Original Article

Symptom Clusters and Relationships to Symptom Interference with Daily Life in Taiwanese Lung Cancer Patients

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Abstract

The number one cause of cancer death in Taiwan is lung cancer. Of the few studies describing the experience of patients living with lung cancer, most use bivariate analyses to test associations between individual symptoms. Few have systematically investigated multiple symptoms. This prospective study was undertaken to explore the phenomenon of symptom distress, to investigate the presence of symptom clusters, and to examine the relationship of symptom clusters to symptom interference with daily life in Taiwanese lung cancer patients. A sample of 108 lung cancer patients was recruited using the Taiwanese version of the M. D. Anderson Symptom Inventory. Data were analyzed by hierarchical cluster analysis, factor analysis, Pearson correlation, t*-test, and regression analysis. The top five most-severe symptoms were fatigue, sleep disturbance, lack of appetite, shortness of breath, and general distress. Factor analysis generated a two-factor solution (general and gastrointestinal symptoms) for symptom severity items. Consistent with the result from factor analysis, cluster analysis also indicated the same two cluster groups (general and gastrointestinal symptoms). Both clusters were significantly correlated with symptom interference items; however, the general symptom cluster presented higher correlation coefficients than did the gastrointestinal symptom cluster. These results provide an important basis for developing novel strategies to manage multiple symptoms in lung cancer patients and thereby improve their well-being.* J Pain Symptom Manage 2008;35:258–266. *© 2008 U.S. Cancer Pain Relief Committee. Published by Elsevier Inc. All rights reserved.*

Keywords

Symptom cluster, symptom distress, lung cancer, Taiwan

Introduction

Lung cancer is the number one cause of cancer deaths in Taiwan.[1] The poor prognosis in this patient group signifies that it is of paramount importance to place attention on symptom relief.[2] Because symptoms are the patients' perception of abnormal physiologic

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stress due to disease and its treatment, severe symptoms such as those experienced by many lung cancer patients influence their ability to continue usual activities and enjoy life.

Patients with lung cancer often suffer from numerous symptoms resulting both from the primary disease itself, as well as from its treatment. For example, fatigue is a frequent symptom in lung cancer patients, with nearly 85% of patients experiencing this symptom.[3] Depression often occurs after a diagnosis of lung cancer, with 15%～44% of patients experiencing some form of depression.[4,5] Sleep disturbance among lung cancer patients has been noted but poorly studied. One study demonstrated that those who reported poorer sleep quality and sleep during the day had more severe fatigue.[6] Pain, or dyspnea, affects 63%～88% of lung cancer patients cared for by palliative care services.[7] All of these aforementioned symptoms are likely to interfere with the patients' ability to participate in their usual physical activities.[8]

Cancer patients may experience multiple concurrent symptoms, or symptom clusters. Symptom clusters are variously defined as three or more concurrent symptoms that are related to each other,[9] or two or more symptoms related to each other that occur together.[10] Whether the definition accepted is two or three or more symptoms, key to the concept is that the symptoms occur in groups and are related to one another. When the National Institutes of Health held a State-of-the-Science Conference on symptom management, they listed the most common cancer symptoms as pain, depression, and fatigue.[11] These symptoms have been studied in isolation, despite the fact that they often occur simultaneously and their interaction may exacerbate the severity of each.[12–14] Although the etiology of symptom clusters has not yet been determined, tumor and treatment-related factors, psychosocial factors, physical condition, medical comorbid condition, and personal profile (such as age) have been proposed as potential contributors to symptom severity.[15]

Gift and colleagues[2] explored symptom clusters over time in a sample of 112 patients with newly diagnosed lung cancer. They found that a cluster of seven symptoms had an internal consistency that was still evident at three and six months. The mean symptom severity and the number of symptoms at diagnosis were correlated with later ratings, but the severity of symptom distress decreased over time. A similar decrease in the severity rating was seen for each individual symptom in the cluster. The symptom cluster remained over the course of the cancer and was an independent predictor of death.

