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# Impact of Respiratory Symptoms and Pulmonary Function on Quality of Life of Long-term Survivors of Non-Small Cell Lung Cancer\*

Linda Sarna, RN, DNSc; Lorraine Evangelista, RN, PhD; Donald Tashkin, MD, FCCP; Geraldine Padilla, PhD; Carmack Holmes, MD; Mary Lynn Brecht, PhD; and Fred Grannis, MD, FCCP

*Purpose:* To describe respiratory symptoms and pulmonary function among long-term survivors of non-small cell lung cancer (NSCLC), and their relationship to quality of life (QOL).

Methods: Cross-sectional survey of disease-free, 5-year minimum survivors of NSCLC (n = 142; 54% women; average age, 71 years); the majority (74%) had received a lobectomy. Analysis included frequency of self-reported respiratory symptoms (cough, phlegm, wheezing, breathlessness) as measured by the American Thoracic Society questionnaire, pulmonary function findings from hand-held spirometry, and QOL (Short Form-36).

Results: Two thirds of survivors reported at least one respiratory symptom (mean, 1.3; SD, 1.2): 25% cough, 28% phlegm, 31% wheezing, and 39% dyspnea. Twenty-one percent reported that they spent most of the day in bed in the past 12 months because of respiratory symptoms. Average FEV<sub>1</sub> percentage predicted was 68% (SD, 23); 21% had < 50% predicted FEV<sub>1</sub>. Based on spirometry results, 36% had a moderate/severe obstructive and/or restrictive ventilatory disorder. Survivors exposed to second-hand smoke (28%) were more than three times as likely to report respiratory symptoms. Respiratory symptom burden contributed to diminished QOL in several domains.

Conclusions: The majority of these survivors experienced respiratory symptoms, and more than one third reported dyspnea, including one of five patients with seriously diminished pulmonary function. Symptom burden, rather than ventilatory impairment, contributed to diminished QOL. Further study is needed to determine the patterns and effective management of posttreatment respiratory symptoms on survivors of lung cancer. (CHEST 2004; 125:439-445)

**Key words:** cancer survivors; chronic lung disease; lung neoplasms; pulmonary function; quality of life; respiratory symptoms; tobacco, smoking

**Abbreviations:** ATS = American Thoracic Society; df = degrees of freedom; FEF<sub>25-75%</sub> = maximum expiratory flow rate; NSCLC = non-small cell lung cancer; QOL = quality of life; SF-36 = Short Form-36

The long-term consequences of the curative treatment for non-small cell lung cancer (NSCLC) on pulmonary status, the frequency of respiratory symptoms, and the impact of these pulmonary consequences on the quality of life (QOL) of such survivors have not been previously reported. Respiratory distress, even among the 14% of patients with

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NSCLC who are disease-free survivors,<sup>1</sup> may negatively affect QOL. Dyspnea and other respiratory symptoms have been reported to negatively impact QOL in those with COPD and other chronic lung conditions,<sup>2–8</sup> but little information is available about the impact on people with cancer.<sup>9</sup> One study<sup>10</sup> suggests that patients with NSCLC may actually have better QOL than those with severe COPD.

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Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (e-mail: permissions@chestnet.org).

Correspondence to: Linda Sarna, RN, DNSc, School of Nursing, University of California, Los Angeles, 700 Tiverton Ave, Box 9569182, Factor 4-262, Los Angeles, CA 90095-6918; e-mail: lsarna@sonnet.ucla.edu The perception of respiratory symptoms among long-term survivors of lung cancer may be affected by a myriad of variables. Aging, tobacco use, and comorbid conditions, in particular, may influence respiratory symptoms and level of pulmonary function. 11–12 Approximately 50% of patients with lung cancer have already stopped smoking at the time of diagnosis, 13 but tobacco-related effects on pulmonary function and respiratory symptoms may continue. Gender differences in respiratory symptoms of lung cancer also have been reported. 14–15

The degree of lung resection (pneumonectomy, lobectomy, sleeve resection, segmental wedge resection) has been associated with varying degrees of pulmonary and functional status compromise. <sup>13,16–20</sup> However, pulmonary function assessment alone has been a poor predictor of patients' perceptions of physical disruptions in day-to-day activities. <sup>21–22</sup>

