Published in final edited form as:

J Pain. 2009 March ; 10(3): 323–328. doi:10.1016/j.jpain.2008.10.006.

Persistent Smoking after a Diagnosis of Lung Cancer is Associated with Higher Reported Pain Levels

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Abstract

The purpose of this study is to evaluate the impact of smoking status after a diagnosis of lung cancer on reported pain levels. We conducted a telephone survey of patients with lung cancer identified from four participating sites between September 2004 and July 2006. Patients were asked to rate their usual pain level over the past week on a 0-10 rating scale on which 0 was 'no pain' and 10 'pain as bad as you can imagine'. We operationally defined persistent smokers as patients who reported continuing to smoke after their lung cancer diagnosis. A logistic regression analyses was used to test the hypothesis that persistent smokers report higher usual pain levels than non-smokers. Overall, 893 patients completed the survey. The majority (76%) was found to have advanced cancer (Stages IIIb and IV). The mean age was 63 (SD=10). Seventeen percent of the patients studied were categorized as persistent smokers. The mean pain score for the study sample was 3.1 (sd=2.7) and 41% reported moderate (4-6) or severe pain (7-10). A greater proportion of persistent smokers reported moderate or severe pain than non-smokers or former smokers ($p<.001$). Logistic regression analysis revealed that, smoking status was associated with the usual pain even after adjusting for age, perceived health status and other lung cancer symptoms such as dyspnea, fatigue and trouble eating. In conclusion, patients who continue to smoke after a diagnosis of lung cancer report higher levels of usual pain than non-smokers or former smokers. More research is needed to understand the mechanisms that relate nicotine intake to pain and disease progression in late-stage lung cancer.

Perspective—This article examines the relationship between pain and persistent smoking in patients with lung cancer. Although more research is needed to understand the mechanisms that relate nicotine intake to pain and disease progression, physicians can promote smoking cessation in patients with lung cancer to improve health and quality of life.

Introduction

The association between cigarette smoking and lung cancer is well accepted. Despite the morbidity and mortality of lung cancer and its strong relationship with smoking, a significant proportion of patients continue to smoke even after they have been diagnosed with lung cancer.¹⁴ Several studies have examined the effects of continued smoking after lung cancer diagnosis

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and found that it impairs healing, reduces the efficacy of cancer treatments, diminishes overall quality of life, increases risk for recurrence and a second primary cancer, and decreases survival.^{3,10,11,12,27, 28}

Among patients diagnosed with lung cancer, approximately 40-50% report smoking at the time of diagnosis.^{4,7} Research suggests that about half of these smokers quit smoking once the diagnosis of lung cancer is made.^{4,12} A recent study of patients with lung cancer referred to a pulmonary clinic (predominantly early-stage disease) found that patients who quit smoking after their diagnosis had better performance status compared to those who continued to smoke.⁴

Few studies have examined the clinical significance of persistent smoking in late-stage patients with lung cancer. Although it is reasonable to presume that a diagnosis of lung cancer would be sufficient motivation for anyone to quit smoking, a patient with late-stage lung cancer may feel that there is nothing to be gained from quitting.

Despite advances in treatment options and improvements in survival, symptom control and quality of life remain important outcomes in patients with late-stage lung cancer. Among the most commonly reported symptoms are pain, dyspnea, cough, and fatigue.¹² Pain can have multiple physiologic sources (e.g. bony metastases, tumor compressing a nerve or side effects of surgery or radiation) and is frequently associated with increased psychological distress.²³

In the general population, the association between smoking and pain is not clear. While animal studies indicate that nicotine has analgesic properties,¹ human studies show mixed results depending upon pain modality and pain tolerance.¹³ In a recent probability sample of participants undergoing a health examination, a dose response relationship was found between heavy smoking and pain intensity.¹⁸ Current heavy smokers reported more pain locations and higher pain intensity compared to never smokers. These findings suggest that smoking may contribute to pain in an otherwise healthy population.

The objective of this study was to evaluate the relationship of smoking status after a diagnosis of lung cancer (predominantly late-stage disease) to ratings of usual pain. We hypothesize that patients who reported they continued to smoke after diagnosis would report higher levels of pain.

Methods/Design

Study population

Patients with lung cancer were recruited from the Duke University Medical Center's Thoracic Oncology Program (Duke), the Durham Veteran's Administrative Medical Thoracic Oncology Clinic (Durham VA), the University of North Carolina Medical Center's Multidisciplinary Thoracic Oncology Program (UNC), and the Division and Program of Thoracic Oncology, H. Lee Moffitt Cancer Center and Research Institute (Moffitt) from September 2004 – July 2006. The study received IRB approval from each of the four participating sites.

