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A Brief Symptom Index for Advanced Lung Cancer

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Abstract

Background—Advanced lung cancer is often symptomatic; thus, the goals of treatment include maintenance of function and symptom palliation. Symptom management requires accurate, systematic symptom assessment. This study, focused on lung cancer, is part of a larger study to obtain patient input which, in combination with previously obtained physician and nurse input, was used to develop symptom indexes for 11 advanced cancers.

Participants and Methods—Fifty patients with advanced lung cancer were recruited from National Comprehensive Cancer Network (NCCN) member institutions and community support agencies; 10 physician experts were recruited from NCCN institutions. Patients reported symptoms associated with their disease in open-ended format and then completed a checklist of symptoms, rating their five most important symptoms. Patient and provider ratings of symptom importance were tabulated to construct the NCCN-FACT Lung Symptom Index-17 (NFLSI-17). Patients also completed the Functional Assessment of Cancer Therapy-Lung (FACT-L), which was used to preliminarily validate the NFLSI-17.

Results—Based on combined patient, physician and nurse input, the NFLSI-17 is comprised of 17 priority symptoms, 11 which are disease-related, three treatment-related, and three related to general function/well-being. Data on 15 of 17 NFLSI-17 symptoms showed good internal consistency ($\alpha = 0.74$) and strong association with the FACT-L total and most subscale scores

($r=0.42-0.92$). Both the NFLSI-15 ($F[2,47]=4.46$, $p=0.017$) and the NFLSI-Disease-Related Subscale (DRS; $F[2,47]=5.56$, $p=.007$) significantly discriminated patients among performance status groups.

Conclusion—The NFLSI-17 reflects the most important patient- and clinician-rated targets of chemotherapy for advanced lung cancer; further validation will follow.

Keywords

lung cancer; symptoms; symptom index; patient-centered; health-related quality of life

Introduction

Lung cancer is the most common cancer worldwide¹, the second most common cancer in the United States and the leading cause of cancer deaths². Despite recent advances in the treatment of lung cancer, the median survival of patients with advanced non-small cell lung cancer (NSCLC) is 8–10 months, with a one-year survival of 30–40%³ and five-year survival rate of only 15%². The majority of all lung cancer is histologically classified as non-small cell cancer (NSCLC), with the remaining being small-cell lung cancer (SCLC).^{4,5} Most lung cancers are undetected until symptoms develop and patients present with advanced (locally or metastatic) disease.⁶ Patients with advanced disease face a shortened life expectancy that is increasingly symptomatic, often due to disease progression. As cure is not an option for advanced disease, the goal of treatment is focused on maintenance of function and symptom palliation while minimizing toxicity.

Symptoms, ranging from mild to debilitating, are common in lung cancer, and usually worsen as the disease progresses.^{7–10} Anti-cancer treatment may alleviate symptom burden, or cause additional symptoms. The most common disease-related symptoms in lung cancer include fatigue, dyspnea, cough, weight loss, anorexia, pain, insomnia, change in mental status, and psychological distress.^{11–16} Multiple symptoms are common, especially in individuals with advanced disease.^{10,17–22} Symptoms may differ at various points in the disease course and by treatment, and some symptoms cluster together.¹⁰ Poorly controlled symptoms can impair patients' daily functioning and health-related quality of life (HRQL)²³ and can affect cancer treatment by causing a patient to interrupt treatment or discontinue anti-tumor therapy altogether, thereby negatively influencing its effectiveness.^{24,25} Despite the availability of effective treatment for many symptoms, patients with advanced cancer experience multiple symptoms that often remain undetected and untreated.^{26–28}

Effective symptom management begins with accurate symptom assessment.²⁹ Systematic symptom assessment and reporting to the provider is associated with reduced symptom distress^{30–31}, better pain control^{32–33} and improved symptom communication. A number of validated multidimensional measures of cancer-specific HRQL also include an assessment of some symptoms.^{34–36} However, brief tumor-specific symptom measures are needed, and, in particular, measures that are psychometrically acceptable and based on both patient and healthcare provider input to ensure clinical relevance. Such measures should be sensitive to the impact of drug therapy³⁷, thereby serving clinical, research and regulatory purposes.