Because of the lack of data describing lung cancer survivors, the primary purpose of this study was descriptive in nature. The specific aims of this report are to describe, in long-term survivors of NSCLC, the following: (1) the frequency, severity, and clustering of respiratory symptoms (cough, phlegm, wheeze, and dyspnea) and characteristics of respiratory illnesses within the past year; (2) pulmonary function abnormalities (as measured by spirometry) and their relationship to symptoms; (3) the relationship of health status and disease/treatment variables to presence of respiratory symptoms; and (4) the relationship of respiratory symptoms and lung function findings to QOL. We hypothesized that impaired pulmonary function and the presence of respiratory symptoms would be associated with diminished QOL. We also anticipated that current smoking, older age, greater extent of surgical resection, and gender would differentially affect respiratory symptoms and pulmonary function.

#### MATERIALS AND METHODS

This cross-sectional survey assessed respiratory status (symptoms and pulmonary function) and QOL of 142 disease-free survivors of NSCLC recruited by mail from local tumor registry and thoracic oncology private practices in the southern California area. This study was approved by the Institutional Review Board of the University of California, Los Angeles. Exclusion criteria included diagnosis with small cell disease or other types of lung cancer (eg, mesothelioma, lung metastasis, carcinoid), and cognitive impairment. The vast majority (98%) of the lung cancer survivors who responded participated in the study. Previous reports from this study have described methods and QOL using a cancer-specific instrument<sup>23</sup> and health perceptions and behaviors of survivors.<sup>24</sup>

## Respiratory Symptoms

The modified version of the Division of Lung Disease/American Thoracic Society (ATS) questionnaire $^{25-27}$  was used to assess

the presence of cough ("Do you usually have a cough?"), phlegm ("Do you usually bring up phlegm from your chest?"), wheezing ("Does your chest ever sound wheezy or whistling?"), and dyspnea ("Do you have to walk slower than other people your age on the level ground because of breathlessness?"). The frequency of multiple respiratory symptoms was tabulated. Details of respiratory illnesses experienced within the past 12 months were recorded, including the frequency of chest illnesses that required bed rest, and the use of prescribed and over-the-counter medications for lung problems.

#### Pulmonary Function

Measurement of lung function was performed using an automated flow-sensing spirometer (Spirovit; Schiller America; Tustin, CA) with determination of FEV<sub>1</sub>, maximum expiratory flow rate (FEF  $_{25-75\%}$  ), and FVC, and calculations of FEV  $_{1}$  /FVC ratio. This easily transportable spirometer has been shown by the manufacturer to fulfill all ATS criteria for spirometry equipment performance characteristics.<sup>28-31</sup> Spirometry was performed at least in triplicate without bronchodilators using standardized procedures conforming to all ATS recommendations for adequacy of spirometry performance.<sup>28-31</sup> If at all possible, at least three and up to a maximum of eight forced expiratory maneuvers were performed in an effort to obtain at least three satisfactory and two reproducible spirometric curves.31 The highest reproducible values for FVC and FEV1 were recorded for use in analysis, regardless of the spirometric curve from which the measurement was derived. The FEV<sub>1</sub>/FVC ratio was calculated from the highest values of FEV1 and FVC. Values for spirometric indexes were recorded both as absolute volumes and flow rates in liters and liters per second, respectively, and as percentage of published predicted values.<sup>30</sup> Personnel performing spirometry were trained, supervised and monitored by one of the coinvestigators (D. Tashkin, Director of the UCLA Medical Center Pulmonary Function Laboratory). In addition, spirometric records (including flow-volume and volume-time curves and calculated results from all trials) were reviewed by Dr. Tashkin for quality assessment. Specific contraindications for pulmonary function testing included recent (within 3 weeks) respiratory infection, recent (within 3 months) chest or abdominal surgery, myocardial infarction or congestive heart failure, recent (within 1 month) cataract surgery, or other recent surgery or serious medical conditions. Recent (within 6 to 12 h) use of bronchodilator medication (inhaled or oral) was noted.

