Symptom Clusters and Quality of Life in Hospice Patients with Cancer

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Abstract

Background: Symptom control is an important part of palliative care and important to achieve optimal quality of life (QOL). Studies have shown that patients with advanced cancer suffer from diverse and often severe physical and psychological symptoms. The aim is to explore the influence of symptom clusters on QOL among patients with advanced cancer. Materials and Methods: 709 patients with advanced cancer were recruited to participate in a clinical trial focusing on symptom management and QOL. Patients were adults newly admitted to hospice home care in one of two hospices in southwest Florida, who could pass mental status screening. The instruments used for data collection were the Demographic Data Form, Memorial Symptom Assessment Scale (MSAS), and the Hospice Quality of Life Index-14. Results: Exploratory factor analysis and multiple regression were used to identify symptom clusters and their influence on QOL. The results revealed that the participants experienced multiple concurrent symptoms. There were four symptom clusters found among these cancer patients. Individual symptom distress scores that were the strongest predictors of QOL were: feeling pain; dry mouth; feeling drowsy; nausea; difficulty swallowing; worrying and feeling nervous. Conclusions: Patients with advanced cancer reported various concurrent symptoms, and these form symptom clusters of four main categories. The four symptoms clusters have a negative influence on patients’ QOL and required specific care from different members of the hospice healthcare team. The results of this study should be used to guide health care providers’ symptom management. Proper attention to symptom clusters should be the basis for accurate planning of effective interventions to manage the symptom clusters experienced by advanced cancer patients. The health care provider needs to plan ahead for these symptoms and manage any concurrent symptoms for successful promotion of their patient’s QOL.

Keywords: Symptom cluster- symptom distress- quality of life- advanced cancer patients

Introduction

An individual’s symptom experience and ability to function in everyday life are increasingly being acknowledged as important health outcomes for individuals with cancer (Liposcomb et al., 2005). Patients with cancer are known to suffer from a number of severe physical, social and psychological symptoms. These symptoms seldom occur in isolation in patients with advanced cancer. Some symptoms may be directly associated with progression of the disease, whereas others are associated with the treatment (Chang et al., 2000; Cohen and Mount, 2000; Cooley et al., 2003; Portenoy et al., 1994). Dodd et al., (2001) defined symptom cluster as three or more concurrent symptoms that are related to each other but do not necessarily share the same etiology. Dodd et al., (2001) also proposed that if a key symptom in the group of commonly occurring symptoms could be treated then the associated symptoms may be relieved. Kim et al., (2005) redefined symptom cluster as follows: “A symptom cluster consists of two or more symptoms that are related to each other and that occur together. Symptom clusters are relatively independent of other clusters, and may reveal specific underlying dimensions of symptoms. Relationships among symptoms within each cluster should be stronger than relationships among symptoms across different clusters. Symptoms in a cluster may or may not share a common etiology” (p. 278). Most of the attributes of a symptom cluster proposed by Kim et al., (2005) reflect symptom clusters empirically derived from an exploratory factor analysis.

Studies dealing with cancer patients have focused on the occurrence of multiple symptoms or symptom clusters. Dodd et al., (2001) were among the first to use the term symptom clusters in their work on pain, fatigue, and sleep disturbances; and together with others they found that the occurrence of multiple symptoms independently predicts changes in patients’ function, treatment outcomes and quality of life (QOL) if poorly managed (Diegel-Vandyk et al., 2012). In palliative care, the primary goal is alleviating...
symptom distress resulting from multiple symptoms and enhancing QOL for patients and their families (WHO, 2009). To meet the patients’ multiple needs, it is generally recommended that the care provided for them is holistic, multidisciplinary and patient- as well family-centered. To achieve the goal of successful symptom management and to promote optimal QOL in patients with advanced cancer, it is essential to identify the most prevalent and distressing symptoms and discern their impact (Kirkova et al., 2010).