Despite increasing numbers of studies that describe symptom-related phenomena as a major aspect of morbidity in cancer care,[16] very limited research effort has been directed toward exploring relationships among symptoms. Moreover, even fewer studies to date have explored symptom clusters in culturally diverse populations. One study conducted by Chen and Tseng[17] investigated symptom clusters in a Taiwanese sample; however, this study recruited patients with various types of cancer. It is unknown whether different cancer types present unique patterns of symptom clusters. Because lung cancer is the leading cause of cancer-related death in Taiwan, understanding the associations among symptom clusters for this particular group of patients is of increased importance. Unrelieved symptoms can have deleterious effects on patients' functional status, mood status, and quality of life.[18] A more careful examination of symptom clusters may help both in understanding the underlying mechanism of these symptoms and in developing more effective treatments. Researchers have recommended that, even though research focusing on single symptoms needs to continue, it is imperative that symptom management research begins to focus on evaluating multiple symptoms using cross-sectional and longitudinal study designs.[19] Therefore, this study was undertaken to, first, explore the experience of symptoms, and second, to examine symptom clusters and their relationships to symptom interference in Taiwanese patients with lung cancer.

Methods

Sample and Settings

A cross-sectional design was used for this study. Patients were recruited from the oncology inpatient and outpatient units at two

medical centers and one teaching hospital in Taiwan. One hundred and eight participants ($n = 108$) completed the study. Participants were referred by their physicians and were enrolled after meeting the following eligibility criteria: All patients (62% inpatients and 38% outpatients) were diagnosed with lung cancer confirmed by pathology, had no other cancer diagnosis within the previous year, were over the age 18, had no cognitive impairments, and were able to communicate in Mandarin or Taiwanese.

Instruments

Demographic and Medical Characteristics. Demographic and medical information was obtained from the patient's chart and through a face-to-face patient interview. A demographic questionnaire provided age, gender, marital status, education, religious affiliation, and employment. Medical information included cancer stage, elapsed time since diagnosis, treatments (i.e., surgery, chemotherapy, radiotherapy), and laboratory data (i.e., WBC, neutrophils, lymphocytes, monocytes, eosinophils, basophils, RBC, Hb, Ht, MCV, MCHC, RDW, platelet, NA, K, Cl, Ca, albumin).

Taiwanese Version of the M. D. Anderson Symptom Inventory (MDASI-T). The MDASI-T was used to measure the severity of symptoms and the degree to which they interfered with daily life. The MDASI[16] has been established as a valid and reliable tool for assessing cancer-related symptoms, regardless of therapy or specific diagnosis. It contains 13 core symptom severity items (i.e., fatigue, sleep disturbance, pain, drowsiness, lack of appetite, nausea, vomiting, shortness of breath, numbness, difficulty remembering, dry mouth, distress, and sadness) and six symptom interference items (i.e., general activity, mood, work, relations with other people, walking, and enjoyment of life). A severity composite score was computed by averaging the scores for the 13 severity items. An interference composite score was computed by averaging the scores for the six symptom interference items. The MDASI is rated from 0 (symptom has not been present) to 10 (the symptom was as bad as I could imagine it to be) for each item. Internal consistencies of the symptom severity and the symptom interference were 0.82 to 0.94, respectively, for the English version of the MDASI.[16] The known-group validity of these items was examined by testing groups stratified according to disease severity and treatment status.

The MDASI-T was developed using the standard translation/back-translation procedure that has been used to create other validated versions of the MDASI. It has been demonstrated to be a reliable and valid tool in assessing multiple symptoms in a Taiwanese sample.[20] The internal consistency Cronbach's α was 0.89 for the symptom severity items and 0.94 for the interference items in 556 Taiwan patients with diverse types of cancer. The test−retest reliability over a 3-day interval was 0.97 for the severity composite score and 0.96 for the interference composite score. The construct validity of the MDASI-T was supported by factor analysis, which revealed a two-factor structure. Concurrent validity was supported by a significant correlation with the SF-36 subscales scores.