Spirometry was interpreted as normal or as indicating the presence of a mild, moderate, or severe obstructive and/or restrictive ventilatory abnormality according to criteria described by the ATS.31 Spirometry was considered normal if both the FVC and the FEV<sub>1</sub>/FVC ratio were in the normal range according to the predicted values of Crapo et al.30 An obstructive abnormality was interpreted when the FEV<sub>1</sub>/FVC ratio was below the normal range. In the latter case, the obstruction was considered to be mild, moderate, or severe if the  $FEV_1$  was < 100% and > 70% of predicted, < 70% and  $\ge 50\%$  of predicted, or < 50% of predicted, respectively. Since measurements of total lung capacity were not performed, a restrictive ventilatory defect was considered to be present if the FVC was reduced in the absence of a reduction in the FEV<sub>1</sub>/FVC ratio. In this case, the restriction was interpreted as mild, moderate, or severe if the FVC was below the lower limit of normal but  $\geq 70\%$  of predicted, < 70%predicted and  $\geq 50\%$  predicted, or < 50% of predicted, respectively. When both FVC and the FEV<sub>1</sub>/FVC ratio were reduced, it was often not possible to distinguish with certainty between a true restrictive process (independent of the associated obstructive abnormality) vs a reduction in FVC due to air-trapping secondary to obstruction. In some cases in which the FVC

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appeared disproportionately reduced in relation to the degree of reduction in the  ${\rm FEV_1/FVC}$  ratio, a restrictive defect was considered in combination with obstruction.

#### QOL

The multidimensional Short Form-36 (SF-36) was used as a generic measure of QOL to allow us to compare our findings to population norms.  $^{32-33}$  This 36-item self-report evaluates eight concepts (physical functioning, bodily pain, role limitations due to physical health, role limitations due to emotional problems, emotional well being, social functioning, vitality/fatigue, and general health perceptions). The time frame for all items is within the last 4 weeks. Higher scores indicate better QOL. The SF-36 has well-established reliability and has been reported to be sensitive to changes after thoracic surgery for NSCLC19 and for severity of COPD and chronic lung diseases.  $^{2.5-7}$  Cronbach  $\alpha$  coefficients of the subscales for this study were acceptable (ranging from 0.76 to 0.92).

#### Disease, Treatment, Demographic, and Health Status Information

Information about disease and treatment (type of NSCLC, stage of disease, type of surgery, time since diagnosis) was determined using the medical record. Demographic variables included age, gender, race/ethnicity, marital status, and education level. Self-reported health status assessment (comorbidity) and smoking status were assessed by questions on the Lung Health Study assessment.<sup>25</sup> Chart review was used to verify and supplement data. All survivors were weighed, and body mass index at the time of interview was calculated.

Current tobacco use, tobacco use history, and exposure to second-hand smoke within the past week were assessed through standard questions in the ATS questionnaire. Biochemical validation of smoking status was performed with a urine sample and cotinine dipstick that allows for immediate results.<sup>34</sup>

#### Data Analysis

Statistical analysis was carried out using SAS Version 6.12 (SAS Institute; Cary, NC) and SPSS Version 11.0 (SPSS; Chicago, IL). Descriptive statistics were used to profile the frequency of cough, phlegm, wheezing, dyspnea, concurrent respiratory symptoms (eg, cough and phlegm), and details of past respiratory illnesses, including use of medications for respiratory symptoms. We computed a total respiratory symptom score (possible range, 0 to 4) by adding the affirmative answers for the presence of cough, phlegm, wheeze, and dyspnea.

The frequency of pulmonary function abnormality according to the spirometry measurement was noted, including the combination of ventilatory abnormalities (*ie*, obstructive and restrictive impairment). After reviewing frequency distributions, we created two categories for comparison (normal/mild and moderate/severe). Subjects with mixed impairment were placed in the category with the greatest disruption (*ie*, those with mild obstructive and moderate restrictive abnormalities were placed in the "moderate" category).

We used likelihood ratio  $\chi^2$  and t tests (two-tailed) to test for associations of demographic, health status, disease/treatment, and severity of ventilatory abnormalities to the presence/ absence of respiratory symptoms. Statistically significant variables were entered in blocks: (1) gender; (2) number of comorbid conditions, current smoking, pack-years, exposure to second-hand smoke, use of bronchodilators; and (3) severity of ventilatory impairment and were then entered into multivariate logistic

regressions to investigate the contribution of these variables to the presence of respiratory symptoms, in general, and the presence or absence of each specific symptom (cough, wheeze, phlegm, and dyspnea).

