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Effect of cigarette smoking on quality of life in small cell lung cancer patients

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Abstract

Background—Continued cigarette smoking after small cell lung cancer (SCLC) diagnosis has been shown to shorten patients' survival, but little is known about the impact of smoking and cessation on quality of life (QOL) profile (e.g., overall QOL, pain, fatigue, cough, dyspnea, appetite change, and performance status) in SCLC survivors (who survived at least 6 months post initial diagnosis). In this study, we sought to evaluate the relationship between cigarette smoking and QOL profiles in SCLC patients.

Methods—A total of 223 survivors were classified into five groups: never smokers, former smokers (quit more than 1 year prior to diagnosis), recent quitters (quit within 1 year surrounding diagnosis), late quitters (quit after 1 year post diagnosis) and never quitters. One hundred and sixty-eight of these survivors were matched with 334 lung-cancer-free controls on age, gender, and smoking status for comparative analysis. QOL scales were scored from 0 (worse) to 100 (best). Conditional logistic regression, linear mixed-effect models, and Wilcoxon signed rank tests were used.

Results—SCLC survivors consistently showed a significant deficit in QOL profile; e.g., mean overall QOL in patients was 17.5 points worse than the controls ($p < 0.0001$). Among all smokers, former smokers reported the best QOL profile, while late or never quitters reported the worst. The recent quitters showed an improving trend in QOL profile and lower percent of reduced appetite (an average of 43%) compared to the late or never quitters (58%).

Conclusions—Our study confirmed the negative impact of smoking on SCLC survivors' QOL and found that smoking cessation surrounding the time of diagnosis could improve overall QOL and symptoms. The findings of this study provide evidence for oncologists to recommend smoking cessation to their SCLC patients.

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Conflict of interest statement

All authors have no conflict of interest to disclose.

Keywords

Quality of life; Cigarette smoking; Small cell lung cancer; Symptom burden

1. Introduction

Health-related quality of life (QOL) has become a very important outcome for cancer therapy especially when the treatment intent is supportive or palliative or the survival benefits are modest. Therefore, although survival is generally the most important measurement for treatment efficacy, patients and physicians are giving greater consideration to multiple dimensions of QOL including symptom burden. Indeed, QOL at baseline may be as important as stage and performance status in predicting non-small cell lung cancer (NSCLC) survival,¹ but the QOL of small cell lung cancer (SCLC) has not been well documented. SCLC represents approximately 13% of all lung cancer² and is the most aggressive cell type among all subtypes. From the time of diagnosis, the median ranges of survival for limited stage and extensive stage SCLC are 15–20 months and 8–13 months, respectively.^{3,4} Despite that a modest improvement has been achieved in the past two decades in treating SCLC,^{5–7} treatment bears positive and negative effects on patients' QOL. Specifically, side-effects from various therapies could severely deteriorate patients' conditions.

Cigarette smoking is the most predominant risk factor in SCLC prognosis. A personal history of cigarette smoking has been associated with decreased overall survival among patients receiving treatment for both SCLC and non-small cell lung cancer (NSCLC).^{8–11} Our recent study of a series of 284 SCLC patients also showed that compared to continuing smokers (those who never quit smoking), patients who quit at or after diagnosis cut the risk of death by 45%,⁷ but little is known about smoking's effects on patients' QOL in SCLC survivors. The negative effects of cigarette smoking on QOL in general and specific disease populations have been well established, including NSCLC patients.^{12–19} In this study, we sought to determine the relationship between smoking and QOL profile, including overall QOL and selected symptoms, in a relatively large series of SCLC survivors. We hypothesised that cigarette smoking would have a negative effect on the QOL profile of SCLC survivors, and we specifically evaluated the differing effects of the timing of smoking cessation.