Procedures

After the hospital ethics committee approved this study, eligible subjects were recruited, and patients who met the selection criteria were invited to participate in the study. The research assistant contacted all patients and provided a verbal explanation of study. All patients were informed that their participation was voluntary, they would remain anonymous, they could withdraw from the study at any time without penalty, and all information would be kept confidential. After obtaining consent, all participants completed the MDASI-T. Research assistants were available on site during the administration of the MDASI-T to answer questions and provide clarification.

Statistical Analysis

Descriptive statistics were used to summarize demographic and disease variables. Pearson correlation coefficients were computed for relationships among symptoms and between symptom clusters and physiologic conditions. The *t*-test was used to determine two contrasting groups and whether the demographic or disease and physiologic conditions had significant relationships with symptom clusters. Exploratory factor analysis and hierarchical cluster analysis were used to identify groups of similar items. Clusters were formed using

the average linkage between groups whereas distances between symptoms were calculated using squared Euclidian distances. Hierarchical cluster analysis gave an overall view of the structure of patient responses to the total set of items. Because the mean is close to the median for major variables in this study, data are given as the mean (M)±standard deviation (SD) unless otherwise noted.

Results

Participant Characteristics

The sample consisted of 108 lung cancer patients (69 males, 39 females). Demographic and medical characteristics are displayed in Table 1. The average age of the participants was 67.52 (SD = 10.48; range from 41 to 90). Most of the participants were married (75%), retired (75%), receiving radiotherapy (81%), and had cancer that had remained localized (74%).

Symptom Severity and Symptom Interference

Descriptive statistics on symptom severity and interference are shown in Table 2. The five most severe symptoms, ranked in order, were fatigue (6.68 ± 3.04), sleep disturbance (6.04 ± 3.29), lack of appetite (5.83 ± 3.33), shortness of breath (5.59 ± 3.43), and distress (5.27 ± 3.11). Average severity of symptoms was 4.78 ± 3.16. Patients reported that symptoms interfered most severely with work (6.58 ± 3.90), general activity (6.53 ± 3.38), and walking (6.43 ± 3.75). The average score of symptom interference items was 6.16 ± 3.54.

Factor Analysis

The scree test indicated a two-factor solution. The confirmatory factor analysis generated a two-factor solution (general and gastrointestinal symptoms) for symptom severity items. Two factors had eigenvalues greater than 1.00, accounting for 66.21% of the total variance.

Factor loadings of the MDASI-T with oblimin rotation are shown in Table 3. The first factor (named general symptoms) included fatigue, sleep disturbance, pain, drowsiness, lack of appetite, shortness of breath, numbness, difficulty remembering, dry mouth, distress, and sadness. The second factor (named gastrointestinal symptoms) included nausea and vomiting.

Table 1
Demographic and Medical Characteristics of Patients ($n = 108$)

Variable	*n* (%)
Age (Mean (SD))	67.52 (10.48)
Gender	
Male	69 (63.5)
Female	39 (36.1)
Marital status	
Married	81 (75)
Divorced	8 (7.4)
Single	3 (2.8)
Widowed	16 (14.8)
Educational level	
Elementary	47 (43.52)
Junior high	11 (10.19)
Senior high	13 (12.04)
College or above	38 (35.19)
Religious affiliation	
Buddhism	40 (37)
Protestant	17 (15.7)
Catholic	2 (1.9)
Taoism	30 (27.8)
None	19 (17.6)
Employment	
Employed	27 (25)
Unemployed or retired	81 (75)
Patient status	
Inpatient (including hospice)	67 (62)
Outpatient	41 (38)
Metastasis	
Yes	28 (25.9)
No	80 (74.1)
Stage ($n = 37$)	
I	3 (8.1)
II	13 (35.1)
IV	21 (56.8)
Treatment ($n = 37$)	
Operation	
Yes	10 (27)
No	27 (73)
Chemotherapy	
Yes	25 (67.6)
No	12 (32.4)
Radiotherapy	
Yes	30 (81.1)
No	7 (18.9)

SD = standard deviation.