Though patients with advanced cancer experience significant psychological and physical distress, there is limited evidence on how their symptoms cluster together. Previous studies have identified physical symptoms, distress, functional status, psychological symptoms, interpersonal status and social interaction, environmental impact, impact on caregivers, and spiritual outlook to be the most significant factors that should be addressed in palliative care settings (Adler et al., 2009; Teunissen et al., 2007; WHO, 2009). Fatigue and pain are the most prevalent, severe and distressing symptoms at the end of life (EoL), irrespective of the underlying type of cancer, and/or clinical setting (Chang et al., 2000; Cohen et al., 2001; Tranmer et al., 2003). Symptom severity and symptom distress represent distinctive features of QOL. Symptom distress is defined as physical or mental upset, anguish, or suffering reported as a result of specific symptoms (Rodhes et al., 1998). McMillan and Small (2002) studied cancer patients receiving home health based hospice care. The investigators found that lack of energy, dry mouth, pain, feeling bloated and difficulty sleeping were most distressing problems reported by patients, in fact, symptom distress was a significant predictor of QOL. The earlier work of (Cheung et al., 2009), recognized that two distinctive symptom clusters exist in advanced cancer outpatients and these include a psychological cluster (anxiety and depression) and a physical cluster (fatigue, drowsiness, nausea, decreased appetite, and shortness of breath), and both were influenced by the site of the primary cancer. The factors that contribute to the symptom distress include proximity to death, age, disease severity, and functional status (Tranmer et al., 2003).

Even with the advances in our understanding of cancer biology and symptom control, the negative effects of unalleviated symptoms are still common and lead to disruption of treatment (Rosenthal et al., 2007; Hadi et al., 2008; Cleeland et al., 2011; Thong et al., 2011), decreased functioning in everyday life (Dodd et al., 2001), and impaired QOL (Chang et al. 2000). Therefore, symptom clusters are clinically important and influence patient outcomes (Doddet al., 2001; Fox and Lyon, 2006; Griff et al., 2004). The process of managing the symptom experience for patients with cancer is complex partly because the as symptoms are dynamic and have numerous causes and effects. For instances, a study of breast cancer patients revealed that a specific symptom cluster (pain, fatigue, sleep disturbances, and depression) fluctuated among four subgroups of outpatients, and the subgroups with high severity levels of all four symptoms reported poorer functional status and QOL (Dodd et al., 2010). Another study reported that as the breast cancer disease or treatment progresses, the symptom severity changed, such that, the increase in severity of sleep disturbance, fatigue, and depression during chemotherapy was similar to that newly diagnosed stage I-III breast cancer patients (Liu et al., 2009).

Few studies have explicitly tested the demographic variates in symptom patterns among advanced cancer patients (Husain et al., 2007; Jodhory et al., 2001; Walsh et al., 2000; Zimmermann et al., 2010), and none have studied the influence of such variates on symptom clusters. To our knowledge, this is the first study to explore symptom clusters and to test the relationship between symptom clusters and QOL in hospice cancer patients. Cognizance of age and related symptom variant may help to improve and provide better symptom directed interventions for particular subgroup of patients with cancer receiving hospice care. A good understanding of these identified contributors to symptom distress can help to provide effective comprehensive care to all patients with cancer (Hughes et al., 2012). Therefore, knowledge from the current study may be useful when planning intervention studies to manage multiple concurrent symptoms in patients with cancer receiving hospice care and when providing clinical care with goal of palliation of cancer symptoms to improve QOL. The aim of this study was to identify symptom clusters in oncology patients receiving hospice care and examine whether symptom clusters are related to demographic, health, and QOL variables. The study aims to meet the following objectives:

1) Identify symptom cluster in oncology patients receiving care at large not for profit- hospices in the southeastern United States;
2) Examine whether symptom clusters in cancer patients receiving hospice care are related to demographic (particularly age), and QOL variables.

Conceptual Framework
The conceptual framework that was used for the identification of symptom clusters in this study was the Theory of Unpleasant Symptoms (Lenz et al., 1997). The theory explains the concept of multiple symptoms as those which that occur simultaneously and may be interrelated. The theory suggests that each symptom can vary in duration, intensity, quality, and distress, and that multiple symptoms can occur together as a result of distinct event or one symptom can precede another. Therefore, the relationships among symptoms are multiplicative rather than additive in nature. For instance, a patient’s complaint of lack of energy gets considerably worse when lack of appetite and difficulty sleeping are experienced concurrently. The development of symptom clusters affects patient outcomes and may be influenced by the patient’s demographic and clinical characteristics. The theory of Unpleasant Symptoms is a good fit for the current study because it clearly defines phenomenon of symptom clusters as well as the relationship among symptoms and QOL. In the current study QOL was considered as one of the outcome of symptom clusters.
Materials and Methods

Design and Sampling
This descriptive, cross-sectional study used self-reported questionnaires to obtain information from a sample of 709 patients with advanced cancer who had been receiving cancer care in the community and were newly admitted to hospice home care in one of two hospices in southwest Florida. English-speaking adults who were receiving care from these hospices participated in the study. Eligible patients were adults with a terminal cancer diagnosis who were able to pass a mental status screening.