Variables significant at an  $\alpha < 0.05$  in the univariate analysis were included in the step-wise multiple regression and were used to explore respiratory predictors for each of the eight dimensions of QOL. Variables were entered in blocks: (1) demographic (marital status), (2) health status (number of comorbidities, number of symptoms and use of bronchodilators), and (3) each of the symptoms (cough, wheeze, phlegm, dyspnea). Default entry (0.05) and removal (0.0) criteria were used. Significance was set at an  $\alpha < 0.05$  for all analyses.

#### RESULTS

#### Sample

One hundred forty-two 5-year minimum NSCLC survivors participated in this study. The majority of survivors (51%) received diagnoses within the previous 10 years (range, 5 to 22 years), had adenocarcinoma (59%), and received a lobectomy (74%). Twelve percent had received a pneumonectomy, and 11% had received a segmental or wedge resection. Twelve survivors (9%) had a second primary or recurrent lung cancer > 5 years prior to the interview. Sixty-six percent were stage I at diagnosis.

The average age of the participant was 71 years (80% were  $\geq$  65 years old); 51% had received diagnoses > 10 years prior to the interview. Fifty-four percent were women, and 52% were married or living with a significant other. The majority were white (83%) and had more than a high school education (72%).

According to self-report, 9% were current smokers, 76% were former smokers, and 16% were never-smokers. With verification of urine cotinine, an additional 7 subjects could be classified as current smokers, for a total of 17 current smokers (13%). From available data of 79 survivors, 60% reported > 40-pack-year history of smoking (mean, 46 packyears). More than one fourth (28%) reported exposure to second-hand smoke at least once a week; 17% described  $\geq 3$  days of exposure. Participants had an average of 1.4 comorbid conditions (SD, 1.4; range, 0 to 7), with the most common conditions being heart disease (29%) and self-reported emphysema (19%). Twenty-two patients (16%) had a history of other malignancies (breast cancer, n = 4; prostate cancer, n = 3; lymphoma, n = 2; endometrial cancer, n = 2; colon cancer, n = 2; head and neck cancer, n = 4; and others, n = 5).

## Respiratory Symptoms

The frequency and severity of respiratory symptoms are displayed in Table 1. Over two thirds of

Table 1—Frequency and Severity of Respiratory Symptoms (n = 142)

Respiratory Symptoms	No. (%)
Cough	35 (24.7)
> 4 d/wk	29 (20.4)
Morning	28 (19.7)
Day and night	33 (23.2)
> 3 mo	32 (22.5)
Phlegm	40 (28.2)
> 4 d/wk	32 (22.5)
Morning	39 (27.5)
Day and night	33 (23.2)
> 3 mo	32 (22.5)
Cough and phlegm > 3 wk in the past year	28 (19.7)
Wheezing	57 (40.1)
Wheezing with a cold	57 (40.1)
Wheezing apart from colds	43 (30.3)
Wheezing most days and nights	16 (11.3)
Short of breath in past year due to wheezing	21 (14.8)
If yes, > 2 episodes of shortness of breath	20 (95.2)
Shortness of breath	90 (63.4)
Short of breath with hurry	90 (63.4)
Walk slower than people your age because of	55 (38.7)
breathlessness	
Stop for breath when walking	45 (31.7)
Stop for breath every 100 yards	33 (23.2)
So breathless that can't leave house, or breathless on dressing/undressing	15 (10.6)