2. Methods and materials

2.1. Patients follow-up and clinical data

This study was undertaken within a prospectively followed lung cancer patient cohort at Mayo Clinic in Minnesota starting on January 1, 1997, and was approved by the Mayo Clinic Institutional Review Board. Informed consent was obtained from the subjects and/or proxies. Details of patient enrollment, diagnosis confirmation, follow-up procedures, data collection, and quality assurance have been previously reported.^{20,21} In brief, at enrolment, each patient's medical record was reviewed and the diagnosis was confirmed. SCLC was classified into the two stage system: limited stage SCLC is defined as disease confined to the ipsilateral hemithorax and within a single radiotherapy port and extensive stage SCLC is defined as evident metastatic disease outside the ipsilateral hemithorax.²² To acquire complete follow-up information, all patients were actively followed by a series of questionnaires, including QOL and symptom questions beginning within 6 months post diagnosis and then annually thereafter. Of all patients in this study who answered their first questionnaire within 12 months post diagnosis, 9.4% answered between months 3–6 and 90.6% answered between months 7–12.

Information on current and past use of tobacco products was self-reported and collected each time during follow-up through a structured questionnaire. A never smoker was defined as one who had smoked less than 100 cigarettes in his or her lifetime. Current smokers were individuals who reported tobacco use within the same year of their diagnosis. In order to evaluate the impact of timing on the QOL profile in this study, we categorised survivors according to time of smoking cessation in relation to diagnosis time: early quitters (more than 1 year prior to the date of diagnosis), recent quitters (within 1 year surrounding diagnosis, either prior to or after the date of diagnosis), late quitters (after 1 year post diagnosis) and never quit.

2.2. Health-related quality of life (QOL) assessment

The QOL measure was a built-in component of the lung cancer follow-up questionnaire. The Lung Cancer Symptom Scale (LCSS) was used at the outset, starting in October 1999. In April 2005, the Linear Analogue Self-Assessment (LASA) was implemented and the redundant LCSS items were dropped to minimise patients' burden yet expand QOL measures beyond symptoms. Both are previously validated QOL tools.^{23,24} For the purpose of this study, we focused on the five overlapping items between these two tools: pain, fatigue, cough, dyspnea and overall QOL. Two additional domains included were patient-reported Eastern Cooperative Oncology Group (ECOG) performance status (PS) and appetite change since diagnosis. Appetite was self-rated using a previously validated item.²⁵ For each QOL item, patients were asked to provide their best answer during the past week, and we summarised all above-mentioned measures as 'QOL profile'.

To understand the QOL profile of SCLC patients relative to the normal population, we compared each QOL item in SCLC patients who returned a questionnaire within 1 year post diagnosis to controls using a matched case-control design. Controls were from Mayo Clinic-based computed tomography (CT) scan trials of healthy heavy smokers over 50 years of age as described in previous publications,²⁶ and pulmonary medicine patients who had a chest CT-scan and pulmonary function test; all individuals were free of any lung cancer at the time of the QOL data collection.

2.3. Statistical analyses

The primary goal of this study was to describe the health-related QOL profile in SCLC patients in relationship to smoking status and time of smoking cessation. Original scores of pain, fatigue, cough, dyspnea and global QOL were translated onto a 0–100 point scale for comparability and ease of interpretability,²⁷ with higher scores representing better status. For example, higher overall QOL scores indicate better quality of life; higher pain scores correspond to less pain. PS was re-grouped into three levels: fully active versus light work restricted versus worse. Appetite change was summarised by two levels: increased or same versus reduced.

Patient characteristics were summarised by limited versus extensive stage SCLC, and the differences were compared using a Chi-square test (or Fisher's exact test) for categorical variables and a two sample *t*-test (or Wilcoxon rank sum test) for continuous variables. Descriptive statistics are provided for each QOL item, PS, appetite change, and smoking status at each follow-up time point and these data are also presented graphically. A one-way analysis of variance (ANOVA) was used to test the difference among the five groups (year 1 through year 5) for continuous QOL items, and a Chi-square test was used for PS, appetite change, and smoking status. Changes from within 1 year versus over 2 years post diagnosis were calculated and tested using Wilcoxon signed rank tests. A change in the magnitude of one-half standard deviation (SD) of QOL, which was considered clinically meaningful,²⁷

was examined overall and by smoking status to explore the impact of smoking status on patient QOL.