Instruments
The study instruments used to collect data were comprised of the revised Memorial Symptom Assessment Scale (MSAS), Hospice Quality of Life Index-14, and demographic data form. The demographic data form was used to collect data about the participant’s age, gender, education level, marital status, religion. This form included data about cancer type.

The MSAS is a patient-rated and multidimensional instrument designed to evaluate the intensity and distress from a list of 33 symptoms. The scale consists of five-point Likert-type response choices for each item, including physical symptoms as well as psychosocial symptoms. The higher the scores on the distress items, the more distressing the symptoms are for the patient (Portenoy et al., 1994). This study used a revised MSAS that was modified for use for hospice patients. The revised MSAS has 25 items rated from 0 – 4 for distress and the resulting subscale scores for distress range from 0 – 100. The construct validity and high reliability of the revised MSAS for use among patients with cancer in hospice care were supported in other studies (McMillan and Small, 2002).

The HQLI-14 is a 14-item shortened version of the previously used and validated Hospice Quality of Life Index (McMillan and Weitzner, 1998). The original version of the HQLI addresses three aspects of overall QOL and these include psychophysiological well-being, functional well-being, and social/spiritual well-being (McMillan and Weitzner, 1998). The validity and reliability of the HQLI were in previous studies (McMillan and Mahon, 1994). The HQLI-14 was developed for repeated clinical use with hospice patients and it measures the overall QOL using three subscales, including psychophysiological well-being (six items), functional well-being (four items) and social/spiritual well-being (four items). Each item is scored using a ten-point scale where 10 indicate the most favorable response and lower scores represent poorer QOL.

Data Collection Procedure
The study was approved by the administration of each hospice before it was submitted to the Institutional Review Board (IRB) at University of South Florida. All study participants provided informed consent. A total of 709 patients had completed data on all of the study measures required for the analysis. The participants were screened each morning by reviewing the face sheet of each patient admitted to the hospice. The patients who had cancer diagnoses and designated caregivers were asked for permission for a home visit to explain the study. During the first home visit, consent was obtained and baseline data were collected.

Statistical Analysis
Data were analyzed using SPSS Version 20.0 (SPSS, Inc., Chicago, IL, 2009). Descriptive statistics were performed to describe the participants’ demographic and clinical characteristics, and symptom experiences. After all assumptions of the statistical analysis were tested and met, exploratory factor analysis was used to determine the number of symptom clusters. Stepwise multiple regression analysis was used to determine the predictive ability of symptoms to predict QOL. An exploratory factor analysis (EFA) was performed to identify the number of symptom clusters based on symptom distress ratings. Exploratory factor analysis with principal components (rotated component matrix with varimax rotation) was used to extract factors using eigenvalues of 1.0 and expressed only factor loadings greater than 0.3 (Hair et al., 2009). The maximum likelihood estimation procedure was used to extract the factors from the variable data. Kaiser’s rule was used to determine which factors were most eligible for interpretation because this rule requires that a given factor is capable of explaining at least the equivalent of one variable’s variance. This is not unreasonable given that factor analysis aims at reducing several variables into fewer factors. The Kaiser-Meyer-Olkin (KMO) was used to examine sampling adequacy or deciding whether factor analysis is appropriate. The communalities were used to observe the level of shared variance between items. These results met criteria and supported the use of factor analysis for this data. Regarding testing of the clustering, all symptoms with factor loadings above 0.30 and loaded on more than one factor were considered and explored through the Pearson’s r correlations. The Cronbach’s alpha coefficient was used to determine the internal consistency and reliability of the clusters that were derived from the factor analysis; if it was more than 0.60. Cronbach’s alpha coefficient was used to test the clustering of symptom clusters which were derived from the factor analysis. Naming and describing the factors were based on the symptoms with higher loadings and correlations. Naming of a symptom cluster was based on the most symptoms presented within that cluster.