To that end, in 2003 we conducted a comprehensive survey of physician and nurse experts at 17 National Comprehensive Cancer Network (NCCN) member institutions to examine the priority symptoms endorsed by oncology experts.³⁸ Using questions from the Functional Assessment of Cancer Therapy (FACT) measurement system and data from this survey of experts, we constructed tumor-specific indexes comprised of the most important symptoms and concerns to monitor in evaluating treatment for nine advanced cancers, including lung. The results of this survey demonstrated good agreement between expert physicians and nurses on the relative importance of symptoms in this survey. However, patient ratings of symptom relevance and severity often differ from those of providers^{26, 39–42}, especially regarding psychological symptoms and concerns.^{43–44} While items derived from the FACT measurement system are based on patient input, and the nine indexes were largely comprised of items from this measurement system, there remained the possibility that the symptom indexes did not capture the full range of patient priority symptoms.

Therefore, we sought to identify patients' highest priority cancer symptoms for an expanded range of advanced cancers (eleven), compare their priority ratings with those of oncology experts, and construct brief symptom indexes utilizing the combined input (i.e., physicians, nurses, patients) to assess these symptoms and concerns. The methodology used was similar to that used with clinical experts³⁸ and has been reported on elsewhere⁴⁵ and was implemented 2005–2007. In addition, physician expert input was obtained as to which symptoms associated with each of eleven diseases are considered to be disease-related versus treatment-related. Patient-completed FACT HRQL questionnaires specific to their disease provided data for a preliminary validation of the symptom indexes. This paper will focus exclusively on the symptom index pertaining to advanced lung cancer, the NCCN-FACT Lung Symptom Index-17 (NFLSI-17).

Participants and Methods

Participants in this study included patients diagnosed with lung cancer and physicians who treat patients with lung cancer.

Patient Eligibility and Recruitment

Patients were eligible for the study if they were at least 18 years of age and had stage III or IV lung cancer. Patients must have had prior experience with chemotherapy for at least 2 cycles (one month for non-cyclical chemotherapy), and no other primary malignancy diagnosed and/or treated within the previous five years except non-melanoma skin cancer.

Patients were recruited from a subset of NCCN member institutions and community support agencies. Specifically, patients with lung cancer were recruited from four NCCN institutions, including the Robert H. Lurie Comprehensive Cancer Center of Northwestern University (Chicago, IL), H. Lee Moffitt Cancer Center & Research Institution (Tampa, FL), Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance (Seattle, WA), and Duke Comprehensive Cancer Center (Durham, NC). The NCCN is a not-for-profit, tax-exempt corporation that is an alliance of NCI-approved comprehensive cancer centers. Patients were also recruited through members of the Cancer Health Alliance of Metropolitan Chicago (CHAMC), a coalition of four community support agencies serving the Chicago

metropolitan area. These organizations were selected to provide patient input from community-based practices to balance the preferences of patients from tertiary referral centers, such as NCCN sites.

Physician Eligibility and Recruitment

Physicians were recruited by email sent to all 21 NCCN member institutions by NCCN headquarters staff. Physicians were eligible to complete the disease-/treatment-related survey if they were in practice at any of the 19 NCCN institutions and had at least three years' experience treating a minimum of 100 patients with advanced lung cancer. Physician input was solicited to determine which symptoms they considered to be disease- versus treatment-related.

Procedures

Patient Survey—After completing brief forms for collecting sociodemographic and clinical information, a subset of 33 patients was asked to respond to an open-ended question, “Please think of the full range of your experience receiving drug treatment for your illness. Please tell me what you think are the most important symptoms or concerns to monitor when assessing the value of drug treatment for your illness.” Patients were then asked, “Please tell me on a scale of 0–10 (with 0 being not important and 10 being extremely important) how important each symptom or concern is to you.” This format allowed for the collection of patient input without possible priming effects of providing them with a list of symptoms.

Next, patients were asked to complete a symptom/concern checklist that included 28 items nominated by clinician experts from the FACT-L questionnaire, identical to that administered to NCCN physicians and nurses previously.³⁸ Patients were first asked to select no more than 10 symptoms or concerns that they felt were “the most important symptoms or concerns to monitor when assessing the value of drug treatment for advanced lung cancer.” Of the 10 symptoms/concerns nominated as “the most important,” patients are then asked to select up to five as “the very most important.” Space was provided for respondents to write in symptoms or concerns that are not already listed. Four versions of each checklist were created to control for response bias due to order effect. Patients then completed the FACT-L⁴⁶, which consists of 27 items from the FACT-General (FACT-G)^{35, 47} assessing Physical Well-being (PWB), Functional Well-being (FWB), Social/Family Well-being (SWB) and Emotional Well-being (EWB), plus the Lung Cancer subscale (LCS), which includes additional ten additional lung cancer-specific questions. These data were analyzed by extracting symptom index items from the full-length HRQL questionnaire and conducting preliminary analyses of their reliability and validity.