Cluster Analysis

Hierarchical cluster analysis was used to derive symptoms that were relatively homogeneous. Clusters were formed using the average linkage between groups. The dendrogram presented in Fig. 1 shows the results of a cluster

Table 2
Descriptive Statistics on Symptom Severity and Symptom Interference ($n = 108$)

Symptom Items	Mean	SD
Symptom Severity	4.78	3.16
Fatigue	6.68	3.04
Sleep disturbance	6.04	3.29
Lack of appetite	5.83	3.33
Shortness of breath	5.59	3.43
Distress	5.27	3.11
Drowsiness	5.19	3.30
Dry mouth	5.11	3.07
Pain	5.10	3.49
Sadness	4.87	3.22
Difficulty remembering	4.65	3.16
Numbness	4.01	2.97
Nausea	2.48	3.18
Vomiting	1.35	2.49
Symptom Interference	6.16	3.56
Work	6.58	3.90
General activity	6.53	3.38
Walking	6.43	3.75
Enjoyment of life	6.23	3.56
Mood	5.97	3.23
Relations with other people	5.23	3.53

SD = standard deviation.

analysis that was performed to examine the similarity of the symptom items. Clusters were formed based on the distance between symptom ratings, which was calculated using squared Euclidian distances. Symptoms that join together earlier are more similar than symptoms that join together later. In this current analysis, two clusters were formed. The general symptom cluster included 11 symptoms (i.e., pain, fatigue, sleep disturbance, distress, shortness of breath, difficulty remembering, lack of appetite, drowsiness, dry mouth, sadness, and numbness). The

Table 3
Factor Analysis with an Oblimin Rotation-Pattern Matrix of Symptoms

		Factor loading	
Symptom Item	Symptom	Factor 1	Factor 2
General symptoms	Pain	0.66	
	Fatigue	0.80	
	Sleep disturbance	0.79	
	Distress	0.87	
	Shortness of breath	0.78	
	Difficulty remembering	0.83	
	Lack of appetite	0.79	
	Drowsiness	0.83	
	Dry mouth	0.76	
	Sadness	0.82	
	Numbness	0.54	
Gastrointestinal symptoms	Nausea		0.85
	Vomiting		0.90

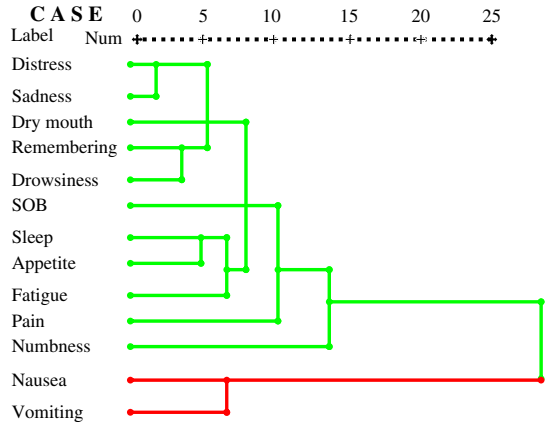

Fig. 1. Dendrograms using average linkages. Clusters were formed based on the distances between symptom ratings that were calculated using squared Euclidian distances.

gastrointestinal symptom cluster included nausea and vomiting.

Relationships Among Symptoms Within Clusters

Symptoms within clusters were all significantly interrelated to each other. The correlation coefficients ranged from 0.33 to 0.85 (Table 4) within the general symptom cluster and was 0.61 within the gastrointestinal symptom cluster. The general symptom cluster is significantly correlated with the gastrointestinal symptom cluster ($r = 0.39$, $P < 0.001$).