Results

Participants’ Characteristics
About two thirds of the sample (n= 400) were male. The mean age of participants was 72.7 years (range= 21 – 95). The majority were married (n=451, 63.3%) and Caucasian (n=690, 96.9%); living with spouse or partner (n=665, 93.4%); and living in suburban area (n=559, 78.7%). The average time since diagnosis was 26.8 months. About one third of patients (34%) had lung cancer, 9.1% had pancreatic cancer, 7.1% had colon cancer, 5.9% had prostate cancer and 5.6% had breast cancer.
Table 1. The Distribution of Symptoms among Patients with Cancer Bother

| Symptoms                          | Occurrence, % | Mean Bother (SD) |
|-----------------------------------|---------------|-----------------|
| Lack of Energy                    | 84            | 2.22 (1.47)     |
| Pain                              | 68.9          | 1.57 (1.44)     |
| Dry Mouth                         | 67.1          | 1.24 (1.36)     |
| Lack of Appetite                  | 58.4          | 1.15 (1.42)     |
| Feeling Drowsy                     | 57.2          | 0.83 (1.21)     |
| Shortness of Breath               | 56.8          | 1.28 (1.47)     |
| Cough                             | 44.1          | 0.77 (1.21)     |
| Constipation                      | 43.2          | 1.07 (1.49)     |
| Worrying                          | 41.4          | 0.89 (1.28)     |
| Difficulty Sleeping               | 41.1          | 0.97 (1.38)     |
| Feeling Sad                       | 40.7          | 0.86 (1.26)     |
| Numbness/tingling in hands or feet| 38.9          | 0.73 (1.22)     |
| Difficulty Concentrating          | 37.0          | 0.64 (1.14)     |
| Dizziness                         | 34.3          | 0.64 (1.12)     |
| Feeling Irritable                 | 31.7          | 0.62 (1.11)     |
| Feeling Nervous                   | 30.4          | 0.60 (1.10)     |
| Nausea                            | 30.4          | 0.66 (1.18)     |
| Feeling Bloated                   | 27.2          | 0.61 (1.19)     |
| Difficulty Swallowing             | 26.6          | 0.60 (1.16)     |
| Sweats                            | 25.7          | 0.46 (1.02)     |
| Problems with Urination           | 23.3          | 0.53 (1.11)     |
| Itching                           | 22.6          | 0.44 (1.11)     |
| Vomiting                          | 15.9          | 0.38 (1.02)     |
| Diarrhea                          | 15.2          | 0.37 (0.99)     |
| Problems with Sexual Interest     | 13.4          | 0.35 (1.01)     |

Symptoms Frequency and Bother

Participants reported an average of 9.8 symptoms (SD= 4.7). The frequency and mean bother score for each of the 25 symptoms are shown in Table 1. The six most commonly reported symptoms were: lack of energy (84%), pain (68.9%), dry mouth (67.1%), lack of appetite (58.4%), feeling drowsy (57.2%), and shortness of breath (56.8%). The most bothersome symptoms were lack of energy, pain, shortness of breath, and dry mouth. The mean symptom bother scores (on a 0 to 4 scale) ranged from 0.35 for problems with sexual interest or activity to 2.2 for lack of energy.

Factor Analysis and Symptom Clusters

Using Kaiser’s rule and Scree plot, 7 factors were extracted. The result shows that the first seven factors together account for 51.3% of the total variance. Table 2 shows the rotated factor loadings (correlations between the variable and the factors). The factors with correlations ≥ 0.3 are highlighted.

As shown in Table 2, 10 symptoms were clearly loaded on more than one factor, with factor loadings above 0.30. Correlations among various symptoms within each factor (cluster) were examined. Pain loaded on factor 1 and factor 4 but the correlations between pain and symptoms within factor 1 were higher than that for factor 4, thus pain was classified within factor 1. Similarly, nausea and vomiting were classified as part of factor 2, shortness of breath was considered to be part of factor 3. Drowsiness, dizziness, and irritability, worrying, feeling sad, difficulty concentrating, lack of energy, and sweating were classified in factor 4. Lack of appetite, difficulty in swallowing, cough and dry mouth were classified in factor 1.

