

# Symptom clusters and quality of life in China patients with lung cancer undergoing chemotherapy

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## Abstract

**Objective:** To explore the symptom clusters and quality of life in patients with lung cancer undergoing chemotherapy.

**Methods:** A cross-sectional survey was completed with 183 patients from three public hospitals in Xi'an, China. Patients completed a demographic questionnaire, the Functional Assessment of Cancer Therapy-Lung Cancer (FACT-L) and the M. D. Anderson Symptom Inventory (MDASI-C). Factor analysis was used to identify symptom clusters based on the severity of patients' symptom experiences. The resulting clusters were correlated with quality-of-life measures.

**Results:** The QOL scores of lung cancer patients on the functioning subscale were the lowest ( $9.70 \pm 5.30$ ), while those of the family subscale were the highest ( $19.28 \pm 3.24$ ). Three symptom clusters were identified: gastrointestinal, emotional and fatigue-related symptoms. There was a negative relationship between the symptom clusters and multiple dimensions of quality of life ( $r -0.178$ – $-0.805$ ,  $p < 0.05$ ). Females, especially those women with low education level / chronic diseases, were experienced greater symptom distress than others.

**Conclusions:** The clusters had a negative relationship with QOL. Identifying symptom clusters helped clarify possible inter-relationships which may lead to the establishment of more effective symptom management interventions for patients with lung cancer in order to improve the quality of life.

**Keywords:** symptom clusters, lung cancer, factor analysis, symptom management, quality of life

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## Introduction

Lung cancer has become the leading cause of cancer deaths in mainland China, and more than 24600 people died of lung cancer in the year 2008[1]. Lung cancer was often diagnosed at an advanced stage with poor prognosis. Anecdotal data shows that 80% of lung cancer cases are diagnosed at stage 3 or 4 in the general hospitals in China. Patients with lung cancer experience a variety of distressing symptoms, many of which begin prior to diagnosis and continue throughout the course of the disease and its treatment, adversely affecting functional status and quality of life (QOL). Compared to other types of cancer, the distress associated with symptoms arising from lung cancer has been reported as the most intense[2]. Part of the symptom burden experienced by patients with lung cancer may be the

result of the simultaneous occurrence of symptoms, also known as “clustering” of symptoms. The term “symptom clusters” has been defined as two or more interrelated symptoms that are present together, independent of other symptom clusters, and may or may not suggest a common etiology or underlying mechanism [3-5]. Research has provided evidence that, together, multiple symptoms may have more negative effects on patients' quality of life than the occurrence of single symptoms [6,7].

Most research on symptoms has been directed towards a single symptom, such as pain or fatigue, or symptoms that were correlated with a single symptom. However, the symptoms generally occurred at the same time and there were synergic relationships among them that resulted in negative impact on QOL[8]. Thus, the exploration of the impact of simultaneous symptoms on QOL domains in lung cancer patients, and the understanding of symptom synergism, became important for successful achievement of cancer treatment. Establishing the best strategies to reduce the impact of cancer and treatment-related symptoms, and to improve QOL, are important. Appropriate symptom control, considering symptom interactions, should be a priority for patients with lung cancer. In addition, effective symptom management might lessen or negate these effects and improve lung cancer patients' quality of life.

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Therefore, the objectives of this study were to (1) describe symptom experienced by patients with lung cancer undergoing chemotherapy; (2) explore whether multiple symptoms were clustered into groups of symptoms; (3) examine whether symptom clusters were related to demographic, health characteristics; (4) identify the impact of symptom clusters on QOL dimensions

Various theoretical frameworks were available to guide our understanding of symptom clusters. We used the theory of unpleasant symptoms (TOUS), which has been utilized frequently in symptom cluster research [9-12]. TOUS has three main reciprocal components: symptoms, influential factors, and performance. According to the theory, each symptom has four dimensions: intensity, timing, level of distress perceived and quality. The symptoms of the effecting factor include physiological, psychological, and situational antecedents. Performance is the consequence of the symptom experience, which covered functional and cognitive activities. This model provides a theoretical framework for research on symptom clusters by indentifying multiplicative effects of multiple concurrent symptoms. In the theory of unpleasant symptoms, Lenz[13] proposed that symptom clusters have a resultant effect on important patient outcomes, such as QOL.

## Methods

### *Design*

A cross-sectional study design was used with a convenient sample of patients from three public hospitals in Xi'an from January to June of 2012.

### *Sample and Settings*

The research criteria for the sample was determined to reflect the following conditions: (1) receiving chemotherapy for lung cancer at any stage of their chemotherapy, and any cycle; (2) 18 years of age or older; (3) able to understand and speak Chinese, and (4) absence of cognitive impairment.