survivors (66%) had at least one respiratory symptom (mean, 1.3; SD, 1.2; range, 0 to 4). Dyspnea (39%) was the most common symptom, followed by wheezing (31%), phlegm (28%), and cough (25%). Thirtyfour percent had no symptoms; 26%, one symptom; 26%, two symptoms; 10%, three symptoms; and 5%, four symptoms. Clustering of symptoms was common. The survivors reporting dyspnea, the most common symptom, also frequently reported cough (51%, n = 18) and phlegm (48%, n = 19). Wheezing, the second most common symptom, was commonly accompanied by phlegm (55%) and cough (63%). A post hoc analysis of the disease/treatment, health status, demographic, and symptom (cough, wheeze, phlegm) correlates of the small sample with severe respiratory distress ("can't leave house or dress because of breathlessness") revealed that those in severe distress were significantly more likely to report unstable angina ( $\chi^2 = 7.92$ , degrees of freedom [df] = 1, p = 0.005), to experience wheeze  $(\chi^2 = 8.87, df = 1, p = 0.003)$ , and less likely to be employed ( $\chi^2 = 6.61$ , df = 1, p = 0.01).

Respiratory illness varied. Fifty patients (35%) reported getting a chest cold within the past year, 19 patients (13%) reported bronchitis, and 6 patients (4%) reported pneumonia. Twenty-one percent (n = 30) reported spending most of the day in bed in the past 12 months because of respiratory symptoms.

Table 2—Spirometry Results (n = 140)

Lung Function Value	Mean (SD)	Range	No. (%)
FVC observed value	2.6 (0.9)	0.92-7.05	
FVC % predicted	81.5 (26.6)	12.0-216.9	
FEV <sub>1</sub> observed value	1.6(0.6)	0.5 - 3.1	
FEV <sub>1</sub> % predicted	68.1 (23.0)	20.5-128.3	
$\geq 70\%$			67 (47.9)
< 70%			73 (52.1)
< 50%			31 (22.1)
FEF <sub>25-75%</sub> observed value	3.3(0.6)	2.1 - 4.6	
FEF <sub>25-75%</sub> % predicted	39.9 (25.0)	6.2 - 131.7	
FEV <sub>1</sub> /FVC observed	68.9 (13.2)	19.0-89.9	
$\mathrm{FEV}_{1}/\mathrm{FVC}$ predicted value	80.0 (2.0)	75.1 - 84.6	

The use of medications for respiratory symptoms was low: 28 patients (20%) used a prescribed inhaled bronchodilator; 14 patients (10%) used nasal corticosteroids; 4 patients (3%) used theophylline; and 4 patients (3%) reported use of nonprescribed bronchodilators.

## Pulmonary Function

The results of the spirometry assessment of pulmonary function are displayed in Table 2. Two patients (1%) were unable to complete the spirometry testing; thus, the pulmonary function results are reported for the remaining 140 patients. According to characterizations of ventilatory abnormalities as the result of spirometry assessment (Table 3), the majority of survivors had relatively minor ventilatory impairment with classifications of normal spirometry (23%) or mild (24%) airflow abnormalities; however, 50 patients (36%) had moderate or severe restrictive or obstructive ventilatory abnormalities alone or in combination. In  $\chi^2$  analysis, respiratory symptoms were significantly more common in the presence vs absence of moderate/severe pulmonary function abnormalities: cough (32% vs 16%, p = 0.03), phlegm (39% vs 17%, p = 0.003), wheeze (57% vs 30%,p = 0.003), and dyspnea (60% vs 29%, p = 0.001).

Table 3—Single and Combined Ventilatory Abnormalities  $(n = 140)^*$ 

Type of	Obstruction				Total
Abnormality	None	Mild	Moderate	Severe	Obstructive
None	32 (22.9)	26 (18.6)	19 (13.6)	2 (1.4)	47 (33.6)
Restriction					
Mild	7(5.0)	0(0)	9 (6.4)	3(2.1)	12 (8.6)
Moderate	8 (5.7)	2(1.4)	6(4.3)	11(7.9)	19 (13.6)
Severe	3 (2.1)	0 (0)	5 (3.6)	7 (5.0)	12 (8.6)
Total restricted	18 (12.9)	2 (1.4)	20 (14.3)	21 (15.0)	

<sup>\*</sup>Data are presented as No. (%).

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## Predictors of Symptoms

Results of the step-wise multivariate regression on presence of respiratory symptoms are displayed in Table 4. The presence of symptoms was more than three times as common if survivors were exposed to second-hand smoke. The presence of cough and wheeze was more likely if bronchodilators were used. Phlegm was less likely to be reported by women. The likelihood of phlegm, wheeze, and cough increased in the presence of moderate-to-severe pulmonary function abnormalities. Phlegm was three times more likely to be reported by current smokers as by nonsmokers. Reports of dyspnea were more likely with a greater number of comorbid diseases.