Relationships of Symptom Clusters to Symptom Interference and Disease and Physiologic Variables

An examination was made of the relationships between symptom clusters and symptom interference. Scores for the clusters (general and gastrointestinal) were computed by adding the scores for each of the symptoms within each cluster. Both symptom clusters were significantly related to symptom interference. Symptom interference items were more highly correlated with the general symptom cluster than with the gastrointestinal symptom cluster. The correlation coefficients ranged from 0.75 to 0.87 for the general symptom cluster and from 0.26 to 0.33 for the gastrointestinal symptom cluster, respectively (Table 5). Regression analysis was applied to examine whether the general symptom cluster score or gastrointestinal symptom cluster score was predictive of the

Table 4
Relationships Among Symptoms in the General Symptom Cluster ($n = 108$)

	Pain	Fatigue	Sleep Disturbance	Distress	Shortness of Breath	Difficulty Remembering	Lack of Appetite	Drowsiness	Dry Mouth	Sadness
Fatigue	0.59									
Sleep disturbance	0.48	0.58								
Distress	0.59	0.63	0.71							
Shortness of breath	0.46	0.60	0.62	0.69						
Difficulty remembering	0.46	0.62	0.62	0.68	0.61					
Lack of appetite	0.58	0.67	0.70	0.71	0.61	0.59				
Drowsiness	0.54	0.62	0.70	0.66	0.59	0.74	0.68			
Dry mouth	0.45	0.57	0.55	0.64	0.64	0.61	0.65	0.65		
Sadness	0.62	0.66	0.59	0.85	0.60	0.59	0.65	0.65	0.62	
Numbness	0.33	0.39	0.33	0.55	0.45	0.48	0.40	0.33	0.55	0.49

For all values, $P < 0.01$.

symptom interference composite score after controlling for the KPS score and age. Results showed that only the general symptom cluster score was significant in predicting symptom interference ($\beta = 0.57$, $P = 0.001$). The regression model explained 59.60% of total variance.

Pearson correlations were performed to examine if there was a relationship between laboratory data and symptom clusters; however, no significant correlation was found. We further explored whether older people (>75 years of age) presented a different symptom cluster pattern compared with younger people (<75 years of age). It was found that there were significant differences in scores of sleep disturbance, difficulty remembering, and drowsiness between these two groups (Table 6). Factor analysis and cluster analysis were also performed in these two groups to explore the cluster patterns. Results showed that these two groups presented identical factor patterns and cluster profiles.

T-tests were then performed to test differences in symptom clusters between inpatients vs. outpatients; hospice patients vs. nonhospice patients; and patients with metastasized cancer vs. those with localized cancer. Results showed that inpatients, hospice patients, and patients with metastasized cancer reported significantly higher scores on general symptom cluster than did their counterparts (Table 7).

Table 5
Relationships Between Symptom Clusters and Symptom Interference ($n = 108$)

	General Symptom Cluster	Gastrointestinal Symptom Cluster
General activity	0.87	0.32
Mood	0.87	0.33
Work	0.75	0.26
Relations	0.77	0.29
Walking	0.85	0.26
Enjoyment of life	0.86	0.33

For all values, $P < 0.01$.

Discussion

The results of this study provide important insights into the symptom experiences and the effect of symptom clusters on quality of life (i.e., symptom interference with daily life) in patients with lung cancer in Taiwan. Lung cancer remains the number one cause of cancer death in Taiwan; however, studies describing the experiences of patients living with lung cancer are extremely limited in Taiwan. To our knowledge, this study is the first one in Taiwan to explore symptom clusters as well as their effect on interference with daily life in a homogeneous group of lung cancer patients.

In this study, two major symptom clusters (general and gastrointestinal) were identified based on the distances between symptom ratings. Surprisingly, the pattern of symptom clusters found in this current study is identical to that which was found in other studies using a heterogeneous group of cancer patients in the United States, Japan, China, and Taiwan.[16,20–22] This finding does not support our assumption that lung cancer patients may present a unique pattern of symptom clusters and, therefore, raises a possibility that the mechanism for symptom clusters may not vary across different cancer diagnoses.