A total of 200 patients were approached and invited to participate. Among them, 183 patients responded to the study invitation. Seventeen patients (8.5%) were too sick to complete the questionnaires, or were prevented from participating by a family member.

### *Procedures*

After the hospital ethics committee approved the study, eligible patients were screened and those meeting 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-C, FACT-L and Demographic and Medical questionnaires. Research assistants were available on site during the administration of the questionnaires and provided explanation. The participant's demographic and clinical data was obtained through personal interview and the review of their medical records. The time required to complete the questionnaire was approximately 20-30 minutes.

### *Instrument*

The study instruments included a demographic and clinical questionnaire, the Functional Assessment of Cancer Therapy-Lung Cancer (FACT-L) and the M. D. Anderson Symptom Inventory-the Chinese version- MDASI-C.

### *The demographic and clinical questionnaire*

The demographic information included the gender, age, family monthly income, type of medical insurance, marital status, educational level, religious affiliation and employment status. The clinical information were about the type of cancer, extent of disease, presence of metastatic disease, and whether there was coexistence with other chronic diseases .

### *Chinese Version of the M. D. Anderson Symptom Inventory (MDASI-C)*

The MDASI-T was used to measure the severity of symptoms and the degree to which they interfered with daily life. The MDASI had been established as a valid and reliable tool for assessing cancer-related symptoms, regardless of therapy or specific diagnosis. It contained 13 core symptom severity items (that is: fatigue, sleep disturbance, pain, drowsiness, lack of appetite, nausea, vomiting, shortness of breath, numbness, difficulty remembering, dry mouth, distress, and sadness) which could explain 64% of the variance in symptom interference, and six symptom interference items (that is: 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 was 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 in Chinese version were 0.82 □ 0.94. Most patients completed the form in 5 minutes.

*The Functional Assessment of Cancer Therapy-Lung Cancer (FACT-L)*

Quality of life was measured using the Chinese version of the Functional Assessment of Cancer Therapy V Lung cancer (FACT-L 4.0) developed specifically for patients with lung cancers[14]. Functional Assessment of Cancer Therapy V Lung cancer contained the original FACT-General scales that included a 27-item compilation of general questions divided into 4 primary QOL domains: physical (7 items), social/family(7 items), emotional (6 items), and functional well-being(7 items). The additional 9 items were used to assess disease-specific issues in patients with lung cancer[14]. The subjects circle numbers on a scale were from 0 (not at all) to 4 (very much) indicating their reaction to each statement. Higher scores for the scales and subscales indicated better QOL. The possible total scores ranged from 0 to 144. In this study, internal consistency of FACT-L (Chinese version 4.0) was 0.56 □ 0.82, whereas the test-retest reliability was 0.76 □ 0.82[15].

*Statistical Analysis*

Data were stored and analyzed using SPSS version 13.0. Frequency distributions and descriptive statistics were used to analyze the demographic, socioeconomic, and

clinical data, the scores on each symptom and QOL questionnaires (the subscales and the global QOL scores).

Exploratory factor analysis with principal axis factoring was used to identify symptom clusters. Varimax rotation was used to maximize the variance of the loadings within each component while assuming the independence of the component structure Spearman correlations was utilized to examine correlations between symptom clusters and QOL: total score of all symptoms of each symptom cluster and global QOL score, score of each dimension of QOL.

**Results**

*Demographic characteristics and clinical information*

A total of 183 participants undergoing chemotherapy were recruited. Most of the participants (63.9%) were male. The mean age was 58.25 years (SD = 10.31, range = 32 □ 84). A large number of participants (n = 174) were married (95.1%); 66.7% were unemployed, 56.3% were educated 9 years or less, and 90% had no religious beliefs, a typical characteristic of Chinese culture.

The diagnosis of non-small-cell lung cancer (NSCLC) comprised 80.9% and 31.2% for small-cell lung cancer (SCLC). Patients with stage IV non-small-cell lung cancer (NSCLC) accounted for 38.8%, while those with stage III non-small-cell lung cancer (NSCLC) totaled 22.4%. Patients with extensive-stage small-cell lung cancer (SCLC) comprised only 6.0% of the sample. More details of demographic and clinical data were presented in Table 1.