As a result, 4 symptom clusters were identified that account for 38.55% of the total variance. The four factors were named as follows: Factor 1-physical – related symptom (pain, cough, dry mouth, difficulty swallowing, and lack of appetite); Factor 2-gastrointestinal – related symptom (nausea and vomiting); Factor 3- respiratory – related symptom (shortness of breath); and Factor 4 - psychological – related symptom (difficulty concentrating, feeling sad, irritability, sweating, dizziness, drowsiness, worrying, and lack of energy). The variance explained in all symptoms of these factors was 22.09%, 6.28%, 5.48%, and 4.68%, respectively. There were two symptom clusters which had a Cronbach’s alpha coefficient greater than 0.60 and these were the psychological – related symptom (α= 0.77) and gastrointestinal related symptom (α= 0.76).

Relationships of Symptoms clusters to Demographics and Quality of Life

The correlations among the clinical variables of interest are shown in Table 3. The four symptom clusters were significantly related to QOL. In all cases, the correlations were negative, indicating that higher ratings of distress or intensity were correlated with lower QOL scores. Age was significantly and positively correlated
Table 3. Variables Correlation Matrix of Demographic Data with Symptom Clusters and QOL Scores

| Variable          | Age | Years / Schooling | Time since diagnosis (months) | QOL |
|-------------------|-----|-------------------|-----------------------------|-----|
| Factor 1          | -0.141*** | 0.011             | 0.044                       | -0.549*** |
| Factor 2          | -0.187*** | 0.071             | 0.068                       | -0.303*** |
| Factor 3          | -0.137*** | 0.034             | 0.049                       | -0.420*** |
| Factor 4          | -0.221*** | 0.05              | 0.053                       | -0.584*** |

*p < .05; ** p < .01; Factor 1, (Physical-related symptoms); Factor 2, (Gastrointestinal-related symptoms); Factor 3, (Respiratory-related symptoms); Factor 4, (Psychological-related symptoms)

Table 4. One Way ANOVA of QOL Scores by Marital Status and Living Area and Cancer Diagnosis (N= 709)

| QOL Scores    | N   | M    | SD   | F   | p   |
|---------------|-----|------|------|-----|-----|
| Marital Status|     |      |      |     |     |
| Never Married | 35  | 98.05| 16.99|     |     |
| Married       | 430 | 100.97| 17.36|     |     |
| Separated     | 8   | 99   | 15.75|     |     |
| Divorced      | 81  | 100.22| 16.06|     |     |
| Never Married | 126 | 107.9| 17.66|     |     |
| Living Area   |     |      |      |     |     |
| Urban Area    | 9   | 102  | 15.81|     |     |
| Suburban Area | 538 | 101.33| 17.19|     |     |
| Rural Area    | 134 | 105  | 17.99|     |     |
| Cancer Diagnosis|   |      |      |     |     |
| Lung          | 234 | 102.7| 17.55| 2.33| 0.05|
| Pancreas      | 61  | 97.6 | 17.03|     |     |
| Colon         | 49  | 106.57| 16.27|     |     |
| Prostate      | 38  | 106.15| 17.27|     |     |
| Breast        | 37  | 101.75| 17.85|     |     |

N, (Sample size); M, (Mean); F, (Value of ANOVA test)

Table 5. Summary of Multiple Regression Analysis for Statistically Significant Symptom Clusters Predicting QOL (N= 709)

| Model                      | B    | SE   | Beta | t   | Sig |
|----------------------------|------|------|------|-----|-----|
| Factor 1 (Physical-related | -0.742| 0.168| -0.256| -4.418| 0.000|
| symptoms)                  |      |      |      |     |     |
| Factor 2 (Gastrointestinal | 0.368| 0.356| 0.042| 1.034| 0.301|
| related symptoms)          |      |      |      |     |     |
| Factor 3 (Respiratory      | -0.678| 0.418| -0.076| -1.62| 0.106|
| related symptoms)          |      |      |      |     |     |
| Factor 4 (Psychological     | -0.999| 0.113| -0.375| -8.846| 0.000|
| related symptoms)          |      |      |      |     |     |
| Age                        | 0.052| 0.045| 0.036| 1.145| 0.253|
| Years of Schooling         | -0.52| 0.179| -0.088| -2.908| 0.004|

Beta, (Standardized Regression Coefficients); t, (t-test); Sig, (p value)

with QOL ratings and negatively associated with symptom clusters. Other significant correlations were observed between years of schooling and QOL.