This study has not only identified symptom clusters but has documented the impact of symptom clusters on quality of life (symptom interference) in Taiwanese patients with lung

Table 6
Comparisons of Individual Symptom Severity and Symptom Clusters Between Patients Less Than 75 Years Old and Patients 75 Years Old or Older

Symptom Severity	< 75 Years Old ($n = 78$); Mean ± SD	≥ 75 Years Old ($n = 30$); Mean ± SD	*t*-value	*P*-value
Individual Symptoms				
Pain	5.00 ± 3.43	5.37 ± 3.69	−0.49	0.63
Fatigue	6.68 ± 3.01	6.67 ± 3.17	0.02	0.98
Nausea	2.79 ± 3.18	1.67 ± 3.06	1.67	0.10
Sleep disturbance	5.64 ± 3.30	7.07 ± 3.08	−2.05	0.04[a]
Distress	5.08 ± 3.18	5.77 ± 2.92	−1.03	0.31
Shortness of breath	5.69 ± 3.41	5.33 ± 3.55	0.49	0.63
Difficulty remembering	4.21 ± 3.20	5.80 ± 2.78	−2.40	0.02[a]
Lack of appetite	5.59 ± 3.50	6.47 ± 2.78	−1.36	0.18
Drowsiness	4.79 ± 3.41	6.23 ± 2.80	−2.25	0.03[a]
Dry mouth	5.22 ± 3.13	4.83 ± 2.95	0.58	0.56
Sadness	4.79 ± 3.26	5.07 ± 3.15	−0.39	0.70
Vomiting	1.51 ± 2.73	0.93 ± 1.66	1.34	0.18
Numbness	4.06 ± 3.05	3.87 ± 2.79	0.31	0.76
Symptom Clusters				
General symptom cluster	56.76 ± 28.49	62.47 ± 26.58	−0.95	0.34
Gastrointestinal symptom cluster	4.31 ± 5.29	2.60 ± 4.40	1.57	0.12

SD = standard deviation.
[a] $P < 0.05$.

cancer. The study found that symptom interference items were more highly correlated with the general symptom cluster than with the gastrointestinal symptom cluster. Furthermore, it was found that the general symptom cluster score remained a significant predictor for symptom interference after other confounding variables were controlled. It appears that the general symptom cluster has a more negative impact on quality of life (symptom interference) for patients with lung cancer in Taiwan. Therefore, symptoms within the general symptom cluster may require more attention from clinicians in order to prevent a negative impact to patients from these symptoms. Cancer symptom severity, whether due to cancer itself or to treatment, severely reduces a patient's ability to function in daily life, with the greatest impact seen in the areas of work, general activity, and walking.

In this study of Taiwanese lung cancer patients, most suffered from multiple symptoms. Of these, fatigue and sleep disturbance were the primary symptoms. These findings agree with those of Wang et al. who studied a sample of 249 cancer patients in China.[22] Fatigue may appear primarily as a complaint of decreased physical function, but it may also manifest itself as decreased mental attentiveness, alertness, and motivation. Alternatively, fatigue

Table 7
Comparisons of the General Symptom Cluster and the Gastrointestinal Symptom Cluster Align Most with Clinical Information in Patients with Lung Cancer

	Mean ± SD	Mean ± SD	*t*-value	*P*-value
	Inpatient ($n = 67$)	*Outpatient ($n = 41$)*		
General symptom cluster	71.60 ± 20.57	36.68 ± 24.88	−7.55	0.00[a]
Gastrointestinal symptom cluster	4.18 ± 5.00	3.27 ± 5.25	−0.90	0.37
	Hospice ($n = 46$)	*Non-hospice ($n = 62$)*	1.67	0.10
General symptom cluster	78.78 ± 10.50	43.18 ± 27.24	9.40	0.00[a]
Gastrointestinal symptom cluster	4.91 ± 5.44	3.03 ± 4.71	1.92	0.06
	Metastasis ($n = 80$)	*Non- metastasis ($n = 28$)*	0.49	0.63
General symptom cluster	66.56 ± 25.75	34.86 ± 19.67	5.93	0.00[a]
Gastrointestinal symptom cluster	3.94 ± 4.90	3.54 ± 5.71	0.36	0.72