Physician Survey—Physicians completed an online survey administered by Survey Monkey™. The survey asked respondents to rate each advanced lung cancer symptom/concern on a 5-point scale as to whether it is “exclusively disease-related,” “predominantly disease-related,” “too close to determine,” “predominantly a treatment side effect,” or “exclusively a treatment side effect.” Physicians were also provided the option of rating symptoms as neither disease- nor treatment-related.

Data Analysis/Selection of Items for Index—Checklists were tabulated according to the frequency with which patients selected a particular symptom/concern as one of the five most important. The criterion for item retention was based upon the probability of chance endorsement as one of the top five symptoms. We determined the number of patients that would be expected to endorse a symptom by chance by dividing 5 [the number of VERY most important symptoms/concerns endorsed] by the number of items on the checklist [28], and then multiplying by the number of patients [50]. Those items endorsed at a frequency that exceeded chance probability were retained as candidates for the final symptom index. To err on the side of inclusion, any item that appeared within one point of the chance cut-off was retained.

The process of how the relative and absolute patient and physician ratings were used to assemble a symptom index is detailed elsewhere⁴⁵; a brief description is provided here. If a symptom/concern was endorsed as very important at a frequency substantially greater than other symptoms, a second item targeting the same aspect of the symptom experience was considered for inclusion. Where possible, items to be added were extracted from the Functional Assessment of Chronic Illness Therapy (FACIT) measurement system (of which the FACT is a subset) because of previously demonstrated ease of use, validation and translation qualities. If a symptom/concern was *not* endorsed by patients as among the very most important at a rate exceeding chance but *was* rated so by providers in the previous NCCN FACT study³⁸, it was retained in the index because of its potential clinical significance.

The open-ended patient-generated lists of important symptoms and/or concerns were also reviewed for the presence of new concepts that warranted inclusion in a priority symptom list. Symptoms judged by experts to be primarily disease-related were included if greater than 10% of patients reported it to be important. Symptoms judged by experts to be primarily treatment-related were included if they were reported by more than 20% of patients. For disease groups having a high percentage of patients volunteering medication or treatment side-effects as one of the most important symptoms or concerns to monitor, the item “I am bothered by side effects of treatment” from the FACIT measurement system was added to each index. The symptoms and/or concerns patients wrote in at the bottom of the checklists were also reviewed for existence of new concepts. If greater than 5% of patients in a disease category reported a particular new symptom/concern that was not judged to be treatment-related (or > 10%, if the symptom/concern was judged to be primarily treatment-related), it was considered for item inclusion.

The physician surveys were reviewed for classification of each index item as “exclusively/predominantly disease-related,” “exclusively/predominantly treatment-related,” or “too close to determine/neither.” If more than 50% of physicians indicated an item was exclusively/predominantly treatment-related, these items were categorized in the Treatment Side-Effect (TSE) subscale. The remainder of items was determined to be either exclusively/predominantly disease-related (DRS subscale).

Results

Sample

Table 1 summarizes the sociodemographic and clinical characteristics of the sample of patients with advanced lung cancer (n=50). Patients had a median age of 63 years. The sample was predominately female (64%), White (90%), well educated (58% with some college or college degree) and retired (39%). Using the Eastern Cooperative Oncology Group [ECOG] performance status rating [PSR] five-point scale (0=no symptoms, 1 = some symptoms but does not require bedrest during the waking day, 2 = requires bedrest for less than 50% of the waking day, 3 = require bedrest for more than 50% of the waking day, 4 = unable to get out of bed), most (58%) patients reported normal activity with some symptoms.

Of the sample of 10 physicians who were surveyed about advanced lung cancer, four were female, mean age was 47 years, and duration of practice ranged from 3–5 years (n=3), to 11–15 years (n=2), to 16–20 years (n=3) to over 20 years (n=2).

Patient Symptom Rankings

The first step required patients to spontaneously generate a list of symptoms or concerns related to their lung cancer and to rate their importance on a scale from 0 to 10. Table 2 displays the number of patients spontaneously generating specific responses to the open-ended question about the symptoms they had experienced receiving treatment for their lung cancer and the 0–10 ratings of importance patients assigned to those symptoms.