Predicting Quality of Life

When the cancer patients’ QOL scores were further analyzed with respect to cancer patients’ demographics (marital status, years of schooling, living area, and cancer diagnosis), significant differences in QOL scores were found between groups using one-way ANOVA test (Table 4) which shows that there was a statistically significant difference in QOL scores by marital status, and cancer diagnosis.

Regression analysis (see Table 5) of the symptom clusters showed that factor 1 and factor 2 were the strongest predictors of QOL. On the other hand, years of schooling were also a strong predictor of QOL.

Discussion

Patients with advanced cancer often experience diverse symptoms, which can vary widely in severity. These symptoms may be caused by the disease (cancer), treatment side effects, or by concomitant conditions. The resulting symptom burden is often high in the affected population (Teunissen et al., 2007; McCarthy et al., 2000), and quality care for such patients necessitates various palliative interventions (Riechelmann et al., 2008) which might put these patients at high risk for potential drug interaction (Riechelmann et al., 2007), and poor QOL (Bekelman et al., 2009). Therefore, recognizing symptom clusters in cancer patients and identifying the factors that influence them and the subsequent QOL is paramount for clinical practice.

Very few studies have explicitly tested the influence of demographic variables on symptom patterns among advanced cancer patients (Husain et al., 2007; Jodhory et al., 2001; Walsh et al. 2000; Zimmermann et al., 2010), and none have studied the influence of such variants on symptom clusters. To our knowledge, the current study is the first to explore symptom clusters and to examine the relationship between symptom clusters and QOL in patients with advanced cancer. The current study identified symptom clusters in patients with advanced cancer newly admitted to hospice home care and examined whether they are associated with specific demographic, and QOL variables.

The findings of the study show that lack of energy, pain, dry mouth, lack of appetite, feeling drowsy, and shortness of breath were the most prevalent symptoms. This result is similar to what has been reported by previous studies (Bender et al., 2005; Tsai et al., 2010; Stark et al., 2012). The participants also reported that the most bothersome symptoms were cough, constipation, worrying difficulty sleeping, and feeling sad, this also has been reported in other studies (McMillan and small, 2002; Stark et al., 2012).

The symptom experience is dynamic and therefore causes different symptom clustering. The factor analysis of the participants’ symptoms showed that they were mainly four categories. The four categories were: physical-related symptoms (pain, lack of appetite, cough, dry mouth, and difficulty in swallowing); gastrointestinal-related symptoms (nausea and vomiting); respiratory-related symptoms (shortness of breath); and psychological-related symptoms (difficulty concentrating, sad, sweating, worrying, feeling drowsy, lack of energy, dizziness, and feeling irritable). Literature shows that until now cancer symptom research has
mostly focused on a single symptom at a time, despite the awareness that patients with advanced cancer often have multiple concurrent symptoms that may exacerbate one another. It is important to systematically and comprehensively assess the dynamics of concurrent symptoms because they are key elements in effective symptom management of cancer patients and therefore improvement of QOL.

The other findings of the current study show that age is significantly associated with all the symptoms highlighted by the study results. The relationships with age appear to suggest that younger patients with advanced cancer perceive greater symptom intensity and distress and worse QOL. It may be that clinicians need to tailor interventions for younger patients who are having greater difficulty coping with the disease and symptoms. The relationship between age and cancer symptom intensity has been previously reported (Jordhy et al., 2001; Baumann et al., 2009; Schmidt et al., 2005). Other significant relationships found (marital status, the level of education, and months since cancer diagnosis) were very weak.

The findings show that newly admitted hospice cancer patients had low QOL scores at admission. Generally, MSAS severity total score and Global distress total score were negatively correlated with QOL scores, indicating that higher rating of distress was related to lower QOL scores. Furthermore, the findings revealed that distress from pain, dry mouth, cough, lack of appetite, feeling drowsy, difficulty in swallowing, worrying, lacking of energy, dizziness, difficulty concentrating, sad, and feeling irritable predicted QOL.

The oncology patients newly admitted to hospice care have symptoms which are more related to the care that they received in the community rather than the hospice care. Therefore, the current study is unique because the symptoms that formed clusters were not predetermined, but rather considered and analyzed all the multiple symptoms patients presented with to identify how they clustered. The large sample size for the current study also provided sufficient statistical power to examine this problem. The findings of the present study provide us important insights into the symptom experiences and relationships between symptom clusters and QOL in cancer patients newly admitted to hospice home care and support the definition suggested by previous studies for symptom cluster as consisting of two or more symptoms that are related to each other and that occur together. There is a need for further studies about the impact of symptoms clusters on patient outcomes in hospice cancer patients.