**Table 1** Demographic characteristics and clinical information

Variable	n	□ % □	M(SD)	Variable	n	□ % □
<b>Age</b>			□ 58.25±10.31 □	<b>Diagnosis</b>		
<b>Gender</b>				Small cell lung cancer	35	19.1%
Male	117	63.9%		Non-small cell lung cancer	148	80.9%
Female	66	36.1%		<b>Stage of disease</b>		
<b>Marital status</b>				Non-small cell lung cancer II	36	19.7%
Singe	4	2.2%		Non-small cell lung cancer III	41	22.4%
Married	174	95.1%		Non-small cell lung cancer IV	71	38.8%
Divorced	5	2.7%		Limited-stage small cell lung cancer	24	13.1%
<b>Education</b>				Extensive-stage small cell lung cancer	18	9.8%
Primary school	53	29.0%		<b>Family monthly income</b>		
Junior school	50	27.3%		Less than 1,000	79	43.2%
Senior school	44	24.0%		1,000 □ 2,000	40	21.9%
College/university	36	19.7%		2,000 □ 3,000	33	18.0%
<b>Occupation</b>				More than 3,000	31	16.9%
No	122	66.7%		<b>Coexistence with other chronic diseases</b>		
Yes	61	33.3%		Yes	53	29.0%
<b>Medical insurance</b>				No	130	71.0%
No	10	5.5%				
Yes	173	94.5%				

*The prevalence and severity of lung cancer patients' symptoms*

The top three prevalent symptoms among participants were tiredness (99.5%); distressed (98.9%), and lack of appetite (97.3%); whereas the rarest symptom was numbness (43.2%). The average symptom

severity was graded 4.0, which indicated symptoms disturbance with a mild-to-moderate level. Moreover, the top three severe symptoms experienced by the participants were fatigue, dry mouth, and shortness of breath. The prevalence and severity of symptoms were listed in Table 2.

**Table 2** Prevalence and severity of Lung cancer patients' symptom

	Prevalence n(%)	Severity Mean(SD)
Fatigue	182 □ 99.5% □	6.24 ± 1.70
Lack of appetite	178 □ 97.3% □	4.86 ± 2.11
Shortness of breath	164 □ 89.6% □	4.88 ± 2.52
Disturbed sleep	175 □ 95.6% □	4.58 ± 2.07
Distressed	181 □ 98.9% □	4.26 ± 1.96
Nausea	150 □ 82.0% □	3.91 ± 2.66
Dry mouth	174 □ 95.1% □	4.96 ± 2.01
Pain	130 □ 71.0% □	3.78 ± 3.01
Drowsiness	79 □ 43.2% □	3.64 ± 2.00
Vomiting	138 □ 75.4% □	3.29 ± 2.63
Sadness	171 □ 94.4% □	3.56 ± 2.16
Disturbed sleep	142 □ 77.6% □	2.36 ± 1.87
Numbness	79 □ 43.2% □	1.39 ± 2.03

*Symptom clusters*

The exploratory factor analysis with principal axis factoring was used to extract symptom clusters, and the Varian rotation was used to simplify the factor structure. In this study, variables with item–total correlation coefficient less than 0.4 were excluded because statistically a correlation with a lower than that will produce too many factors in factor analysis. Three

distinct factors with Eigen values greater than 1.0 were retained, accounting for 69.4% of the total variance. The first factor, that is, gastrointestinal symptom cluster included nausea and vomiting. The second factor, fatigue-related cluster includes feeling fatigued, pain, and disturbed sleep. The third factor, emotional cluster, consisted of symptoms of sadness, and distress (Table 3).

**Table 3** The Symptom Clusters in lung cancer (n=183)

Symptom clusters	Symptoms	Factor Loading		
		Factor1	Factor2	Factor3
Gastrointestinal	nausea	0.873		
	vomiting	0.887		
Emotional	distressed		0.724	
	sad		0.818	
Fatigue related	disturbed sleep			0.826
	disturbed sleep			0.527
	pain			0.450

*Relationship of symptom clusters to demographic and clinical information*

For demographic variables, the gender differences were identified as statistically significant in each factor, which indicated that females reported statistically higher

troubling symptoms than males. Education differences among the three symptom clusters were statistically significant. Chronic illnesses were significantly related to gastrointestinal symptom clusters as shown in table 4.

**Table 4** The correlations among demographic characteristics

Variable	Factor1		Factor2		Factor3	
	t/F	P	t/F	P	t/F	P
Gender	-2.99	.01	-2.32	.02	-2.18	.03
Stage of disease	5.73	.001	5.94	.001	4.81	.001
chronic diseases	2.45	.04				

*Relationship between symptom clusters and quality of life*

The results demonstrated the descriptive statistics for the FACT-L total and its subscales. The highest HRQOL score for the total sample was the lung cancer subscale dimension, followed by the social dimension.

