

SYMPTOM CLUSTERS IN THAI PATIENTS WITH ADVANCED LUNG CANCER

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ABSTRACT: The purpose of this study was to explore the characteristics of symptoms and to explore the presence and composition of symptom clusters in Thai patients with advanced lung cancer based on the "Theory of Unpleasant Symptoms". One hundred and sixty five patients with advanced lung cancer were purposely selected from outpatient and inpatient oncology units at two tertiary hospitals in Bangkok to complete a demographic questionnaire and symptom record based on the Memorial Symptom Assessment Scale (MSAS). The results found that patients with advanced lung cancer stages IIIA, IIIB and IV, aged between 35 and 84 years, with a mean age of 62.4 years, accompanied by multiple symptoms, and averaged 14.65 symptoms. Coughing was the most common symptom reported, lack of appetite was reported to be most frequently occurring symptom. The symptom of pain was reported to be the most severe as well as the most distressful. Using principal component analysis, with varimax rotation, seven symptom clusters were identified and labeled as body image symptom cluster, neuropsychological symptom cluster, sleep alteration symptom cluster, digestive impairment symptom cluster, dermatologic and dizziness symptom cluster, bowel-emotional dysfunction symptom cluster, and pain related discomfort symptom cluster. Because symptoms usually occur together, identifying symptom clusters may lead to an investigation and management of several symptoms within the cluster. The results intimately suggest nursing intervention on symptom management for better quality of life in Thai patients with advanced lung cancer.

Keywords: Advanced lung cancer, Symptom clusters, Factor analysis, Thai patients

INTRODUCTION

Patients with advanced lung cancer often suffer from numerous symptoms resulting both from the disease itself as well as from its treatment [1]. The majority of patients with lung cancer experience a rapid and fatal course, which includes the development and progression of symptoms. Common symptoms experienced in patients with lung cancer at any stage include fatigue, cough, dyspnea, pain, sleep disturbance, and loss of appetite. All of these symptoms are likely to interfere with patients' physical activities [1]. Patients with advanced lung cancer often present with multiple symptoms [1-3], which Dodd and colleagues have identified as a "symptom cluster" that refers to three or more symptoms that correlate

to each other [4]. Prior studies found that patients who experienced three or more symptoms concurrently had poorer physical functioning and quality of life than those who experienced only one or two symptoms [1, 5]. Therefore, identifying symptom clusters may promote our understanding of the pathophysiology of advanced lung cancer and the etiology of symptoms. Moreover, in research on symptom management, if a specific therapeutic symptom is examined, the other symptoms in that cluster should be evaluated as outcome measures thus ensuring that an important therapeutic effect is not overlooked [6]. However, before nurses can determine the type of assistance patients with lung cancer may require, information is needed about patients' experience with the symptoms and symptom cluster. The term "symptom cluster" was first used in the literature by Dodd and colleagues [4], they defined a

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symptom cluster as “When three or more concurrent symptoms (e.g. pain, fatigue, sleep insufficiency) are related to each other”. Symptoms within a cluster do not need to share the same etiology, for instance pain may be caused by the cancer, fatigue by the cancer and treatment, insomnia by selected types of chemotherapy agents [4]. Because of the limited definition in the literature, many studies use this term “three or more concurrent symptoms that are related to each other” to study symptom clusters [4, 7- 10]. Many others have suggested the definition of symptom cluster to have at least two symptoms that are significantly correlated and which occurs together [11]. Some studies have investigated three or more concurrent symptoms that were related to each other but the selected symptoms have varied somewhat, as has the strength of the inter-correlations among the symptoms [4, 7, 8, 10]. Symptom cluster studies are well conducted in other countries [1-8, 10]. However, there is a need to conduct symptom studies with multiple other cancer sites, stages of cancer and treatment trajectories [12]. Moreover, even fewer studies to date have explored symptom clusters in culturally diverse populations. One study conducted by Suwisith [9] investigated symptom clusters in Thailand. However, this study recruited patients with breast cancer undergoing chemotherapy. The study was limited because it focused only on the patients with breast cancer and therefore the findings cannot be generalized into other populations, particularly in advanced lung cancer, which recognized having more symptoms than other cancer patients [9]. In 2011, Chaiviboontham and colleagues investigated symptom clusters in Thai people with advanced cancer. Although this study was conducted in various types of advanced cancer patients in Thailand, the result cannot be generalized to lung cancer patients because the sample size of advanced lung cancer in this study was very small with only 33 subjects [12]. Lung cancer being one of the leading cause of cancer-related death in Thailand, it is important to understand the association between symptom clusters for this group of patients. Unrelieved symptoms can affect patients’ functional status and quality of life. Therefore, the purpose of this study was first to explore the common symptoms experienced in advanced lung cancer patients and second to examine symptom clusters in Thai patients with advanced lung cancer.

