatigue as a consequence of their cancer or treatment, and these symptoms may persist, or develop, even after treatment ends.[1] However, clinical and research evidence suggests individual variability in the symptoms patients experience.[2–4] Additionally, although cancer patients frequently experience multiple co-occurring symptoms, these symptoms have traditionally been studied and treated in isolation.[5]

The study of multiple symptoms has become an area of active investigation and has diverged along two conceptually different lines. The first approach examines the clustering of symptoms to determine which symptoms cluster together.[5,6] A second approach examines how patients reporting similar symptoms group together to form patient subgroups based on their specific symptom cluster.[5] Patients may differ in terms of symptom severity and/or type of symptom. This approach focuses on individual variation among patients to determine if subgroups differ on clinical outcomes. The present study focuses on this second approach.

Address correspondence to: Nancy E. Avis, PhD, Department of Social Sciences and Health Policy, Wake Forest School of Medicine, Medical Center Blvd., Winston-Salem, NC 27157, USA. E-mail: navis@wakehealth.edu

Latent class analysis (LCA) and cluster analysis (CA) are methods exemplifying this second approach[2–4,7–10] and typically focus on symptom severity.[4,7,8,10] Although these approaches can be useful for identifying patients with high symptom burden, they do not provide information on patients experiencing qualitatively different symptom profiles. Few researchers have studied the combination of symptom severity and symptom type.[2–4]

LCA, CA,[6] path analysis,[11] and cross-sectional comparisons of patient clusters at each time point[12] have been used with longitudinal data. However, none of these methods provides insight into symptom subgroup transition. Patient transition from one symptom subgroup to another is particularly relevant for understanding the impact of beginning or ending treatment and/or response to an intervention. The application of methods suitable for longitudinal analysis of symptoms has appeared only recently in the literature. The hidden Markov model (HMM) is a longitudinal extension of latent class analysis that avoids separately analyzing repeatedly measured data by time point and is able to derive an entire trajectory of subgroup membership for each individual.[13,14]

The present study takes advantage of HMM analysis to examine symptom evolution based on previously identified important symptoms for cancer patients.[1] The present analysis had four objectives. We used HMM to 1) identify subgroups of breast cancer patients based on their symptom profiles and 2) estimate the probability of an individual patient changing subgroup membership over 18 months. We further 3) examined sociodemographic factors, disease and treatment characteristics, and psychosocial factors for their association with subgroup membership in bivariate and multivariate analyses. Finally, we 4) evaluated the association between subgroup membership and quality of life (QOL).

Methods
Study Sample
This was a secondary analysis of a longitudinal study of age-related differences in adjustment to breast cancer.[15] Details on study recruitment and eligibility are reported elsewhere. All sites obtained approval from their institutional review boards. Data were collected at five time points: the first survey (administered within eight months of breast cancer diagnosis), and 3, 6, 12, and 18 months after completion of the first survey. The self-administered questionnaire included questions on symptoms, sociodemographics, QOL, and psychosocial factors. A medical chart review was performed one year after the first survey to obtain treatment-related data.

Measures
Symptoms. Study participants completed a 39-item symptom checklist based on the Women's Health Initiative study[16] and adapted from the Breast Cancer Prevention Trial Symptom Scale.[17] For all symptoms, participants were first asked whether it occurred during the past month. If the symptom did occur, participants were asked if the symptom was mild (did not interfere with usual activities), moderate (interfered somewhat with usual activities), or severe (so bothersome that usual activities could not be performed). For the purpose of these analyses, we selected six symptoms common among cancer survivors and typically studied as part of a symptom cluster: fatigue or low energy level, restless sleep, general aches and pains, joint pains, feeling depressed, and difficulty concentrating.[1]

Quality of Life. The Functional Assessment of Cancer Therapy−Breast (FACT-B) was used to measure cancer-related QOL.[18] The FACT-B consists of the FACT General (FACT-G) subscale (26 items) and the Breast-Specific Concerns subscale (nine items). Items are based on a five-point Likert scale and refer to the past seven days. Items are summed, and higher scores reflect better QOL.

The following variables, some of which were time varying, were evaluated for their association with symptom subgroups.

Sociodemographic Variables. Sociodemographic variables, all time-invariant, included age at diagnosis, race (white vs. nonwhite), ability to pay for basics (very or somewhat hard vs. not at all hard), educational level (high school or less vs. more than high school), and marital/partner status.

Cancer-Related Variables. Cancer-related variables obtained from the medical chart included cancer stage (I, II, or II) as defined at diagnosis based on tumor size, lymph node status, and metastases,[19] and two time-varying treatment variables: chemotherapy status (yes/no at given time point), and radiation (yes/no at given time point).

Psychosocial Factors. Psychosocial factors included two measures that were both time varying. The Illness Intrusiveness Ratings Scale assesses the degree to which breast cancer diagnosis and treatment affect 13 life areas: health, diet, paid work, active recreation, passive recreation, financial situation, relationship with spouse, sex life, family relations, other social relations, self-expression, religious expression, and community.[20] Total scores range from 16 to 112, with higher scores indicating greater intrusiveness (coefficient $\alpha = 0.93$). Social support was assessed by the RAND Social Support Scale,[21] which contains 19 items measuring four aspects of support: emotional support, tangible support, affection, and social interaction.