In conclusion, patients with advanced cancer reported various concurrent symptoms, and these form symptom clusters of four main categories: physical, gastrointestinal, respiratory and psychological related symptoms. The four symptoms clusters have a negative influence on patients’ QOL and required specific care from different members of the hospice healthcare team. Therefore, the current study findings provide us with additional understanding of the symptom clusters which could help health care providers develop more comprehensive assessment tools and care plans to ensure more effective symptom management strategies to improve QOL for cancer patients receiving hospice care.

Conflict of Interest
None disclosed.

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References

Adler ED, Goldfinger IZ, Kalman J, Park ME, SMieier DE (2009). Palliative care in the treatment of advanced heart failure. Circulation, 120, 2597–2606.
Baumann R, Putz C, Rohrig B, Hofiken K, Wedding U (2009). Health – related quality of life in elderly cancer patients. Eur J Cancer Care, 18, 457-65.
Bekelman DB, Rumsfeld JS, Havranek EP, et al (2009). Symptom burden, depression, and spiritual well-being: a comparison of heart failure and advanced cancer patients. J Gen Intern Med, 24, 592–8.
Bender CM, Ergyn FS, Rosenzweig MQ, Cohen SM, Sereika SM (2005). Symptom clusters in breast cancer across 3 phases of the disease. Cancer Nurs, 28, 219-25.
Chang VT, Hwang SS, Feuerman M, Kasimis B (2000). Symptom and quality of life survey of medical oncology patients at a Veterans Affairs medical center: A role for symptom assessment. Cancer, 88, 1175-83.
Cheung WY, Le LW, Zimmermann C (2009). Symptom cluster in patients with advanced cancers. Support Care Cancer, 17, 1223-30.
Cohen SR, Mount BM (2000). Living with cancer: ‘good’ days and ‘bad days - what produces them. Cancer, 89, 1854-65.
Cleeland CS, Mendoza TR, Wang, XS, et al (2011). Levels of symptom burden during chemotherapy for advanced lung cancer: differences between public hospitals and a tertiary cancer center. Clin Oncol, 29, 2859-65.
Cooley ME, Short, TH, Moriarty HJ (2003). Symptom prevalence, distress, and change over time in adults receiving treatment in lung cancer. Psychooncology, 12, 694-708.
Dodd MJ, Cho MH, Cooper BA, Miaskowski C (2010). The effect of symptom clusters on functional status and quality of life in women with breast cancer. Eur J Oncol Nurs, 14, 101-10.
Dodd MJ, Miaskowski C, Paul SM (2001). Symptom clusters and their effect on the functional status of patients with cancer. Oncol Nurs Forum, 28, 465-70.
Digel-Vandyk A, Harrison MB, Macartney G, Ross-White A, Stacey D (2012). Emergency department visits for symptoms experienced by oncology patients: A systematic review. Support Care Cancer, 20, 1589-99.
Fox SW, Lyon DE (2006). Symptom clusters and quality of life in survivors of lung cancer. Oncol Nurs Forum, 33, 931-6.
Gift AG, Jablonski A, Stommel M, Given CW (2004). Symptom clusters in elderly patients with lung cancer. Oncol Nurs Forum, 31, 203 – 10.
Hadi S, Fan G, Hird AE, et al (2008). Symptom clusters in patients with cancer with metastatic bone pain. J Palliat Med, 11, 591–600.
Hair JF, Black WB, Babin BJ, Anderson RE (2009). Multivariate data analysis (7th Edition). Amazon, pp 68-83.
Hughes EF, Wu AW, Carducci MA, Snyder CF (2012). What can I do? Recommendations for responding to issues identified by patient-reported outcomes assessments used in clinical practice. Supp Oncol, 10, 143-8.
Husain A, Myers J, Selby D, Thomson B, Chow E (2011). Subgroups of advanced cancer patients clustered by their symptom profiles: quality-of-life outcomes. *J Palliat Med*, 14, 1246-53.

Kim HJ, McGuire DB, Tulman L, Barsevick AM (2005). Symptom clusters: concept analysis and clinical implications for cancer nursing. *Cancer Nurs*, 28, 270-82.