MATERIALS AND METHODS

Study design and sample

This study was a cross-sectional descriptive study, it was conducted from July 2010 to February 2011 to investigate symptom clusters of patients with advanced lung cancer during the course of advanced disease (inoperable or presence of metastases). The purposive samples were selected from King Chulalongkorn Hospital and Bhumipol Hospital that treated large numbers of cancer patients. One hundred and sixty five subjects (n= 165) participated in the study. The subjects were enrolled after meeting the following criteria: 1) diagnosed Non-Small Cell Lung Cancer (NSCLC) (clinical stages; III A, IIIB, or IV), 2) having no other cancer diagnosis within the previous year, 3) having ability to read and speak Thai, 4) aged at least 18 years or older, and 5) willing to participate in this study and having signed a written consent form. Subjects were excluded from the study if they had 1) Co-morbidities of AIDS, congestive heart failure, renal failure, cirrhosis, or Tuberculosis because the pathophysiologic manifestations of these diseases would confound the larger study’s finding, or 2) Had psychiatric morbidity or cognitive impairment and were unable to answer the questionnaires.

Instrument

Thirty two symptoms were evaluated by using the tool to measure multiple symptoms; the researcher used the Memorial Symptom Assessment Scale (MSAS) [13]. The MSAS is a multidimensional symptom assessment instrument that measures the symptom prevalence, frequency, severity and distress associated with 32 physical and psychological symptoms experienced during the prior week. The instrument asked each subject to respond either “yes” = 1 or “no” = 0 concerning whether she/he had experienced each symptom during the past week. Symptom frequency was rated from 1 to 4 ranging from 1 (rarely) to 4 (almost constantly). Symptom severity was measured as 1 (mild) to 4 (very severe), and symptom distress was rated as 0 (not at all) to 4 (very much). The MSAS demonstrated reliability and validity in cancer inpatient and outpatient populations. In this study the researcher modified a Thai version of the Memorial Symptoms Assessment Scale (MSAS) translated by Nongluck Suwisith, in the study of symptom clusters and functional status of women with breast cancer. Reliability analysis was reported with an internal consistency of 0.96. The Pearson Correlation ranging from 0.82 to 0.88 respectively for the

Table 1 Symptom prevalence, level of symptom frequency, severity and distress of patients reporting the symptoms (n= 165)