SD = standard deviation.
[a] $P < 0.001$.

may be described as a combination of both decreased physical function and decreased mental attentiveness, alertness, and motivation.[23] Gift et al.[2] report that fatigue is both the most frequent, and most debilitating, symptom in lung cancer patients.[24] The exact cause of this fatigue is unknown.[25]

As might be expected, those who report poorer sleep quality and sleeping during the day experience more severe fatigue.[6] This supports our findings that sleep disturbance is associated with fatigue. In this study, older patients (>75 years of age) reported higher levels of sleep disturbance than did younger patients (<75 years of age). As a result, older lung cancer patients are at a greater risk of suffering from sleep disturbance.

Patients with lung cancer have more severe symptom distress than patients with other cancers.[2] Across all cultures and nationalities, symptom management for lung cancer patients undergoing treatment or follow-up is an essential component of cancer care. Symptom clusters need to be emphasized to lead to the development of novel symptom management strategies.[18] Gift et al.[15] note that it is not known whether the same cluster of symptoms would be found in all ethnic groups. Focusing on testing symptom clusters as an assessment tool for patients with lung cancer is crucial, especially in Taiwanese patients, a group with a high mortality rate. Our study results agree with two other studies,[21,23] which show that there are three similar components: (1) distress and sadness, (2) fatigue and sleep disturbance, and (3) nausea and vomiting. Symptom clusters may reveal specific underlying dimensions of symptoms. Symptom clusters may also provide insights into the underlying mechanisms associated with the occurrence of multiple symptoms.

There are several limitations in this study. First, the study targets lung cancer patients whose cancers have remained localized, but lung cancer falls within a range of stages. The group of the most seriously ill lung cancer patients is not represented, so our findings cannot be generalized to that population. In addition, the average age of the subjects was 67.52 (range, 41～90) years old, but a significant difference existed in the symptom experience of older vs. younger patients. Results may not be applicable to individuals of other ages, especially younger patients. Lastly, this study used a cross-sectional design, meaning that change in symptom clusters over time was not investigated.

Based on the results of this study, future research directions are indicated. First, studies using a longitudinal design are needed to explore the changes of symptom clusters over the course of lung cancer disease. Second, a comprehensive picture of the determinants of symptom clusters, such as stage of cancer, and other comorbidities needs to be addressed. Thirdly, more work should be done to explore the relationship between symptom clusters and their underlying biological mechanism. Finally, further studies should be directed at molecular and biochemical mechanisms underlying symptoms. These types of research may lead to the development of novel interventions for symptom management.

In conclusion, past research on cancer symptoms tends to assume a single symptom framework.[12–14] Cancer symptoms, however, often occur in groups or clusters. The strength of this study was its use of a sample with homogeneous clinical characteristics, that is, lung cancer patients who presented with symptom clusters that caused symptom interference with daily life. By addressing an understudied problem, this study provides essential information for investigators who are moving toward evaluating multiple symptom clusters. Moreover, the results of this study provide a basis for developing novel strategies to manage multiple symptoms in lung cancer patients. A management strategy targeting the most common symptoms that occur simultaneously may have a great potential to improve the quality of life for patients with lung cancer in Taiwan.

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References

1. Taiwan Cooperation Oncology Group (TCOG), National Health Research Institutes. Cancer practice guideline: lung cancer. Available from http://www.sars.nhri.org.tw/publish 2004.

2. Gift AG, Stommel M, Jablonski A, Given W. A cluster of symptoms over time in patients with lung cancer. Nurs Res 2003;52:393–400.

3. Hollen PJ, Gralla RJ, Kris MG, Potanovich LM. Quality of life assessment in individuals with lung cancer: testing the Lung Cancer Symptom Scale (LCSS). Eur J Cancer 1993;29A:S51–S58.

4. Hopwood P, Stephens RJ. Depression in patients with lung cancer: prevalence and risk factors derived from quality-of-life data. J Clin Oncol 2000; 18:893–903.