In the matched case–control analysis, each SCLC case was matched to 1 or 2 controls based on age (within 5 years, age at diagnosis for cases and at the time of QOL data collection for controls), gender, and smoking status (at diagnosis for cases and at time of QOL data collection for controls) using an optimal match algorithm.²⁸ The same questionnaire excluding lung-cancer-specific items was used for controls. Conditional logistic regression was used to model categorical factors accounting for matching and linear mixed-effect models with matched set as random effect for continuous factors. All analyses were performed with SAS software, version 8.2 (SAS Institute, Cary, NC).

3. Results

3.1. SCLC patient cohort

A total of 223 patients with SCLC who were diagnosed between 1998 and 2008 and who have answered a follow-up questionnaire at least once were included in this study. At the time of diagnosis, 85 patients (38%) had extensive disease; the median age was 65 years (range, 37–89 years) and 54% were males; 3% were never smokers, 44% were former smokers, and 53% were current smokers. Forty-one percent of the patients quit smoking more than 1 year before diagnosis; an additional 32% quit before lung cancer treatment and 14% never quit smoking. The median follow-up time for living patients was 3 years with a range of 6 months to 10 years. Table 1 provides more information on patient characteristics and comparisons by disease stage.

3.2. Health-related QOL profile between SCLC patients and comparable controls free of lung cancer

In the analysis comparing baseline QOL to a control group free of lung cancer, 168 SCLC patients who returned a questionnaire within 1 year post diagnosis were successfully matched to 334 controls (166 cases each matched to two controls and two cases each matched to one control). Table 2 summarises characteristics and QOL comparison between the cases and matched controls. Pack-years of cigarette smoking history and smoking cessation were found to be significantly different between the two groups; therefore, these two factors were adjusted in the case–control comparison analysis. SCLC survivors consistently showed a statistically significant worse QOL compared to the matched controls (Table 2). For instance, the mean overall QOL was 63.4 in the SCLC survivors and 80.9 in the controls, a significant 17.5-point difference ($p < 0.0001$).

Table 3 shows the cross-sectional mean QOL profiles of SCLC survivors over a 5-year follow-up period; overall QOL and symptom scales of pain, fatigue, cough, and dyspnea were relatively stable; e.g., mean overall QOL was between 63.0 (year 1, SD 23.2) and 67.6 (year 5, SD 21.1). Pain seemed not to be a major problem in survivors, with mean scores ranging from 74.4 (SD 25.4) to 79.5 (SD 23.6). SCLC survivors scored consistently more severe on fatigue (mean scores between 48.5 and 52.7) and dyspnea (mean scores between 57.1 and 59.0). Coughing was moderate, with a lowest mean score of 66.4 at year 4. For the ECOG PS, most patients were fully active or capable of light work, with roughly one-third unable to work or having worse status (ranging between 25% at year 2 to 33.3% at year 3) except year 5 (10.7%). Higher percentages of reduced appetite were observed earlier in the follow-up period with 52% at year 1 and 32.1% at year 5.

3.3. Impact of smoking status and smoking cessation on health-related QOL among SCLC survivors

We analysed QOL profiles across the 5 years of follow-up for each symptom as well as overall QOL according to smoking status and the time of quitting smoking; data of year 4 and beyond were combined due to fewer survivors. Fig. 1 illustrates the key findings based on mean overall QOL (upper panel) and reduced appetite (lower panel) over follow-up years. Among the three subgroups of smokers, early quitters reported the best overall QOL, while recent quitters reported the best symptoms scores, e.g., the lowest percentage of reduced appetite. Late or never quitters reported the worst QOL, e.g., from year 2 to year 4 they had the lowest overall QOL (56–62) and the highest percentage of reduced appetite (55–70%). Overall, the recent quitters showed an improving trend of QOL profile and lower percentage of reduced appetite at first assessment (43%) compared to the late or never quitters (57%).