## Respiratory Symptoms and QOL

The QOL outcomes are displayed in Table 5. Table 6 displays the stepwise regression results on QOL. The F values reported are for the entire model for each subscale as each variable is added. All of the dimensions of QOL, except mental health, were affected to some degree by the presence, number, and type of respiratory symptoms. Dyspnea provides an important contribution to the explanation of several of the subscales (physical functioning, role limits-physical, and social functioning). Other respiratory symptoms provide only modest improvement in the models for the bodily pain and general health subscales. The severity of ventilatory impairment is significant in only one subscale (social functioning). Symptom burden (total number of respiratory symp-

Table 4—Significant Predictors of Presence of Respiratory Symptoms\*

Predictors	Odds Ratio	95% Confidence Interval	p Value	
Cough				
Bronchodilator use	2.88	1.09 - 7.64	0.03	
Phlegm				
Sex	0.42	0.18 - 0.96	0.04	
Current smoking	3.40	1.04-11.1	0.04	
Ventilatory abnormality	2.50	1.03-6.06	0.04	
Wheeze				
Bronchodilator use	4.69	1.61-13.6	< 0.01	
Ventilatory abnormality	2.51	1.14-5.53	0.03	
Dyspnea				
No. of comorbidities	1.38	1.03-1.85	0.03	
Ventilatory abnormality	3.46	1.03 - 1.85	< 0.01	
Presence of any symptoms				
Exposure to second- hand smoke	3.54	1.01-12.3	< 0.05	

<sup>\*</sup>Variables entered include sex, No. of comorbid conditions, use of bronchodilators, exposure to second-hand smoke, and presence of moderate/severe ventilatory abnormality (df = 1).

Table 5—QOL Outcomes of Lung Cancer Survivors

Rand SF-36 Subscales	Total Sample (n = 142) Mean (SD)		
Physical function	57.7 (28.3)		
Role limits-physical	60.9 (43.6)		
Role limits-emotional	77.9 (36.4)		
Bodily pain	74.5 (25.2)		
Social function	77.9 (36.4)		
Vitality/fatigue	55.5 (23.0)		
Health perceptions	60.4 (24.6)		
Mental health	73.9 (19.7)		

toms) is statistically significant in four of the subscales (physical functioning, general health, vitality, and role-limits physical), but provides a very minor contribution to the overall model.

#### DISCUSSION

Surveillance of symptoms is a recommended component of follow-up care of patients treated for lung cancer with curative intent.<sup>35</sup> Although respiratory symptoms may signal recurrence or second lung primaries, there is little information about the pattern and extent of the expected symptom burden

Table 6—Predictors of QOL Dimensions of SF-36 (n = 142)

Variable	Adjusted $\mathbb{R}^2$	F*	p Value
Physical functioning			
Marital status	0.05	6.78	0.011
No. of comorbidities	0.17	11.60	< 0.001
Total No. of respiratory	0.26	12.74	< 0.001
symptoms			
Dyspnea	0.36	15.41	< 0.001
Role limits-physical			
Marital status	0.08	10.32	0.002
No. of comorbidities	0.19	13.49	< 0.001
Dyspnea	0.25	12.18	< 0.001
Bodily pain			
No. of comorbidities	0.06	8.30	0.005
Phlegm	0.10	6.66	0.002
General health			
No. of comorbidities	0.19	25.39	< 0.001
Total no. of respiratory	0.22	15.16	< 0.001
symptoms			
Cough and phlegm	0.25	11.91	< 0.001
Vitality			
No. of comorbidities	0.07	8.35	0.005
Total respiratory symptoms	0.11	7.11	0.001
Social functioning			
No. of comorbidities	0.12	14.91	< 0.001
Dyspnea	0.16	10.83	< 0.001
Mental health			
No. of comorbidities	0.07	7.19	0.008

<sup>\*</sup>F values for each variable as entered into the model.