Symptom experience	Prevalence		Frequency	Severity	Distress
	n	%	$\bar{x}$ (SD)	$\bar{x}$ (SD)	$\bar{x}$ (SD)
Coughing	127	77.00 ¹	2.63 (0.80)	2.07 (0.93)	2.25 ⁴ (1.01)
Lack of energy	121	73.30 ²	2.68 ³ (0.90)	2.03 (0.74)	2.11 (0.90)
Pain	120	72.70 ³	2.67 ⁴ (0.93)	2.36 ¹ (0.92)	2.51 ¹ (0.96)
Sleeping difficulty	112	67.90 ⁴	2.78 ² (0.70)	2.13 ⁴ (0.90)	2.27 ³ (1.00)
Shortness of breath	104	63.00 ⁵	2.60 (0.83)	2.11 ⁵ (0.82)	2.35 ² (0.96)
Dry mouth	104	63.00 ⁵	2.34 (0.99)	1.56 (0.69)	1.59 (0.79)
Lack of appetite	96	58.20	2.93 ¹ (0.84)	2.23 ² (0.81)	2.24 ⁵ (0.84)
Constipation	92	55.80	2.27 (0.87)	1.97 (0.74)	1.87 (0.84)
Numbness/tingling	91	55.20	2.41 (0.97)	1.67 (0.82)	1.85 (0.89)
Feeling bloated	87	52.70	2.60 (0.88)	1.86 (0.80)	1.97 (0.95)
Dizziness	86	52.10	1.93 (0.82)	1.44 (0.64)	1.60 (0.73)
Irritability	83	50.30	2.17 (0.68)	1.70 (0.68)	1.80 (0.78)
Difficult in concentration	80	48.50	1.96 (0.78)	1.57 (0.68)	1.51 (0.75)
Weight loss	79	47.90	2.21 (1.05)	1.89 (0.95)	2.03 (0.93)
Change in food taste	79	47.90	2.53 (1.05)	1.92 (0.84)	2.01 (0.96)
Worrying	79	47.90	2.38 (0.84)	1.99 (0.72)	2.15 (0.84)
Drowsiness	75	45.50	2.51 (0.89)	1.79 (0.78)	1.70 (0.89)
Sadness	73	44.20	2.10 (0.78)	1.71 (0.73)	1.74 (0.79)
“ I don’t look like myself”	72	43.60	2.60 (1.04)	2.13 ⁴ (0.90)	2.13 (0.96)
Hair loss	69	41.80	2.67 ⁵ (0.99)	2.22 ³ (0.97)	2.08 (0.99)
Itching	67	40.60	1.96 (1.08)	1.49 (0.75)	1.68 (0.86)
Nausea	61	37.00	1.92 (0.90)	1.50 (0.65)	1.61 (0.75)
Change in skin	61	37.00	2.11 (1.15)	1.59 (0.59)	1.48 (0.76)
Problem of urination	56	33.90	2.45 (0.87)	1.52 (0.57)	1.64 (0.64)
Difficult swallowing	56	33.90	2.40 (1.18)	1.88 (0.78)	2.22 (0.87)
Nervousness	50	30.3	2.44 (0.86)	1.98 (0.82)	2.22 (0.75)
Mouth sore	44	26.70	2.09 (0.93)	1.59 (0.72)	1.85 (0.88)
Sweating	42	25.50	1.86 (0.68)	1.57 (0.77)	1.50 (0.94)
Sexual problem	39	23.60	1.72 (0.99)	1.51 (0.72)	1.58 (0.77)
Vomiting	39	23.60	1.61 (0.71)	1.49 (0.64)	1.85 (0.83)
Diarrhea	39	23.60	1.59 (0.71)	1.41 (0.64)	1.72 (0.85)
Swelling arms/legs	35	21.20	1.80 (1.80)	1.71 (1.10)	1.91 (1.04)

Note :¹⁻⁵ = Ranking of top five symptom prevalence, level of symptom frequency, severity, and distress

symptom severity and symptom distress subscales [9]. In this study, the reliability of the Memorial Symptom Assessment Scale (MSAS) reported that Cronbach’s alpha co-efficiency was 0.90.

Data collection

After permission and project approval, the potential subjects were identified from medical records and follow up appointment dates with the oncology department. Informal informed consent was performed with verbal explanation then formal written consent forms were subsequently processed. All subjects were informed that their participation was voluntary, they would remain anonymous, could withdraw from the study at any time without penalty, and all information would be kept confidential. After obtaining consent, all subjects were asked to complete the questionnaires about their symptoms experience in the previous

week. Most subjects preferred to have the researcher read the questionnaires for them. However, if there was missing information, the researcher asked the subjects for completeness of the data. Therefore, there was no missing data in this study.