In order to assess the longitudinal changes of reported QOL over time in the same patients, we evaluated data from 45 patients who answered questionnaires within 1 year after diagnosis and beyond 2 years after diagnosis (Table 4). Among these 45 patients, 3 never smoked cigarettes (removed from further analysis due to small number), 19 were recent quitters (subgroup 1), and the remaining 23 were former smokers and late or never quitters (subgroup 2). Fig. 2 depicts the percentage of patients with clinically significant improvement or decline of their reported QOL profile over the two time intervals; specifically, for example, fatigue (middle panel) improved in 32% and declined in 32% in subgroup 1 although there was no statistically significant change in fatigue status between within-1-year and over-2-years; in subgroup 2, fatigue significantly declined in 61% and improved in only 22% of patients.

4. Discussion

Although it has been shown that SCLC patients who continue to smoke have poorer chances of survival than those who do not,^{7,9,11} the relationship between smoking cessation (timing and duration) and QOL in SCLC patients has not been adequately studied. In this matched analysis, we demonstrated that SCLC patients consistently showed a statistically significant worse QOL. Over the 5-year follow-up period, cross-sectional overall QOL and symptom scales of pain, fatigue, cough, and dyspnea were relatively stable. Smoking status had a significant impact on overall QOL and each individual symptom scale in SCLC patients, with the exception of year 1 after diagnosis. Never smokers reported in general the best QOL profile, while late or never quitters reported the worst. More importantly, recent quitters showed a trend of improvement in overall QOL and better scores on all symptoms in this study than never quitters.

The negative impact of smoking on QOL in both the general patient population and in specific subgroups has been reported in a number of studies.^{12–14,18} Other studies reporting similar findings were based on patients with head and neck cancer, asthma, HIV infection, or other conditions, where current smoking was negatively associated with multiple QOL scales including physical functioning, general health, vitality or energy, cognitive and social functioning, and role-emotional health.^{15–17,19}

The first study of QOL of lung cancer survivors, composed of 142 NSCLC patients, found that smoking status was not predictive of QOL.²⁹ However, this study included only prevalent long-term survivors and had a relatively small number of NSCLC patients; the authors suggested that further study is needed to address this question. In our previous study of the effect of cigarette smoking on QOL in a large series of lung cancer patients (92% with NSCLC),³⁰ we found that continued cigarette smoking is related to a deficit in QOL

measures. One caveat of this study was that SCLC was not separately studied due to small sample size, therefore the results were virtually driven by NSCLC patients.

In our current study, when comparing the baseline QOL of SCLC patients with the matched non-cancer controls, we unsurprisingly found that SCLC patients consistently showed a significantly worse overall QOL. This was the case with four of the five individual symptoms as well as PS and appetite. An unexpected finding was that the controls reported worse pain than the cases, which is believed to reflect one of the important characteristics of subjects in the control groups, i.e., they were heavy smokers participating in lung cancer screening trials or non-cancer patients with lung diseases.

Although the cross-sectional mean QOL and symptom scores were relatively stable during the course of the 5-year follow-up, significant differences were detected when the patient population was divided into five groups by smoking history. In line with the findings from the literature, we found that, except for year 1, never and former smokers with SCLC reported the best QOL in general, while late or never quitters reported the worst. To our best knowledge, our study is the first to confirm the negative impact of smoking on SCLC survivors' QOL by the timing and duration of smoking cessation.

Several limitations should be recognised when interpreting the results in this study. First, only seven selected QOL and symptom scales were analysed: five overlapping items from LCSS and LASA plus patient-reported ECOG PS and appetite change. Further investigation is needed to explore other dimensions of QOL in SCLC patients. Second, we did not observe a meaningful difference in age and smoking cessation status at the time of diagnosis by stage of SCLC; however, this may reflect the cases enrolled in our institution, e.g., 62% being limited stage. Third, although QOL data were collected yearly after SCLC diagnosis, the number of patients who consistently responded to the survey each year is small, particularly among patients with extensive stage SCLC. Due to insufficient longitudinal data, the ability to reach a definitive conclusion about QOL trend during the course of the disease is limited. Finally, QOL data in the control group may not represent the general population; instead, they only represent 'high-risk' people who took CT-scans to rule out lung cancer or other lung conditions. Coupled with the pre-existing medical conditions of the controls, the strength of QOL comparisons between SCLC patients and 'healthy' controls was compromised.