Patients were asked to select symptoms that they considered to be among their top 10 “most important symptoms or concerns to monitor when assessing the value of drug treatment for advanced lung cancer” along with the number of endorsements. This list was led by lack of energy/fatigue, being able to enjoy life, being able to think clearly, being able to sleep well, being content with the quality of one’s life, and shortness of breath. After selecting their top 10 symptoms/concerns, patients were asked to go back and select the top 5 most important symptoms or concerns to monitor during drug treatment (Table 3). Eleven symptoms exceeded the threshold for chance selection (i.e., 8.9), and included 11 of the top 12 symptoms rated as among the patients’ top 10.

In addition to selection symptoms/concerns that represented their “top 10” and “top 5,” patients were provided with an opportunity to write in any symptom or concern that was not listed. Forty-two (84%) of the patients did not add any symptom/concern, and eight (16%) patients offered a total of twelve write-in responses (e.g., inability to donate blood, mouth sores, worry about financial burden), all of which received endorsement by only one patient. Because of their low endorsement frequency (< 5%), none were retained in the final index.

Composition of the NCCN-FACT Lung Symptom Index (NFLSI)

The final NCCN-FACT Lung Symptom Index was composed of 17 symptoms/concerns (see Table 4). Ten of the 17 were retained because they met the threshold of being selected by patients as among their top five “very most important” symptoms to monitor at a rate

exceeding chance (fatigue, shortness of breath, bone pain, worry condition will worsen, ease of breathing, good appetite, sleeping well, nausea, thinking clearly, ability to enjoy life). “I am content with my quality of life right now” was the fifth most frequently endorsed concern by patients in the first step of this study. This item was immediately below the threshold of 8.9 (8.0) for exceeding chance selection as one of the top five symptoms, and it was also added to the index. Three additional symptoms (pain, weight loss, coughing) were not rated by patients as among their top five concerns but were endorsed by providers in the previous NCCN FACT study.³⁸ One symptom (fatigue) was endorsed as very important substantially more than other symptoms, so a second fatigue item (“I feel fatigued”) from the FACIT measurement system was added to complement the “I have a lack of energy” item. The original lung cancer symptom index contained the item “I have certain areas of my body where I experience significant pain,” which was intended to capture bone pain. Thus, “bone pain” had been parenthetically added to the statement on the checklists. However, the item was re-written to “I have bone pain” for inclusion on the NFLSI-17 because our subsequent research indicated that patients were able to understand and respond to this item wording. Hair loss was spontaneously reported by 21% of patients as a significant concern, and 15% voiced concern about treatment side effects, so items related to these issues (“I am bothered by hair loss,” “I am bothered by side effects of treatment”) were retained in the index.

Physician Ranking Data

Table 5 shows the ratings of the ten physician experts in lung cancer that rated symptoms and concerns as to their relation with disease, treatment, both or neither. Eleven of the symptoms were unambiguously identified as disease-related. Neither of the symptoms regarding appetite and sleep were considered to be “exclusively/predominantly treatment-related” by greater than 50% of the physicians, so they were retained on the Disease-Related Subscale (DRS), whereas the items relating to nausea and hair loss met the criterion for being categorized on the Treatment-Related Side Effects Subscale (TSE). Items related to being able to enjoy life and being content with one’s quality of life right now were considered to be descriptive of general function and well-being (F/WB) and were so categorized.

The final index was formatted with each subscale delineated by shaded boxes. The DRS appears first, followed by the TSE subscale and then the F/WB subscale. Within each subscale, positive and negative items were separated (negative items appearing first), and within negative and positive items, physical and psychological items were separated (physical items appearing first).

Preliminary Validation Data

Two of the items on the NFLSI-17 were not in the FACT-L (“I feel fatigued” and “I have bone pain”) (see Table 4). Thus, preliminary analyses of the symptom index included only 15 of the 17 items in the index (“NFLSI-15”).

The 15-item version of the NFLSI showed good internal consistency, with a Cronbach’s alpha of 0.74.