Patients were eligible to participate if they were 18 years of age and older, diagnosed with lung cancer, intended to continue care at one of the study sites, and had at least one family member who smoked. Two methods of identifying patients were used based on IRB site requirements. At UNC and Moffitt, patients were identified in the clinic by study clinicians and coordinators and provided written consent to be contacted by a trained interviewer to complete the baseline survey over the telephone. Patients were provided a brochure with information about the study that they could pass on to family members. At Duke and the Durham VA, a trained interviewer contacted patients using a list provided by the study clinicians to obtain verbal consent. Patients

who were smokers were sent a self-help smoking cessation guide. Patients who reported that they were planning to quit in the next 30 days were also sent a 6-week supply of nicotine patches, if indicated. The research assistant also asked the patient to identify family members and loved ones who smoke for two trials focusing on smoking cessation and genetic risk, obtained contact information on those people, and obtained permission to contact them. Patients with lung cancer completed a telephone-based questionnaire which included smoking history, perceived health status, symptoms, and demographics which are the source of data for this manuscript.

Measures

Non-smokers were defined as those patients who had smoked fewer than 100 cigarettes (five packs) in their lifetime. Former smokers had smoked 100 cigarettes or more in their lifetime but reported quitting prior to the telephone survey. Persistent smokers were those patients who reported they were currently smoking at the time of survey. For the purpose of understanding the effects of persistent smoking, data from non-smokers were combined with that from former smokers.

Other measures included gender, age and race. The education level of the patients was divided into patients having less than a high school education, those having a high school education or equivalent and those having, trade, college or graduate education. Using medical record review, patients' stage of disease was determined using the World Health Organization (WHO) classification of lung cancer stages Ia-IV. Patients with stages Ia-IIIa lung cancer were classified as early-stage and stages IIIB and IV were classified as late-stage based on estimates of survival.⁵

All patients were asked to rate their usual pain using a numeric scale on which 0 was 'no pain' and 10 'pain as bad as you can imagine.' Based on the cut points for pain severity described Palos et al., responses on the pain scale were further divided into two categories: 1) none to mild (0-3) and 2) moderate to severe (4-10).²²

Patients also were asked to provide ratings of the extent they were experiencing other lung cancer symptoms, i.e. fatigue, difficulty keeping down their food, and shortness of breath in the past week.¹⁵ The response categories for these questions were: 1="not at all", 2="a little", 3="quite a bit", and 4="very much." All patients also rated their own health status in the past week as 'Excellent,' 'Good,' 'Fair,' or 'Poor'.

Data Analysis

Frequencies and means (SD) were used to describe the sample and Pearson coefficient was used for correlations. T-test and chi-square test were used to test associations between pain and demographics, stage of cancer (Ia-IV), time since diagnosis, perceived health, smoking status, and lung cancer symptoms. Logistic regression was used to test the hypothesis that smokers would report higher levels of perceived pain controlling for age, race, gender, education, site, time since diagnoses, perceived health status, and other lung cancer symptoms. We used the criteria of $p = 0.15$ for an independent variable to remain in the model using backward selection. Statistical Analysis Software (SAS) V9 was used for these analyses.

Results

Patient Characteristics

The survey was completed by 893 patients with lung cancer. Table 1 outlines the patient characteristics of this sample. As can be seen, the majority (76%) of patients had late-stage disease (stages IIIB and IV). The mean age was 63 years (SD=10) with a range of 33 to 88

years. The study population was predominantly white (89%), half male (50%), with 57% having some form of post secondary education including trade school, 31% having a high school diploma or equivalent and 12% of patients having less than a high school diploma.

Overall, 17 % of patients with lung cancer were defined as ‘persistent smokers’. Of the remaining patients, 10% percent were non-smokers and 73% were former smokers. On average, the patients reported that they began smoking at age 17. Of the persistent smokers (n=151), the mean pack/years was 27 (SD=25) and 86% reported that they planned on quitting in the next 30 days implying that they were in the preparation stage of readiness.²⁴ Of those patients planning to quit smoking, 97% requested cessation material, which included nicotine replacement therapy.

Correlations between Potential Covariates and Pain

As can be seen in Table 2, there were significant correlations between patients’ ratings of pain and other lung cancer symptoms. Patients who reported higher levels of pain were more likely to report higher levels of fatigue, difficulty keeping down their food, and shortness of breath. Pain ratings, however, were not associated with stage of lung cancer.