The lowest score was the role functioning dimension, followed by the emotional dimension. Pearson correlations were computed between the symptom cluster scale scores and the quality-of-life measurements and the results are in table 5.

**Table 5** Worse physical quality of life was associated with higher symptom bother from all symptom clusters

Variables	M(SD)	gastrointestinal	Symptom Clusters	
			emotional	Fatigue related
FACT-L				
Physical well-being	14.38±4.72	-.655	-.697	-.749
Social/family well-being	19.28±3.24	-.178	-.302	-.257
Emotional well-being	13.20±4.37	-.358	-.805	-.617
Functional well-being	9.70±5.30	-.411	-.749	-.696
Lung cancer subscale	20.89±5.55	-.332	-.508	-.485

**Discussion**

The results of this study have provided important insights into the symptom experiences and the relationship between symptom clusters and quality of life in patients with lung cancer in mainland China. Lung cancer remains the leading cause of cancer death in mainland China. However, studies describing the experiences of patients living with lung cancer in mainland China are limited. To our knowledge, this is the first study in mainland China, to explore symptom clusters as well as test the relationship between symptom clusters and quality of life in a homogeneous group of lung cancer patients.

Tiredness, distress, and lack of appetite were the most prevalent symptoms in this study. This result was similar to that from previous studies[16-18]. Concerning severity of symptoms, our result showed fatigue, dry mouth, and shortness of breath as the most severe, was similar to Semiha Akin 's [19] findings. The results of this study indicate lung cancer patients in mainland China suffered from a severe level of symptom distress

similar to what is experienced in Europe and north America. Three factors were identified this study. Gastrointestinal symptom cluster included nausea and vomiting, which was similar to the research of Wang, SY et al[20]. Gastrointestinal symptom cluster probably resulted from the side effects of chemotherapy. Fatigue-related cluster composed of feeling fatigued, pain, and disturbed sleep. These sickness behaviors were considered to be mediated by proinflammatory cytokines[21,22]. Emotional cluster which was a more psychologically related cluster consisted of symptoms of sad, and distressed. Historically, cancer symptom research had focused on a single symptom at a time, but now, we were aware that the patients with lung cancer often have multiple concurrent symptoms and may exacerbate one another. Furthermore, assessing possible symptom grouping simultaneously, systematically and comprehensively and therefore treated; interest in the effectively symptom management of cancer patients should pay more attentions to symptom clusters instead of only to individual symptoms.

It was found to be correlated with all symptom clusters in this study were gender and education. Weakness, psychological vulnerability was the nature of female patients leading to more symptom burden than male. The difference caused by education was similar to the previous research[23]. Patients who received high education will have early recognition of cancer and seek treatment actively. The weak correlations between symptom cluster and chronic disease might be explained by two reasons. Firstly, the symptoms of chronic disease itself will contribute to cancer symptom cluster. Secondly, lung cancer patients with chronic diseases produce more economic and psychological burden than patients without.

In this study, we found lung cancer patients had low QOL scores. The functioning subscale scores were the lowest, while the family subscale scores were the highest. The current study found a negative relationship between symptom clusters and QOL scores. Generally, almost all three symptom clusters were negatively correlated with PWB, EWB, FWB, SWB, and overall QOL. In this study, physical quality of life was highly correlated with all symptom clusters. Another particularly strong relationship was between the emotional cluster and emotional well-being in quality of life. This finding was consistent with other studies[24-26].

Overall QOL was important for patients with lung cancer. Therefore, symptom and QOL assessments were vital for the evaluation of the efficacy of cancer treatments. Patients with cancer experienced different levels of symptom distress according to disease and treatment. According to our finding, symptom management should be taken into account in order to decrease the negative effects of symptom clusters on QOL. Further studies should include a larger sample to more fully describe the potential interactive effects of the dependent variables on QOL.

#### **Limitations and methodological issues:**

Firstly, the MDASI was a relatively short instrument that assessed only 13 symptoms. As we know, using different tools of symptoms may result in different symptom clusters. We therefore suggested a more comprehensive tool should be used to assess symptoms when exploring the phenomenon of symptom clusters. Secondly, the current study of symptom clusters had been conducted by cross-sectional design. A future study was needed to explore long-term changes of symptom clusters and its association with physical, psychological, and clinical variables.

#### **Conclusions**

Lung cancer patients receiving chemotherapy suffered from numerous symptoms simultaneously, due to the disease itself as well as treatment. The results of this study have provided understanding of symptom clusters which could help clinicians develop more comprehensive and useful assessment tools as well as more effective symptom management strategies to improve the quality of life for patients with lung cancer in China.

#### **Conflict of interest**

The authors have no conflict of interest to declare.

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