Data analysis

Descriptive data analysis was used to summarize the characteristics of the subjects and prevalence of symptom occurrence, symptom frequency, symptom severity, and symptom distress. Exploratory factor analysis was used to identify symptom clusters, only symptom distress dimension was used in the analysis because symptom distress influences patients’ capabilities to function, especially in self-management [12]. Thirty-two symptoms were subjected to explanation with an exploratory principle component factor analysis. However, the

Table 2 Exploratory factor analysis using rating of symptom distress

Symptoms	Factor loading						
	F1	F2	F3	F4	F5	F6	F7
Body image symptom cluster							
“I don’t look like myself	0.72						
Weight loss	0.70						
Irritability	0.67						
Difficulty swallowing	0.66						
Hair loss	0.56						
Neuropsychological symptom cluster							
Drowsiness		0.73					
Sadness		0.67					
Difficult in concentration		0.67					
Nervous		0.60					
Numbness/tingling		0.57					
Dry mouth		0.52					
Sleep alteration symptom cluster							
Sleeping difficulty			0.64				
Problem of urination			0.58				
Coughing			0.46				
Digestive impairment symptom cluster							
Nausea				0.69			
Lack of appetite				0.51			
Change in food taste				0.31			
Dermatologic and dizziness symptom cluster							
Itching					0.85		
Change in skin					0.68		
Dizziness					0.48		
Bowel-emotional dysfunction symptom cluster							
Constipation						0.71	
Worrying						0.40	
Feeling bloated						0.37	
Pain related discomfort symptom cluster							
Pain							0.79
Shortness of breath							0.37
Lack of energy							0.34
Variance explained	30.20	9.30	5.93	4.84	4.57	4.48	3.93
Total variance explained							63.24
Alpha	0.79	0.81	0.58	0.66	0.62	0.58	0.62

testing of normal distribution for symptom distress scores revealed deviated distributions in six symptoms. These symptoms were mouth sores, sweating, sexual problems, vomiting, diarrhea, and swelling arms/legs. These symptoms were also reported as having low prevalence (Table 1). In order to have a manageable number of symptoms for factor analysis, 26 symptoms with > 30% prevalence were selected. The results showed that 26 significant symptoms ($X^2 = 1707.431$, $df = 325$, and $p < 0.001$). This means that 26 items had a multivariate normal distribution and that the correlation matrix was not an identity matrix. Moreover, the Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy test showed that the size of the overall KMO was 0.850 (Scores > 0.50 indicate adequate sample size for the analysis). Cronbach’s alpha was used to measure of internal

consistency among factor items.

RESULTS

Characteristics of the sample

The sample consisted of 165 patients, with an age range of 35 to 84 years, with a mean of 62.4 (SD = 10.70) years, 66.10 % were male and 33.90% female. Data on the patients’ co-morbid conditions was present in 42.4 % of the sample, of those 24.2% had a single condition. Hypertension was the most common co-morbidity reported (33.3%). Demographic information showed that 93.90 % of the samples were found in outpatient department, 34.5% of the sample had stage IIIA/IIIB, and 65.5% stage IV. Most patients (84.2%) had metastatic disease. During data collection, most patients were currently undergoing chemotherapy (72.1%), combined treatment of chemotherapy and

radiation therapy (11.52%), palliative treatment (12.12%), radiation therapy (1.82%) and no treatment (2.42%).

Characteristics of symptoms

Patients with lung cancer ($N = 165$) experienced 2 - 32 symptoms with an average of 14.65 symptoms reported during the disease and treatment phases. The prevalence of 32 symptoms is presented in Table 1. Of the 32 symptoms, the most common symptoms reported was coughing (77 %) followed by lack of energy (73.3%), pain (72.7%) sleeping difficulty (67.9%), shortness of breath (63%), and dry mouth (63%). The symptoms most frequently occurred after received treatments or not received treatment within a week were lack of appetite, followed by sleeping difficulty, lack of energy, hair loss, and pain respectively. The symptoms reported to be most severe were pain, lack of appetite, hair loss, sleeping difficulty, "I don't look like myself", and shortness of breath. The symptoms that were reported as most distressful were pain, shortness of breath, sleeping difficulty, coughing, and lack of appetite respectively (Table 1).