Factors associated with moderate to severe pain levels

Table 3 presents information on pain severity status (none to mild vs. moderate to severe) as a function of smoking status and covariates. Persistent smokers had the highest proportion of patients who reported ‘moderate to severe’ pain. Younger age, lower perceived health status and higher levels of other cancer symptoms (fatigue, shortness of breath and difficulty eating) were also significantly associated with a higher likelihood of reporting moderate to severe pain ($p<0.001$).

Table 4 displays the results of the logistic regression model adjusted for age, perceived health status and lung cancer symptoms. Smoking status was associated with the patients’ rating of usual pain. Patients who were persistent smokers reported higher levels of pain (Odds Ratio (OR) =1.6 (95% Confidence Intervals (CI) 1.1-2.4)) compared to non-smokers or former smokers.

Discussion

To our knowledge, this is the first study to report that patients who continue to smoke after lung cancer diagnosis experience significantly higher levels of pain than former and never smokers. Because this was a cross-sectional study, it is impossible to determine whether persistent smoking leads to increased pain or whether increased pain leads patients to smoke. Laboratory studies have shown that nicotine can reduce pain and it is possible that smokers in this study increased their smoking to help them cope with higher levels of pain. Given that pain is often a major concern of both patients with lung cancer and their caregivers,²⁰ further research is needed to examine the causal nature of the relationship of smoking and pain in this population.

This study found that patients who continued to smoke after diagnosis not only reported higher levels of pain, but also higher levels of other lung cancer symptoms (fatigue, shortness of breath and difficulty eating). These findings regarding the relationship of smoking to cancer symptoms are consistent with those of Garces,¹² that found that patients with lung cancer who continued to smoke after their diagnosis had worse scores on all measures of the Lung Cancer Symptom Scale (LCSS) when compared with never smokers.¹²

One of the most interesting findings of this study was that patients who reported high levels of pain also reported high levels of fatigue. This finding agrees with those reported by Hwang

and colleagues in their analysis of independent predictors of fatigue in cancer patients.¹⁶ In a multivariate model they examined a number of possible predictors of fatigue (pain, dyspnea, lack of appetite, feeling drowsy, depressed mood, and feeling irritable) and found that the only independent predictors of fatigue were pain and depressed mood.¹⁶ Visovsky (2003) also reported a significant link between pain and fatigue.²⁹ The reasons for this relationship are not clear. It is possible that pain may interfere with rest, thereby contributing to fatigue. It is also possible that pharmaceutical interventions for pain management such as narcotics increase fatigue. Interestingly, John et al. found that smokers in the general population experience more pain and use more analgesics.¹⁹

It is of clinical interest that persistent smoking and higher levels of pain were both related to increased dyspnea. Dyspnea or shortness of breath, a common symptom of cancer patients, can result from compromise of the respiratory, musculoskeletal, cardiovascular, hematological or psychological systems. In addition, because the cause of dyspnea can not always be reversed, symptom control must be achieved. Dudgeon and colleagues investigated the incidence of dyspnea in advanced cancer patients and found that current smokers were more likely to be short of breath than non-smokers.⁹

In our study, younger patients reported higher pain levels than older patients even after adjusting for perceived health status and symptoms. A study by Kuo et al reported similar findings with younger patients defined as those younger than 40 years old (n=127) and older patients as older than 80 years old (n=184).²¹ The study was developed to investigate lung cancer survival differences in young and old patients in Taiwan. In an analysis of presenting symptoms, younger patients (<40 years of age) reported higher levels of chest pain than older patients (>80 years).²¹ These results were again demonstrated in a review of several studies dealing with pain in cancer patients.²³ Three of the studies in this review found lower reports of pain in older patients.²³ No reliable relationship was observed between pain and histological subtype or stage of disease. One possible explanation is that older patients generally have more co-morbid illnesses and are more accustomed to pain giving them a higher pain tolerance overall. Another explanation is that older patients may be more likely to receive hospice services and receive more supportive care for their pain.²³

Patients with high school or college education were less likely to report pain compared with patients with less than a high school education. This observation is supported by a study examining the role of race and education in coping with pain.⁶ The investigators found that a higher level of education was associated with less pain. One explanation offered was that those with higher education would have more success coping with pain.⁶ Another factor is that those with higher education have a corresponding higher socioeconomic status and therefore better access to medical care that can address their pain.