In conclusion, our study confirmed the negative impact of smoking on SCLC survivors' QOL and found that smoking cessation surrounding the time of diagnosis could improve overall QOL and symptoms. This information provides evidence for oncologists to recommend smoking cessation to their SCLC patients.

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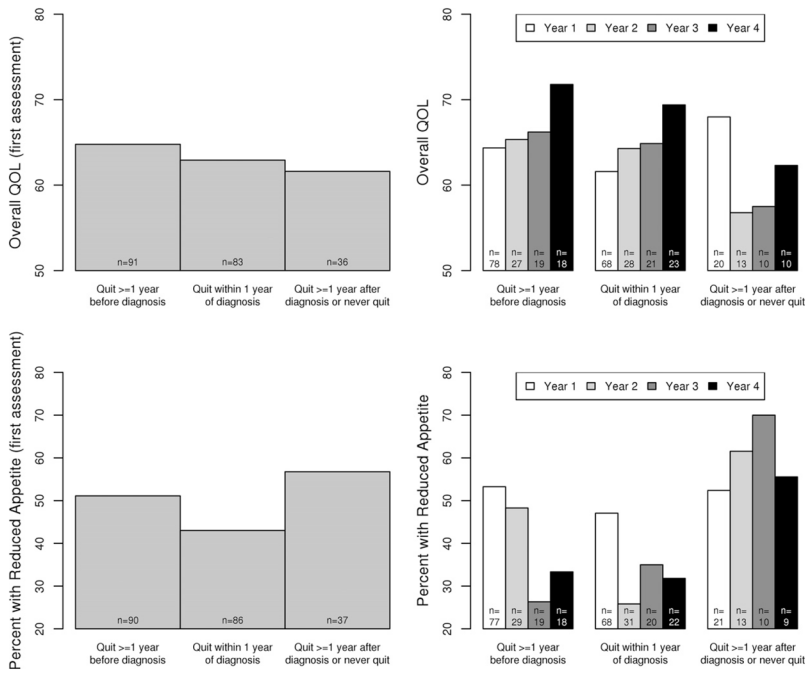


Fig. 1. Time trend of overall quality of life (QOL) and reduced appetite among groups of patients by smoking cessation. Upper panel: mean overall QOL; lower panel: reduced appetite. (footnote: data of year 4 and beyond were combined.)

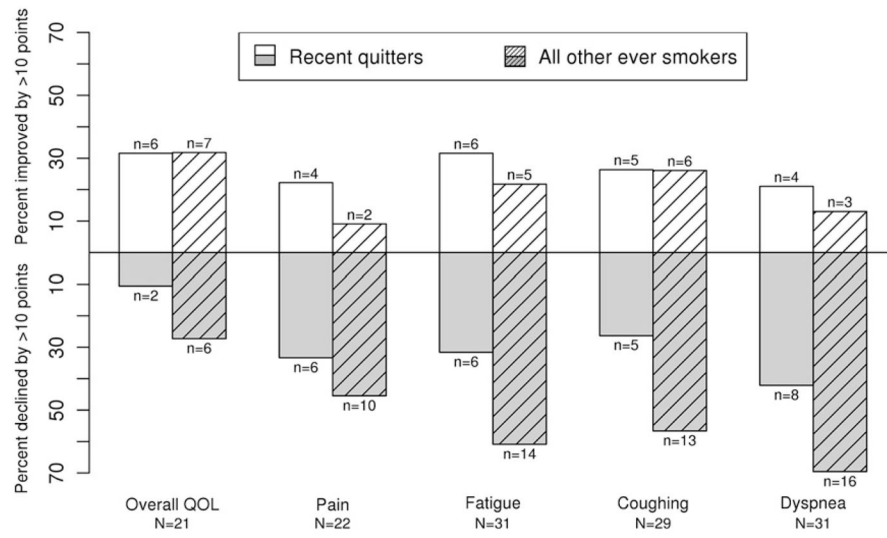


Fig. 2. Difference in overall QOL and selected symptoms for patients with assessments within 1 year and over 2 years post diagnosis of small cell lung cancer (SCLC).