Symptom clusters

A total of 26 symptoms were analyzed for factor structures of symptom distress dimension. As shown in Table 2, with varimax rotation, seven factors were extracted, which accounted for a 63.24% of variance, which means that about 63.24% of the variation in all symptoms is explained by seven factors. The detail of each factor is presented as the following: Factor 1 "body image symptom cluster" this cluster consisted of five symptoms, the percent of variance in all symptoms accounted for by this factor is 30.20 %, which means that about 30.20 % of the variation in all symptoms is explained by this cluster. Factor 2 "neuropsychological symptom cluster", this cluster consisted of six symptoms, which explained 9.30% of the factor's variance. Factor 3 "sleep alteration symptom cluster", this cluster consisted of three symptoms, which explained 5.93% of the factor's variance. Factor 4 "digestive impairment symptom cluster", this cluster consisted of three symptoms, which explained 4.84 % of the factor's variance. Factor 5 "dermatologic and dizziness symptom cluster", this cluster consisted of three symptoms, which explained 4.57% of the factor's variance. Factor 6 "bowel-emotional dysfunction symptom cluster", this cluster consisted of three symptoms, which explained 4.48 % of the factor's variance. Factor 7 "pain related discomfort symptom cluster", this cluster consisted of three symptoms,

which explained 3.93 % of the factor's variance (Table 2). As shown in Table 2, the factor loading scores of these seven clusters ranged from 0.31-0.79 which means that the symptoms in each factor have strong relationships with the factor extracted. Cronbach's alpha coefficient demonstrated medium to high internal reliability in the clusters, with a coefficient ranging from 0.58- 0.81, indicating that the symptoms within each cluster occurred in a homogenous pattern. The name of symptom clusters in this study were based on the sets of symptoms in each factor, such as the symptoms in the factor 1 were more likely related to body image. This factor is then named the-"body image symptom cluster".

DISCUSSION

In this study, of the 32 symptoms assessed, the number of symptoms reported from patients with advanced lung cancer during the disease and treatment phases was high with average 14.65 symptoms, with ranges between 2-32 symptoms reported. The most common symptoms reported were coughing followed by lack of energy, pain, sleeping difficulty, shortness of breath, and dry mouth. The characteristics of symptom experiences in this study found that patients with advanced lung cancer weighted their symptoms differently across symptom dimensions. The most prevalent symptom reported was coughing while lack of appetite was rated as the most frequently occurring a week after receiving treatments. Pain was rated as the most severe and the most distressful symptom in the study. Using principal component analysis with varimax rotation, seven symptom clusters were identified in the dimension of symptom distress in this study. The symptoms within these clusters were found to relate to each other and were homogenous. Using different instruments to evaluate symptoms make the different construction of symptom cluster. A study of Sarna and Bretch [2] examined symptom clusters in distress dimension in women with advanced lung cancer. The symptom distress ratings in that study fit a structure of four factors (1) emotional and physical suffering included the symptoms of pain frequency, pain severity, bowel, appearance and outlook; (2) gastrointestinal distress included the symptoms of nausea frequency, nausea severity and appetite; (3) respiratory distress included the symptoms of insomnia, breathing and cough; and (4) malaise included the symptoms of fatigue, concentration and outlook. However, the reliability and generalizability of their findings were compromised by the sample's small size and lack