Table 6 displays the means and standard deviations of the NFLSI and FACT scale scores. Associations between the NFLSI and FACT-L scale and subscale scores were evaluated with Spearman correlations (Table 7). The NFLSI-15 was highly correlated with the PWB subscale ($r=0.79$), FWB subscale ($r=0.74$), LCS ($r=0.76$), FACT-G total ($r=0.75$), FACT-L total ($r=0.89$) and Trial Outcome Index (TOI; a composite of the PWB, FWB and LC subscales; $r=0.92$), all $p<.0001$. The NFLSI was not as strongly associated with the EWB subscale ($r=0.42$, $P<.01$) and there was no significant association with the SWB subscale. The NFLSI contains four PWB items, three FWB items, and one EWB item, which could produce inflated correlations due to redundancy. However, even after redundant items were removed, correlations were lower but remained significant (range $r=.033 - 0.61$). Similar patterns of correlations, albeit lower in magnitude, were found for the NFLSI-DRS, NFLSI-TSE and NFLSI-F/WB subscales with two exceptions: the TSE subscale was no longer significantly associated with the FACT EWB subscale, and both the SWB and EWB subscales of the FACT were significantly associated with the F/WB NFLSI subscale.

As further preliminary evidence of the NFLSI's validity, we examined its ability to discriminate patients based on ECOG PSR (see Table 8). Because only one patient was in the PSR=3 group, PSR=2 and 3 groups were collapsed. For all NFLSI subscales, the scores across PSR groups were in the expected direction, i.e., patients with the lowest PSR (i.e., best performance status) had the highest NFLSI scores (i.e., better symptom status). Both the NFLSI-15 ($F[2,47]=4.46$, $p=0.017$) and the NFLSI-DRS ($F[2,47]=5.56$, $p=.007$) significantly discriminated patients in the 3 ECOG PSR groups. However, neither the NFLSI-TSE nor the NFLSI-F/WB scores were significantly different among these groups.

Discussion

The primary objective of this study was to identify patients' highest priority cancer symptoms for advanced lung cancer, to compare their priority ratings with those of oncology experts, and to construct a brief symptom index utilizing the combined input (i.e., physicians, nurses, patients) to assess these symptoms and concerns. Priority symptoms were assessed using open-ended qualitative input from patients and surveys of candidate items derived from the FACT-G and the Lung Cancer Subscale. We compared patient input with data already obtained from national and international oncology experts to determine which symptoms/ concerns were most important to monitor in advanced cancers. Seventeen items endorsed most frequently by both patients and medical experts were retained on the new symptom index, the NCCN-FACT Lung Symptom Index. The symptoms represented are consistent with highly prevalent symptoms associated with advanced lung cancer.¹¹⁻¹⁶ The index has been formatted by subscale, separating disease-related (DRS), treatment side-effect (TSE) and general function and well-being (F/WB) items for ease of use and scoring.

In the qualitative, patient-generated phase, patients were provided the opportunity to write in symptoms/concerns that may or may not be present on the symptom checklists. Ultimately, none of these spontaneously generated items were included in the NFLSI-17 because they were reported by no more than 2% of patients. Similarly, after checklists of items from the FACT HRQL measurement system were presented to patients for selection of their top 5 priority symptoms, they were again provided with an opportunity to write-in any

additional items, and none of these met criteria for inclusion in the index. The 17-item NFLSI is comprised of items derived exclusively from the FACT HRQL measurement system. Thus, the results suggest that the FACT HRQL system appears to contain the symptoms and concerns that patients believe are most important to monitor when receiving treatment for advanced lung cancer.

A unique aspect of this study compared to the initial NCCN symptom index study³⁸ was the inclusion of physician expert ratings of symptoms as disease- or treatment-related. In this study, physicians rated 11 symptoms on the NFLSI-17 as “exclusively” or “predominantly” related to disease and three symptoms as related to treatment side effects. An additional three symptom/concerns were retained in the index because of their prevalence in being selected as a priority symptom or concern, but they were considered to reflect more general function or well-being concerns and were so designated in the NFLSI-17 (“NFLSI-F/WB”).

Preliminary validation analyses suggest that the NFLSI-17 represents a psychometrically acceptable brief symptom index for advanced lung cancer, with good internal consistency and evidence of construct validity. As would be expected, the 15-item NFLSI was more highly correlated with FACT subscales that represented physical aspects of well-being (e.g., PWB, FWB, Lung Cancer Subscale (LCS), FACT-G total, FACT-L total and TOI and correlated to a lesser extent (EWB) or not at all (SWB) to psychosocial subscales. The NFLSI-15 showed good internal consistency, and the NFLSI-15 and NFLSI-DRS were able to discriminate among patients grouped by PSR. Neither the NFLSI-TSE nor the NFLSI-F/WB scores were significantly different among these PSR groups, but this is not unexpected, given that the ECOG PSR measures symptomatology and ability to function with/without bedrest, which are not reflected in these subscales. While preliminary results appear encouraging, this index awaits more extensive validation in patient populations with advanced lung cancer.

