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Examining patterns of multivariate, longitudinal symptom experiences among older adults with type 2 diabetes and cancer via cluster analysis

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ABSTRACT

Purpose: Diabetes and cancer are chronic conditions that produce symptoms, some unique to each condition and others common to both. Previous studies have reported on subgroups of patients who experience distinct combinations of symptoms in cross-sectional samples and the univariate longitudinal trajectories of individual symptoms. The literature currently lacks examples of research that take a multivariate longitudinal perspective to understanding patients' symptom experiences. The purpose of this study was to identify subgroups of patients who share distinct multivariate longitudinal profiles with respect to how symptom severity changes over time for a set of five symptoms (pain, fatigue, change in appetite, nausea, and numbness and tingling).

Methods: This exploratory study included 43 participants with pre-existing diabetes from eight community-based cancer centers who were receiving chemotherapy for a solid tumor. Using baseline and 8-week data, a model-based cluster analysis with Bayesian regularization was used to identify subgroups.

Results: Two groups were identified. Group 1 experienced mild symptoms that changed very little at 8 weeks; group 2 experienced mild to moderate symptom severity, with small increases in fatigue, nausea, and numbness and tingling. Effect size confidence intervals suggest that level of depression, length of time with diabetes, and severity of diabetes at baseline may differ between groups.

Conclusions: More research in this area is needed to further test this model, address limitations associated with analyzing a small sample, and explore factors that may be associated with changes in the overall symptom experience for patients with diabetes and cancer.

Introduction

Cancer and diabetes are two conditions that frequently co-occur (Giovanucci et al., 2010; Psarakis, 2006). Individuals with diabetes and cancer have a poorer prognosis, higher mortality rates, higher infection rates, and shorter remission periods compared to individuals with cancer who do not have diabetes (Barone et al., 2008, 2010; Peairs et al., 2011; Psarakis, 2006). Both cancer and diabetes have associated symptoms. Symptoms occurring while individuals are treated with chemotherapy can be attributed to the cancer treatment, cancer disease process, or preexisting comorbidities (Brant et al., 2011). Symptoms associated with diabetes may be confused with cancer-related symptoms and can compound the symptoms experienced during cancer treatment (Clark et al., 2007).

The occurrence of multiple symptoms simultaneously is common in patients with cancer (Enders, 2010; Given et al., 2007). Symptom clusters have been defined as the presence of three or more concurrent symptoms (Enders, 2010) and have been frequently studied in cancer patients (Brant et al., 2011; Dodd et al., 2010; Ellis, 2010; Molassiotis et al., 2010; Roiland and Heidrich, 2011; Ruxton and Neuhäuser, 2010), yet few studies utilize existing comorbidities as a covariate (Bender et al., 2008). Having a comorbid condition increases the risk of experiencing at least two symptoms within a symptom cluster (Fritz et al., 2012).

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Brant et al. (2011) found the presence of comorbidities increased the risk of developing sleep disturbances and fatigue. Most studies examined symptom clusters by using either a most-common symptom approach or an all-possible symptom approach (Xiao, 2010). Both of these approaches primarily use a correlational, cluster, or exploratory factor analysis to identify specific clusters (Xiao, 2010).

Previous studies have reported on subgroups of patients who experience distinct combinations of symptoms in cross-sectional samples (Cherwin, 2012; Enders, 2010; Karabulu et al., 2010) and the longitudinal trajectories of individual symptoms (Brant et al., 2011; Molassiotis et al., 2010; Ruxton and Neuhäuser, 2010), literature adopting a multivariate longitudinal perspective to understanding patients' symptom experiences is lacking. This is important because both diabetes and cancer are associated with many different symptoms, and there is little reason to expect that those symptoms will evolve in the same way over time for all patients. However, there may be discernible patterns in the occurrence and severity of symptoms as they develop. Therefore, we set out to identify subgroups of patients who share distinct multivariate longitudinal profiles with respect to how symptom severity changes over time for five symptoms that are commonly found in patients with either diabetes or cancer: pain, fatigue, change in appetite, nausea, and numbness and tingling (Clark et al., 2007; Miaskowski et al., 2006; Nielsen et al., 2011; Pud et al., 2008; Sullivan et al., 2012). Identifying patterns in how a collection of symptoms tends to change over time could be useful in clinical settings, particularly if it is possible to predict which pattern a patient is likely to experience.