5. Akechi T, Okamuram H, Niskiwaki Y, Uchitomit Y. Psychiatric disorders and associated and predictive factors in patients with unresectable nonsmall cell lung carcinoma: a longitudinal study. Cancer 2001;92:2609–2622.

6. Broeckle JA, Jacobsen PB, Horton J, Balducci L, Lyman GH. Characteristics and correlates of fatigue after adjuvant chemotherapy for breast cancer. J Clin Oncol 1998;16:1689–1696.

7. Potter J, Higginson IJ. Pain experienced by lung cancer patients: a review of prevalence, causes and pathophysiology. Lung Cancer 2004;43:247–257.

8. Chan WHC, Richardson A, Richardson J. A study to assess the existence of the symptom cluster of breathlessness, fatigue and anxiety in patients with advanced lung cancer. Eur J Oncol Nurs 2005;9:325–333.

9. Dodd MJ, Miaskowski C, Paul S. Symptom clusters and their effect on the functional status of patients with cancer. Oncol Nurs Forum 2001;28: 465–470.

10. Kim HJ, McGuire DB, Tulamn L, Barsevick AM. Symptom clusters: concept analysis and clinical implications for cancer nursing. Cancer Nurs 2005; 28:270–282.

11. Agency for Healthcare Research and Quality. Management of cancer symptoms: pain, depression, and fatigue. AHRQ 2002;61:1–5. Available from http://www.ahrq.gov/clinic/epcsums/cansympsum.pdf.

12. Ross DD, Alexander SC. Management of common symptoms in terminally ill patients: part I: fatigue, anorexia, cachexia, nausea, and vomiting. Am Fam Physician 2001;64:807–814.

13. Dodd MJ, Miaskowski C, Lee KA. Occurrence of symptom clusters. J Natl Cancer Inst Monogr 2005; 32:76–78.

14. Esper P, Heidrich D. Symptom clusters in advanced illness. Semin Oncol Nurs 2005;21:20–28.

15. Gift AG, Jablonski A, Stommel M, Given CW. Symptom clusters in elderly patients with lung cancer. Oncol Nurs Forum 2004;31:202–212.

16. Cleeland CS, Mendoza TR, Wang XS, et al. Assessing symptom distress in cancer patients: the M. D. Anderson Symptom Inventory. Cancer 2000;89: 1634–1646.

17. Chen ML, Tseng HC. Symptom clusters in cancer patients. Support Care Cancer 2006;14: 792–794.

18. Miaskowski C. Symptom clusters: establishing the link between clinical practice and symptom management research. Support Care Cancer 2006; 14:792–794.

19. Miaskowski C, Dodd MI, Lee KA. Occurrence of symptom cluster. J Natl Cancer Inst Monogr 2004; 32:76–78.

20. Lin CC, Chang AP, Cleeland CS, Mendoza TR, Wang XS. Taiwanese version of the M.D. Anderson Symptom Inventory: symptom assessment in cancer patients. J Pain Symptom Manage 2007;33:180–188.

21. Okuyama T, Wang XS, Akechi T, et al. Japanese version of the M.D. Anderson Symptom Inventory: a validation study. J Pain Symptom Manage 2003; 26:1093–1104.

22. Wang XS, Wang Y, Guo H, et al. Chinese version of the M.D. Anderson Symptom Inventory: validation and application of symptom measurement in cancer patients. Cancer 2004;101:1890–1901.

23. Valentine AD, Meyers CA. Cognitive and mood disturbance as causes and symptoms of fatigue in cancer patients. Cancer 2001;92:1694–1698.

24. Bozcuk H, Dalmis B, Samur M, et al. Quality of life in patients with advanced non-small cell lung cancer. Cancer Nurs 2006;29:104–110.

25. Cella D, Lai JS, Chang CH, Peterman A, Slavin M. Fatigue in cancer patients compared with fatigue in the general United States population. Cancer 2002;94:528–538.