of male representation [2]. When comparing the evidences of symptom cluster in a study of advanced cancer in Thailand, the result of this study, and other studies, was different even though using the same instruments [12]. The result of other study found that only four symptom cluster occurred when using distress dimension to identify; 1) pain, sickness-behavior, and psychological symptom cluster, 2) anorexia-cachexia symptom cluster, 3) gastro-intestinal and elimination and 4) cutaneous and other [12]. Because the study was conducted in advanced cancer patients, the subject group of advanced lung cancer was very small with only 33 subjects. Therefore, the study has limitations to be representative of advanced lung cancer population in Thailand [12]. In this study, the “body image symptom cluster” and the “neuropsychological symptom cluster” tend to be associated with the side effect of cancer and treatment. In the neuropsychological symptom cluster, some studies included a variety of affective items depending on the scale used to elicit the symptom reports and can include patients’ feeling distress, sadness, lack of appetite, sleeping difficulties, anxiety, and depression [6, 10,12,14-16]. In the “sleep alteration symptom cluster” (sleeping difficulty, problem of urination, and coughing), sleeping difficulty was found to be high in this study (67.90%) but less than another study previously reported in advanced cancer in Thailand (80.4%) [12]. One qualitative study in the exploration of respiratory distress symptom cluster in lung cancer found that coughing led to sleep disturbance because the severity of cough disrupted patients’ sleep, particularly when patients had been in a supine position [17]. In this study coughing was found to be the most common symptom reported (77 %) in patients with advanced lung cancer. The “digestive impairment symptom cluster” (nausea, lack of appetite, and change in food taste) has also been described elsewhere in patients with lung cancer, it was found to predict poor survival in lung cancer patients [3]. Nausea occurs in advanced cancer both in relation to and independent of therapeutic treatment. It has been reported to occur in 34% of lung cancer patients at some stage in their disease [1, 2], also lack of appetite has been ranked by patients in one study as the third most distressing symptom they experience [18], it is believed to occur in 80% of persons with advanced cancer [12]. The etiology of this symptom is multi-factorial and has been linked to overproduction of interferon and cytokines that include tumor necrosis factor, IL-1, and IL-6 [19]. Clustering of these symptoms recognizes that if

someone feels nauseated they will generally limit food intake for fear of stimulating an emesis response [20]. The “dermatologic and dizziness symptom cluster” (itching, changes in skin, and dizziness) is not uncommon in advanced cancer. Each has multiple etiologies that contribute to these individual symptoms. The “bowel-emotional dysfunction symptom cluster” (constipation, worrying and feeling bloated) can be from the disease as well as a side effect of treatment. Constipation and feeling of being bloated are often seen in patients with advanced cancer [21], feeling bloated was found 88.3% [12], and however in this study feeling bloated was found to be lower than previous study. Pain is commonly reported in advanced cancer patients. An estimated 60% to 92.5% of persons with advanced lung cancer report pain, making it one of the most common symptoms of advanced cancer [1, 12]. In the current study, pain was rated as the most severe, and the most distressful symptom in the study. The “pain related discomfort symptom cluster” consisted of three symptoms (pain, shortness of breath and lack of energy); the result is almost similar with other studies. For example Chaiviboontham and colleague [12], reported four symptom clusters, one cluster is “pain, sickness-behavior and psychological which consisted of 11 symptoms (difficulty concentrating, pain, lack of energy, feeling bloated, shortness of breath, worrying, lack of appetite, weight loss and “ I don’t look like myself) [12]. Symptom clusters in this study were reported differently from other studies [1-3, 6, 9, 12]. The variation of symptom clusters may occur according to the heterogeneous characteristics of the sample such as type of cancer, type of treatments ,stage of disease [6, 9, 12] and the evaluation of symptoms with different type of instruments [1-3,6]. However, the result of this study revealed that symptom clusters existed in advanced lung cancer patients in Thailand.

CONCLUSION AND LIMITATIONS

Most research on cancer symptoms to date tends to study a single symptom but as we know, symptoms in cancer patients often occur in groups or clusters. Across all cultures and nationalities symptom management for patients undergoing treatment or palliative care is an essential component for cancer care. The strength of this study is in using a sample with homogenous clinical characteristics of patients with advanced lung cancer with most patients on chemotherapy. The result of this study can be used to develop strategies, such as assessment tools to investigate

and manage symptom clusters. For example, suggestion is made on the assessment of a cluster of shortness of breath, pain, and fatigue which the most common symptoms that occur simultaneously in lung cancer patients. Symptom management strategies such as pain intervention and closely following the effect on fatigue and shortness of breath can improve the quality of life for patients with lung cancer in Thailand. The limitations of this study need to be mentioned, because only a single time period was assessed, the stability of symptom clusters was not evaluated. Statistically derived clusters can differ from clinically defined clusters. The identification of clusters will need to be supported by work related to the biological mechanisms behind the clusters.

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