If a clinician or researcher was interested in measuring both multidimensional HRQL as well as symptoms, s/he might wonder if it is possible to score the NFLSI-17 index from an administration of the FACT-L (37 items). Because the NFLSI-17 includes two items not present in the FACT-L, deriving a symptom index score from the FACT-L requires that the 15 NFLSI items be scored and then pro-rated to a full 17-item index. This is accepted as standard methodology in the FACIT measurement system and has been demonstrated to be superior compared to other methods of handling “missing” data.⁴⁸

The potential uses for the NFLSI-TSE and NFLSI-DRS are more intuitively obvious in that an investigator interested in focusing more exclusively on treatment-related side effects would find the -TSE scale more relevant, whereas a focus on disease-related symptoms would suggest the use of the -DRS scale. The trial outcome index (TOI) was created in order to explore the value of combining subscales relevant to medical clinical trial interventions. The TOI aggregates scores from the PWB, FWB, and 7-item LCS subscales. The 21-item TOI is reliable and sensitive to change in clinical status (e.g., Performance Status Rating), and among FACT-L scores, has been shown to be the most relevant and precise indicator of patient-reported health available for lung cancer patients in oncology clinical trials.⁴⁶

This study is not without limitations. While we attempted to broaden the representativeness of the patient population by including community support agencies in addition to NCCN institutions, it remains possible that patients recruited from clinical settings reflecting different patient mixes and delivery systems would report some additional symptoms and concerns. In addition, those symptoms categorized as associated with treatment side-effects reflect the treatments for advanced lung cancer at the time the study was conducted (2005–2007). As the availability of novel targeted agents expands, the TSE subscale could require updating to reflect increasingly prevalent symptoms associated with these therapies.

Disease-specific symptom assessment has a potentially key role in evaluating patient-related endpoints in clinical trials and in clinical care. In addition to representing an efficient and clinically-relevant means of obtaining information related to the symptom component of QOL, it may also clarify a treatment's toxicity, potential palliative benefit, or need to make a change in the patient's clinical management.¹⁷ In evaluating the efficacy of new chemotherapeutic agents, the ability to demonstrate the amelioration of symptoms specific to a given tumor may represent efficacy in achieving a meaningful patient outcome. Thus, a brief tumor-specific tool to assess symptomatology, such as the NFLSI-17, has a potentially key role to play in evaluating patient-related endpoints in clinical trials. This symptom index was developed using methods that meet industry standards for ensuring content validity, consistent with FDA guidance.⁴⁹ Regulatory review will ultimately determine its acceptability when evaluating the impact of new treatments on the symptoms that matter most to people with advanced lung cancer.

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Table 1

Sociodemographic and Clinical Summary of Patient Sample (n=50)

Age (yrs)		
M (SD)	51.6 (10)	
Median (range)	63.0 (38–79)	
	n	%
Female	32	64
Race		
White	45	90
African-American	4	8
Asian	1	2
Education		
< 12 th grade	3	6
High school diploma or GED	18	36
Vocational college or some college	13	26
College degree	8	16
Professional or graduate degree	8	16
Current occupational status (n=1 missing)		
Homemaker	7	14
Unemployed	2	4
Retired	19	39
On disability	11	23
On leave of absence	3	6
Full-time employed	3	6
Part-time employed	4	8
Patient-rated ECOG Performance Status Rating		
0, normal activities without symptoms	9	18
1, some symptoms, but do not require bed rest during waking day	29	58
2, require bed rest for less than 50% of waking day	11	22
3, require bed rest for more than 50% of waking day	1	2

Table 2Frequency of Spontaneous Patient-reported Symptoms & Ratings^a (n=33)

Rank	# Responses (%)	Exact Stated Symptom/Concern	Mean Importance Rating (0–10)
1	13 (39%)	Nausea	7.9
1	13 (39%)	Fatigue Energy level Tiredness after treatment Slow me down/decrease activity Lack of energy Lose of stamina	7.4
2	8 (24%)	Effectiveness of treatment Effectiveness Quality of chemo treatment Quality of treatment Overall effectiveness of chemo What are benefits? Growth of tumors Be cancer free	9.5
3	7 (21%)	Hair loss	4.6
3	7 (21%)	Breathing Shortness of breath Loss of lung function	9
4	6 (18%)	Pain Back pain Aches/Pain	8.7
5	5 (15%)	Life interference Interferes with time (personal) social Interferes with family time Being able to live normal life Ability to function day to day Interferes with private (individual time)	10
5	5 (15%)	Loss of appetite Appetite problems Could not eat lack of appetite Appetite	8.6