after curative treatment. To our knowledge, this study is the first to report the respiratory status and pulmonary function of long-term survivors of NSCLC and their relationships to QOL. The few available reports 16-22,36 of the pulmonary status and QOL of survivors of NSCLC provide information only over a relatively short-term period following surgery. Symptom reports have primarily focused on advanced stage disease, but most support the importance of symptom burden on QOL. 36-39

Two thirds of the survivors reported at least one respiratory symptom, with dyspnea and wheezing being the most common complaints; combinations of symptoms such as cough and phlegm also were common. Eleven percent of survivors described themselves as so breathless they could not leave the house. The comorbid condition of unstable angina was significantly linked to risk for this level of symptom severity, whereas prior pneumonectomy was not. Further study is needed to evaluate the contribution of comorbid conditions to symptoms and QOL among all cancer survivors, especially those who might be at additional risk due to late effects of tobacco use.

According to the results of spirometry, the majority had values of  $FEV_1 < 70\%$  predicted, indicating significant ventilatory impairment. One of three patients had moderate/severe obstructive and/or restrictive impairment. Severity of impairment was an important predictor of the symptoms of phlegm, wheeze, and dyspnea. Current smokers were more likely to report phlegm than nonsmokers, but smoking was not a factor in the report of other symptoms. It may be that those smokers who were more symptomatic were more likely to have quit smoking. Men also were more likely to report phlegm but were not significantly different from women in their self-report of other symptoms. Survivors exposed to second-hand smoke were three times more likely to report respiratory symptoms. Passive exposure to tobacco smoke is rarely evaluated in assessment of symptoms. Along with assistance with smoking cessation, this may be an important intervention target for those at risk.

The presence of respiratory symptoms contributed to perceptions relating to all dimensions of QOL, except mental health. Not unexpectedly, the presence of dyspnea was associated with reduced levels of physical functioning, limitations in physical role activities, and decreased social functioning. Respiratory symptom burden (number of symptoms) contributed to models of physical functioning, general health perceptions, and vitality/fatigue. These results are similar to the finding of Ruffin et al<sup>2</sup> of the importance of symptom burden (multiple respiratory symptoms) in predicting QOL of patients with

chronic lung disease. Phlegm and the combination of cough and phlegm were related to bodily pain and general health, respectively. The objective assessment of pulmonary function (severity of ventilatory impairment) did not significantly contribute to any of the dimensions of QOL.

These findings underscore the importance of subjective perceptions of symptoms, in addition to objective measures of pulmonary function, as has been reported by studies of patients with chronic lung diseases.<sup>2–8</sup> In particular, dyspnea in relationship to physical function is commonly reported in the setting of advanced lung cancer.<sup>38</sup> As reported in other studies,<sup>2–5</sup> QOL ratings did not always correlate with the severity of pulmonary functional impairment or even the severity of symptoms.<sup>39</sup>

Despite the relative frequency of respiratory symptoms, reported use of medications was not common. For example, 36% reported wheezing and 32% reported needing to stop for breath, but only 18% reported use of prescribed bronchodilators.

There are important limitations to consider in interpreting the results of this study. This was a convenience sample, and more severely impaired survivors may have elected not to participate. The disease-free status of the survivors was not verified by a complete medical workup, and recurrence of disease may have been present but undetected at the time of the interview. Because of the cross-sectional nature of this study, we are unable to determine the changes or the time frame for changes in pulmonary status after treatment for lung cancer. The presence of chronic respiratory symptoms and lung function abnormality may be due to a variety of other factors, including the presence of comorbid diseases such as heart disease, in addition to underlying chronic lung disease. Because of the descriptive exploratory nature of the present analysis, no statistical adjustments were made for multiple tests, so that conservative interpretation is warranted.

This study provides the first known description of respiratory symptoms, pulmonary function, and the relationships of these characteristics to QOL in long-term survivors of NSCLC. Continuing assessment and treatment of respiratory distress may be an important dimension in the evaluation and rehabilitation of the lung cancer survivors. The survivor's perception of symptoms provides important information beyond objective pulmonary function testing. Survivors with dyspnea are at risk for diminished physical and social aspects of QOL. Further research is needed to monitor the course of respiratory symptoms after thoracotomy and to evaluate strategies for reducing symptom burden and improving QOL among these survivors.

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