Kirkova J, Walsh D, Rybicki K (2010). Symptom severity and distress in advanced cancer. *J Palliat Med*, 24, 330-9.

Jordhoy MS, Fayers P, Loge JH, et al (2001). Quality of life in advanced cancer patients: the impact of sociodemographic and medical characteristics. *Br J Cancer*, 85, 1478–85.

Lenz ER, Pugh LC, Milligan RA, Gift A, Suppe F (1997). The middle-range theory of unpleasant symptoms: an update. *ANS Adv Nurs Sci*, 19, 14-27.

Lipscomb J, Gotay CC, Snyder C (2005). Outcomes assessment in cancer: measures, methods and applications. United Kingdom: Cambridge University Press, pp 623-38.

Liu L, Fiorentino L, Natarajan L, et al (2009). Pre-treatment symptom cluster in breast cancer patients is associated with worse sleep, fatigue. *Psychooncology*, 18, 187-94.

McCarthy EP, Phillips RS, Zhong Z, Drews RF, Lunn J (2000). Dying with cancer: Patients’ function, symptoms, and care preferences as death approached. *J Am Geriatr Soc*, 48, 110-21.

McMillan SC, Small BJ (2002). Symptom distress and quality of life in patients with cancer newly admitted to hospice home care. *Oncol Nurs Forum*, 29, 1421-8.

McMillan S, Weitzner M (1998). Quality of life in cancer patients: a revised hospice index. *Cancer Nurs Pract*, 6, 282-8.

McMillan SC, Mahon M (1994). Measuring quality of life in hospice patients using a newly developed hospice quality of life index. *Qual Life Res*, 3, 437-47.

McMillan SC, Small BJ, Haley WE (2011). Improving hospice outcomes through systematic assessment: A clinical trial. *Cancer Nurs*, 34, 89-97.

Portenoy RK, Thaler HT, Kornblith AB (1994). Symptom prevalence, characteristics and distress in a cancer population. *Qual Life Res*, 3, 183-9.

Rhodes VA, McDaniel RW, Matthews CA (1998). Hospice patients and nurses perceptions of self-care deficits based on symptom experience. *Cancer*, 21, 312-19.

Riechelmann RP, Krzyzanowska MK, O’Carroll A, Zimmerman C (2007). Symptom and medication profiles among cancer patients attending a palliative care clinic. *Support Care Cancer*, 15, 1407–12.

Riechelmann RP, Zimmerman C, Chin SN, et al (2008). Potential drug interactions in cancer patients receiving supportive care exclusively. *J Pain Symptom Manage*, 35, 535-43.

Rosenthal DI, Mendoza TR, Chambers MS, et al (2007). Measuring head and neck cancer symptom burden: The development and validation of the M. D. Anderson symptom inventory, head and neck module. *Head Neck*, 29, 923–31.

Schmidt CE, Bestmann B, Kucher T, Longo WE, Kremer B (2005). Impact of age on quality of life in patients with rectal cancer. *World J Surg*, 29, 190-7.

Stark L, Tothagen C, Visovsky C, McMillan S (2012). The symptom experience of patients with cancer. *J Hosp Palliat Nurs*, 14, 61-70.

Teunissen SC, Wesker W, Kruijtewagen C, et al (2007). Symptom prevalence in patients with incurable cancer: a systematic review. *J Pain Symptom Manage*, 34, 94–104.

Tranmer JE, Heyland D, Dudgeon D (2003). Measuring the symptom experience of seriously ill cancer and noncancer hospitalized patients near the end of life with the Memorial Symptom Assessment Scale. *J Pain Symptom Manage*, 25, 420-9.

Tsai JS, Wu CH, Tai-Yuan, Chiu TY, Chen CY (2010). Significance of symptom clustering in palliative care of advanced cancer patients. *J Pain Symptom Manage*, 39, 655-62.

Walsh D, Donnelly S, Rybecki L (2000). The symptoms of advanced cancer: Relationships to age, gender, and performance status in 1,000 patients. *Support Care Cancer*, 8, 175-9.

World Health Organization (2009). WHO definition of palliative care. Geneva: World Health Organization. Available from: http://www.who.int/cancer/palliative/en/.

Zimmermann C, Burman D, Follwell M, et al (2010). Predictors of symptom severity and response in patients with metastatic cancer. *Am J Hosp Palliat Care*, 27, 175-81.