Table 1

Characteristics of 223 small cell lung cancer patients by stage.

	Limited stage (n = 138)	Extensive stage (n = 85)	Total (n = 223)	p-Value*
<i>Age at diagnosis</i>				
				0.5797 ^a
<i>N</i>	138	85	223	
Mean (standard deviation (SD))	64.4 (9.8)	65.2 (10.0)	64.7 (9.8)	
Median	65.0	66.0	65.0	
Range	(38.0–87.0)	(37.0–89.0)	(37.0–89.0)	
<i>Sex</i>				
				0.0223 ^b
Female	72 (52.2%)	31 (36.5%)	103 (46.2%)	
Male	66 (47.8%)	54 (63.5%)	120 (53.8%)	
<i>Race</i>				
				0.5388 ^c
Non-Caucasian**	8 (5.8%)	3 (3.5%)	11 (4.9%)	
Caucasian	130 (94.2%)	82 (96.5%)	212 (95.1%)	
<i>Smoking status at diagnosis</i>				
				0.8631 ^c
Never smoker	4 (2.9%)	2 (2.4%)	6 (2.7%)	
Former smoker	59 (42.8%)	40 (47.1%)	99 (44.4%)	
Current smoker	75 (54.3%)	43 (50.6%)	118 (52.9%)	
<i>Pack-years of smokers</i>				
				0.1089 ^c
Missing	0 (–)	1 (–)	1	
0–40	34 (24.6%)	27 (32.1%)	61 (27.5%)	
41–60	54 (39.1%)	20 (23.8%)	74 (33.3%)	
>60	46 (33.3%)	35 (41.7%)	81 (36.5%)	
<i>Smoking cessation</i>				
				0.4507 ^c
Early quitters (Quit 1 year before diagnosis)	53 (38.4%)	39 (45.9%)	92 (41.3%)	
Recent quitters (Quit within 1-year of diagnosis)	56 (40.6%)	32 (37.7%)	88 (39.5%)	
Late quitters (Quit 1 year after diagnosis)	5 (3.6%)	0 (0.0%)	5 (2.2%)	
Never quitters	20 (14.5%)	12 (14.1%)	32 (14.3%)	

* p-Value for between stage comparison;

^a Wilcoxon rank sum;^b Chi-square;^c Fisher's exact.