^a Only those symptoms endorsed by 10% of patients are included here

Table 3

Frequency of Symptoms Rated among “Top 5” (n=50)

Symptom/Concern	Frequency Ranking
Lack of energy (fatigue)	22
Being able to enjoy life	15
Worry that my condition will get worse	15
Being able to sleep well	13
Nausea	13
Shortness of breath	13
A good appetite	12
Being able to think clearly	12
Being able to breathe easily	11
Being able to enjoy the things I usually do for fun	9
Experiencing significant pain (bone pain) in certain areas of my body	9
(Threshold for chance selection = 8.9)	
Being content with the quality of my life right now	8
Worry about dying	8
Being able to swallow naturally and easily	7
Pain	7
Because of my physical condition, having trouble meeting the needs of my family	6
Losing hope in the fight against my illness	6
Feeling ill	5
Feeling sad	5
Tightness in my chest	5
Weight loss	5
Being able to work (include work at home)	4
Being forced to spend time in bed	4
Coughing	4
Coughing up blood	4
Satisfaction with my sex life	3
Feeling nervous	2

Table 4

Comparison of NCCN/FACT-Lung Symptom Index and FACT-L Items

	Revised NCCN/FACT Lung Symptom Index items	Item on FACT-L?
	I have a lack of energy	Yes
	I have pain	Yes
	I am losing weight	Yes
	I have been short of breath	Yes
	I feel fatigued	No
DRS	I have been coughing	Yes
	I have bone pain	No
	I worry that my condition will get worse	Yes
	Breathing is easy for me	Yes
	I have a good appetite	Yes
	I am sleeping well	Yes
	I have nausea	Yes
TSE	I am bothered by hair loss	Yes (not scored)
	I am bothered by side effects of treatment	Yes
	My thinking is clear	Yes
F/WB	I am able to enjoy life	Yes
	I am content with my quality of life right now	Yes
FACT-L items (LCS) not in Revised NCCN/FACT Lung Symptom Index		
	I feel tightness in my chest	
	I regret my smoking (not scored)	

DRS=Disease-Related Symptoms, TSE=Treatment Side Effects, F/WB=Function/Well-Being

Table 5Physician Ratings of Symptoms as Disease- or Treatment-related (n=10)^a

Symptom	Frequency (percent)					Neither
	Exclusively Disease-Related	Predominantly Disease-Related	Too Close to Determine (both)	Predominantly Treatment-Related	Exclusively Treatment-Related	
Lack of energy		6 (60)	4 (40)			
Pain	2 (20)	8 (80)				
Weight loss		7 (70)	3 (30)			
Shortness of breath	2 (20)	7 (70)	1 (10)			
Coughing	2 (20)	8 (80)				
Bone pain	2 (20)	8 (80)				
Worry condition will get worse	2 (20)	7 (70)				1 (10)
Breath easily	2 (20)	7 (70)		1 (10)		
Good appetite		2 (20)	4 (40)	4 (40)		
Able to sleep well	1 (10)	4 (40)	5 (50)			
Nausea			1 (19)	9 (90)		
Hair loss				4 (40)	5 (50)	1 (10)
Think clearly		1 (10)	5 (50)	4 (40)		
Able to enjoy life	1 (10)	4 (40)	4 (40)	1 (10)		
Content with quality of life now		3 (30)	7 (70)			

^a Only those symptoms retained on final NCCN/FACT Lung Symptom Index are shown

Table 6

Functional Assessment of Cancer Therapy – Lung (FACT-L) and NCCN-FACT Lung Symptom Index (NFLSI) Scale Scores (n=50)