Methods

Research design

This exploratory study presents a secondary analysis of previously collected data (Hershey, 2011). Participants were recruited from eight community-based cancer centers in Michigan and Ohio. Baseline data were collected via a self-administered survey; follow-up data were collected 8 weeks later via phone survey. This allowed enough time for participants to receive at least two chemotherapy cycles between baseline and follow-up.

Sample

The 43 participants were selected to represent a population of persons who met all of the following criteria: 1) 50 years of age or older, 2) dually diagnosed with diabetes (either type 1 or 2) and a solid tumor cancer, and 3) eligible for or currently undergoing outpatient chemotherapy (either intravenous or oral), 4) taking medication for diabetes (e.g., daily insulin or an oral hypoglycemic), 5) could read, write, and speak English, 6) could follow written and oral instructions, and 7) had access to a telephone and were able to use it. The exclusion criteria eliminated people who: 1) could not hear or use a telephone, 2) self-reported a history of Alzheimer's or dementia, or 3) were unable to understand written and oral communications. Ability to read and understand English was assessed by the site personnel (clinic nurses) who were familiar with the patient prior to approaching them about the study, and then further assessment was done by the PI at time of initial contact with the participant after the consent form was received.

Two individuals died prior to the follow-up survey at week 8. Because symptom data for them was not observable in principle at that time point, we excluded them from the sample prior to conducting the imputation and analyses ($N = 41$).

Data collection

Recruitment began once we obtained ethics approval from institutional review boards at Michigan State University and the individual cancer centers. We acquired a convenience sample using rolling enrollment. Clinic staff assisting in recruitment identified potential participants using an inclusion/exclusion criteria checklist. The study investigator provided cancer center staff with an educational session on the study protocol and inclusion and exclusion criteria, then nurses at the cancer centers approached potential participants. Nurses gave each patient willing to participate a packet containing the baseline written survey, consent form, a study brochure, and a self-addressed, stamped envelope. Once the survey and signed consent forms were returned to the study investigator, we contacted patients to reconfirm their willingness to participate in the study and to schedule a date for the follow-up survey. The study investigator administered phone surveys 8 weeks after the participants enrolled in the study. All participants who participated were assigned a study ID number, all data was collected and entered into the data files utilizing the study ID number. Files which linked the participant to the ID number were kept in a separate password protected thumb drive and stored in a secured file cabinet in order to maintain confidentiality.

Study variables and measures

Individual characteristics. The sociodemographic variables of age, sex, education level, income status, marital status, race, and ethnicity were considered individual characteristics. These variables were obtained at baseline.

Clinical characteristics. Clinical characteristics included general health, symptoms, number of medications, and number of comorbidities, as well as diabetes and cancer-specific characteristics. The total number of medications participants took daily and as needed and the number of comorbidities they had were reported at baseline.

The total number of comorbidities for each patient was determined by a self-report instrument based on Katz's Comorbidity Questionnaire (Katz et al., 1996), consisting of binary items assessing the presence of chronic diseases: hypertension; asthma; other chronic lung problems; congestive heart failure; heart attack; stroke; neurological conditions; arthritis; emotional, nervous, or psychological problems; and other conditions. For other conditions, patients provided a list. The comorbidities were counted by summing the first nine items and adding the number of unique other conditions after excluding those that overlapped with the first nine items.

Finally, patients completed the seven-item depression subscale from the Hospital Anxiety and Depression Scale (HADS) (Snaith, 2003). The HADS is measured using a 4-point Likert scale, ranging from 0 to 3. The depression subscale has a reported reliability of 0.86 (Snaith, 2003).

Three diabetes-specific clinical characteristics were measured: self-reported length of illness (in years) and self-reported type of diabetes (type 1 or type 2). Finally, diabetes severity was measured by the Diabetes Complications Index, which is the sum of six binary indicators of specific complications associated with diabetes (Fincke et al., 2005).

Four cancer-specific clinical characteristics were also measured. Patients provided information on the type of cancer they had and whether metastasis had occurred, which was a binary indicator; what type of cancer treatment they had received (oral chemotherapy, intravenous [IV], or both); whether or not they had received radiation treatments; and the total number of days they had been in chemotherapy (6 missing values were imputed).

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