** Non-Caucasian includes Hispanic and Alaskan/Native American.

Table 2

Characteristics of matched cases and controls.^a

	Cases (n = 168)	Controls (n = 334)	p-Value
<i>Race</i>			0.6360 ^e
Missing	0 (–)	1 (–)	
Non-Caucasian	6 (3.6%)	15 (4.5%)	
Caucasian	162 (96.4%)	318 (95.5%)	
<i>Pack-years among smokers</i>			0.0004 ^e
Missing	0 (–)	6 (–)	
0–40	44 (26.2%)	137 (41.8%)	
41–60	59 (35.1%)	97 (29.6%)	
>60	59 (35.1%)	82 (25%)	
<i>Smoking cessation^b</i>			<0.0001 ^e
Early quitters (Quit 1 year before diagnosis/questionnaire)	85 (50.6%)	177 (53%)	
Recent quitters (Quit <1 year before diagnosis/questionnaire)	64 (38.1%)	20 (6%)	
Never quitters	19 (11.3%)	137 (41%)	
Overall quality of life (QOL) ^c , N	163	334	<0.0001 ^f
Mean (SD)	63.4 (23.2)	80.9 (15.9)	<0.0001 ^g
Range	(0.0–100.0)	(20.0–100.0)	
Pain, N	163	333	<0.0001 ^f
Mean (SD)	79.6 (23.0)	69.2 (25.3)	<0.0001 ^g
Range	(0.0–100.0)	(10.0–100.0)	
Fatigue, N	168	334	<0.0001 ^f
Mean (SD)	48.5 (23.0)	63.8 (25.2)	<0.0001 ^g
Range	(0.0–100.0)	(0.0–100.0)	
Coughing, N	167	334	0.0059 ^f
Mean (SD)	68.6 (23.5)	74.7 (22.9)	0.0017 ^g
Range	(5.0–100.0)	(0.0–100.0)	
Dyspnea, N	168	333	0.0003 ^f
Mean (SD)	58.5 (26.9)	67.8 (26.2)	0.0022 ^g
Range	(0.0–100.0)	(0.0–100.0)	
<i>Eastern Cooperative Oncology Group (ECOG) performance status^c</i>			<0.0001 ^e
Missing	2 (–)	0 (–)	
Fully active	21 (12.7%)	185 (55.6%)	
Light work	100 (60.2%)	136 (40.8%)	
Unable to work and worse	45 (27.1%)	12 (3.6%)	
<i>Appetite change^{c,d}</i>			<0.0001 ^e
Missing	5 (–)	0 (–)	
Increased/same	78 (47.9%)	260 (77.8%)	
Reduced	85 (52.1%)	74 (22.2%)	

^a Matching variables: age, sex, and smoking status.

^b Time relative to diagnosis date for cases and date of questionnaire for controls.

^c Used the first questionnaire returned within the 1-year time frame for cases.

^d Appetite change since diagnosis for cases and appetite change since 1 year ago for controls.

^e Conditional logistic regression.

^f Mixed-effect model with matched set as a random effect.

^g Mixed-effect model with matched set as a random effect, includes pack-years and smoking cessation as covariates.

Table 3

Follow-up questionnaire variables (QOL, performance status (PS), appetite change, and smoking status).*

	1 year (N = 177)	2 years (N = 78)	3 years (N = 54)	4 years (N = 48)	5+ years (N = 29)	p-Value**
<i>Overall QOL</i>						0.0382
<i>N</i>	173	72	52	47	29	
Mean (SD)	63.0 (23.2)	63.8 (25.4)	64.8 (24.5)	67.4 (26.8)	67.6 (21.1)	
Range	(0.0–100.0)	(0.0–100.0)	(0.0–100.0)	(0.0–100.0)	(24.0–94.0)	
<i>Pain</i>						0.1220
<i>N</i>	172	71	51	46	29	
Mean (SD)	79.1 (23.6)	76.0 (25.4)	79.5 (23.6)	77.9 (23.9)	74.4 (25.4)	
Range	(0.0–100.0)	(6.0–100.0)	(3.0–100.0)	(3.0–100.0)	(14.0–100.0)	
<i>Fatigue</i>						0.6735
<i>N</i>	177	74	53	47	29	
Mean (SD)	48.5 (22.9)	50.8 (27.1)	52.7 (21.4)	49.7 (21.3)	49.1 (24.8)	
Range	(0.0–100.0)	(0.0–100.0)	(2.0–94.0)	(0.0–98.0)	(4.0–92.0)	
<i>Coughing</i>						0.4874
<i>N</i>	176	75	53	43	29	
Mean (SD)	69.4 (23.3)	67.6 (24.2)	72.1 (24.8)	66.4 (24.1)	71.2 (24.7)	
Range	(5.0–100.0)	(3.0–100.0)	(3.0–100.0)	(8.0–100.0)	(3.0–100.0)	
<i>Dyspnea</i>						0.6662
<i>N</i>	177	74	53	46	29	
Mean (SD)	59.0 (26.9)	58.1 (27.7)	57.6 (27.7)	57.9 (28.7)	57.1 (29.2)	
Range	(0.0–100.0)	(0.0–100.0)	(5.0–100.0)	(0.0–100.0)	(6.0–96.5)	
<i>ECOG PS</i>						0.0154
Missing	2 (-)	2 (-)	0 (-)	0 (-)	1 (-)	
Fully active	22 (12.6%)	17 (22.4%)	7 (13%)	8 (16.7%)	11 (39.3%)	
Light work	107 (61.1%)	40 (52.6%)	29 (53.7%)	26 (54.2%)	14 (50%)	
Unable to work and worse	46 (26.3%)	19 (25%)	18 (33.3%)	14 (29.2%)	3 (10.7%)	
<i>Appetite change since diagnosis</i>						0.0048
Missing	4 (-)	1 (-)	3 (-)	3 (-)	1 (-)	
Increased/same	83 (48%)	46 (59.7%)	31 (60.8%)	28 (62.2%)	19 (67.9%)	