Variable	Mean	SD	Minimum	Maximum
Physical Wellbeing (PWB)	20.15	5.04	1.00	28.0
Social Wellbeing (SWB)	23.34	4.25	11.67	28.00
Emotional Wellbeing (EWB)	17.84	4.73	7.00	24.00
Functional Wellbeing (FWB)	16.90	5.87	6.00	28.00
FACT-G Total	78.23	13.89	51.00	107.00
Lung Cancer Scale (LCS)	52.15	11.25	15.43	69.43
FACT-L Total	130.38	21.22	87.43	171.29
Trial Outcome Index (TOI)	89.20	17.97	41.43	120.86
NCCN-FACT Lung Symptom Index-15 (NFLSI-15)	40.68	8.06	26.00	56.00
NCCN-FACT Lung Symptom Index-17 (NFLSI-17)	46.11	9.14	29.47	63.47
NCCN-FACT Lung Symptom Index-Disease Related Subscale (NFLSI-DRS)	29.41	6.50	14.67	41.56
NCCN-FACT Lung Symptom Index-Treatment-related Side Effects (NFLSI-TSE)	8.84	2.63	0.00	12.00
NCCN-FACT Lung Symptom Index-Function/Well-being (NFLSI-F/WB)	7.78	2.62	1.00	12.00

Table 7

Spearman Correlation Coefficients of NFLSI^a with FACT-L Scales (n = 50)

	PWB	SWB ^c	EWB	FWB	LCS	FACT-G ^b	FACT-L ^b	TOI ^b
NFLSI-15, unadjusted	0.79 <.0001	0.23 0.1134	0.42 <.01	0.74 <.0001	0.76 <.0001	0.75 <.0001	0.89 <.0001	0.92 <.0001
NFLSI-15, adjusted for overlap	0.61 <.0001	NA	0.33 <.05	0.57 <.0001	0.45 <.001	NA	NA	NA
NFLSI-DRS, unadjusted	0.67 <.0001	0.12 0.4209	0.43 <.01	0.57 <.0001	0.80 <.0001	0.58 <.0001	0.80 <.0001	0.83 <.0001
NFLSI-DRS, adjusted for overlap	0.49 <.001	NA	0.29 <.05	0.50 <.001	0.39 <.01	NA	NA	NA
NFLSI-TSE ^b	0.62 <.0001	0.24 0.0994	0.07 0.6336	0.42 <.01	0.37 <.01	0.46 <.001	0.51 <.0001	0.57 <.0001
NFLSI- F/WB ^b	0.50 <.001	0.32 <.05	0.40 <.01	0.83 <.0001	0.43 <.01	0.73 <.0001	0.68 <.0001	0.66 <.0001

NFLSI = NCCN Functional Assessment of Cancer Therapy – Lung Symptom Index; DRS = disease-related symptoms; TSE = treatment-related side effects; F/WB = Functional/Well-being-related symptoms

^aTwo items from NFLSI are not on FACT-L, so 15-item NFLSI was used in analyses

^bCorrelations adjusted for overlap not calculated-too few items remained

^cNo overlap, adjusted correlations not needed

Table 8

NFLSI and FACT-L Scale Scores by ECOG Performance Status Groups

ECOG Rating Group	N	Physical Wellbeing F(2,47) = 8.56 P<.001		Social Wellbeing F(2,47) = 0.11 P=0.895		Emotional Wellbeing F(2,47) = 1.14 P=0.329		Functional Wellbeing F(2,47) = 4.98 P=0.011		Lung Cancer Subscale F(2,47) = 3.02 P=0.059		FACT-G Total F(2,47) = 5.45 P=0.007		FACT-L Total F(2,47) = 6.15 P=0.004	
		M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
0	9	23.68	4.21	22.80	5.07	19.11	5.09	20.11	4.76	58.86	10.16	85.69	13.44	144.54	21.43
1	29	20.78	3.91	23.56	4.55	18.14	4.46	17.52	6.00	52.14	9.04	80.03	13.37	132.17	18.90
2/3	12	15.97	5.58	23.23	2.92	16.17	5.06	12.92	4.31	47.14	14.72	68.29	10.52	115.43	18.62

ECOG Rating Group	N	Trial Outcome Index 7.30 P=0.002		NFLSI-15* F(2,47) = 4.46 P=0.017		NFLSI-DRS F(2,47) = 5.56 P=0.007		NFLSI-TSE F(2,47) = 0.12 P=0.886		NFLSI-F/WB F(2,47) = 1.88 P=0.163	
		M	SD	M	SD	M	SD	M	SD	M	SD
0	9	102.63	17.73	46.33	8.75	34.22	6.23	9.22	2.39	9.11	2.03
1	29	90.47	15.04	40.70	7.54	29.54	5.69	8.79	2.48	7.72	2.93
2/3	12	76.03	17.11	36.40	6.55	25.46	6.44	8.67	3.28	6.92	1.88