	1 year (N = 177)	2 years (N = 78)	3 years (N = 54)	4 years (N = 48)	5+ years (N = 29)	p-Value**
Reduced	90 (52%)	31 (40.3%)	20 (39.2%)	17 (37.8%)	9 (32.1%)	
<i>Smoking status</i>						0.2508
Never smokers	6 (3.4%)	3 (3.8%)	2 (3.7%)	2 (4.2%)	1 (3.4%)	
Former smokers	140 (79.1%)	60 (76.9%)	41 (75.9%)	35 (72.9%)	24 (82.8%)	
Current smokers	31 (17.5%)	15 (19.2%)	11 (20.4%)	11 (22.9%)	4 (13.8%)	

* The table reports multiple responses per person, but all p-values were calculated after subsetting to each case's first response.

** The analysis of variance (ANOVA) method was used to test the difference among the five groups (1 year through 5 year) for continuous factors, and Chi-square test for categorical factors.

Table 4

Difference in overall QOL and selected symptoms at within 1 year versus over 2 years post diagnosis of small cell lung cancer.

QOL	Mean (SD) <1 year	Mean (SD) 2 years	Signed rank test p-value	Percent (%) declined by 10 points	Percent (%) improved by 10 points
<i>All patients (n = 45*) with <1 and 2 years QOL assessment</i>					
Overall QOL	65.8 (19.9)	69.0 (22.5)	0.14	18.18	31.82
Pain	81.7 (20.4)	73.5 (22.5)	0.02	37.21	13.95
Fatigue	54.5 (19.4)	47.5 (23.7)	0.06	44.44	24.44
Coughing	69.6 (20.1)	66.2 (20.1)	0.21	40.00	26.67
Dyspnea	68.9 (23.3)	56.0 (26.0)	<0.01	55.56	17.78
<i>Sub-group 1** (n = 19); recent quitters</i>					
Overall QOL	61.9 (17.6)	69.7 (20.8)	0.07	10.53	31.58
Pain	76.3 (22.6)	75.4 (20.9)	0.49	33.33	22.22
Fatigue	50.2 (18.6)	48.4 (26.8)	0.84	31.58	31.58
Coughing	70.1 (18.6)	70.3 (18.5)	0.85	26.32	26.32
Dyspnea	68.0 (21.3)	58.6 (29.8)	0.17	42.11	21.05
<i>Sub-group 2*** (n = 23); early quitters, late or never quitters</i>					
Overall QOL	67.5 (22.0)	66.2 (24.6)	0.90	27.27	31.82
Pain	85.0 (18.9)	69.2 (23.8)	0.01	45.45	9.09
Fatigue	56.2 (19.4)	44.7 (21.1)	0.03	60.87	21.74
Coughing	68.4 (21.5)	61.1 (20.7)	0.07	56.52	26.09
Dyspnea	68.2 (25.5)	51.5 (22.2)	0.01	69.57	13.04

* Three (3) of the 45 patients were never smokers and removed from the subgroup analysis regarding quitting smoking time.

** Subgroup 1: recent quitters were patients who quit smoking within 1 year of diagnosis.

*** Subgroup 2: former smokers and late or never quitters were patients who were smokers, not in sub-group 1.