Our study has several limitations. The patient survey was designed to describe overall health and smoking status of patients with lung cancer and to identify family members who smoke. Patients with very high pain may have been unable to participate in the telephone survey.² A longitudinal study that includes a more frequent and detailed assessment of smoking behaviors and pain indices (e.g. measures of the quality, duration, location of pain) could provide more a more definitive analysis of the relationship of smoking to pain. An intriguing possibility that could be investigated using an intensive longitudinal study design is that smoking leads to immediate positive effects (e.g. relief in pain) but long-term negative effects (e.g. increased mean levels of pain).

Additionally, the survey did not explore possible causes of persistent smoking. Patients were not asked, what if any benefit they felt they were experiencing by continuing to smoke, such as reduction in stress or anxiety. In a small study (n=43) of patients with lung cancer undergoing

surgical resection for a primary tumor, 44% of patients had started smoking again by six months after surgery.³⁰ The main factors associated with relapse were depression and lack of social support.³⁰ This could mean that future interventions for smoking cessation in patients with lung cancer will have to include a mental health component whether based in counseling or pharmaceuticals.

Patients with lung cancer represent an especially at-risk group for whom smoking cessation is paramount for survival. However, they are a special population and the stresses of diagnosis and treatment as well as the guilt associated with their smoking habit could be barriers to quitting. A few smoking cessation interventions have been tested in patients with lung cancer with mixed results.^{7,25,26} If, as our findings suggest, patients who continue to smoke after lung cancer diagnosis indeed experience higher levels of pain, then it may be useful to include training in pain coping skills as one component of smoking cessation protocols. Such a comprehensive protocol may enhance the effects obtained with more traditional smoking cessation interventions.

Gritz and colleagues conducted a comprehensive literature review which highlighted the significance of a cancer diagnosis as a teachable moment that can be used to encourage smoking cessation¹⁴. The study found an increase in motivation and interest in cessation after cancer diagnosis. In addition, many patients relapsed 1-6 months after treatment.¹⁴ This implies that there is not only a window of opportunity for beginning cessation but also a period when the patient, their clinician and their support system must be vigilant in order to avoid relapse.

Perhaps one of the most daunting consequences of continued smoking is the increased risk of a second primary tumor. The patient must once again face the challenges associated with treatment and survival. In a ten-year longitudinal study of more than 1000 patients with head and neck malignancies, Do and colleagues found that more than 20% of current smokers developed a second primary tumor compared with 8.8% of non-smokers.⁸ A review by Johnson found that the overall risk of developing a second malignancy was 1%-2% per year in non-small cell lung cancer and 6% per year in small cell lung cancer. This risk was increased in patients that continued to smoke.¹⁷

Promoting smoking cessation is a challenge. For those surgeons and oncologists caring for patients with lung cancer, it is all the more challenging because the patients may not think there are any benefits to quitting. Those benefits are improved effectiveness of treatment, increased survival, improved quality of life and perhaps decreased pain. Interventions that emphasize benefits could be a strong motivator for cessation.

Acknowledgments

This work was supported by National Cancer Institute grant 5UO1-CA-92622.

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Table 1

Characteristics of patients with lung cancer (N=893)

Patient Characteristics	N (%)
Age, mean (SD)	63 (10)
Race:	
White	796 (89)
African-American	82 (9)
Other	12 (2)
Gender:	
Male	442 (50)
Female	451 (50)
Education:	
Less than High School	103 (12)
High School	273 (31)
Post High School	517 (57)
Recruitment site:	
Duke	351 (39)
UNC	109 (12)
Durham VA	65 (7)
USF/Moffitt	368 (42)
Stage of disease:	
Ia/b	123 (14)
IIa/b	48 (5)
IIIa	47 (5)
IIIb	196 (22)
IV	479 (54)
Time since diagnosis:	
Less than 90 days	252 (28)
More than 90 days	641 (72)
Perceived health status	
Poor	144 (16)
Fair	316 (35)
Good	348 (39)
Excellent	85 (10)
Lung cancer symptoms:	
Fatigue	

Patient Characteristics	N (%)
Not at all	237 (27)
A little	329 (37)
Quite a bit	236 (26)
Very Much	91 (10)
Shortness of breath	
Not at all	501 (56)
A little	308 (34)
Quite a bit	69 (8)
Very Much	15 (2)
Trouble eating	
Not at all	712 (80)
A little	125 (14)
Quite a bit	41 (4)
Very Much	15 (2)
Smoking status:	
Never	91 (10)
Former smoker	651 (73)
Persistent smoking	151 (17)
Reported pain level:	
None (0)	234 (26)
Mild (1-3)	296 (33)
Moderate (4-6)	237 (27)
Severe (7-10)	126 (14)

Table 2
Correlation – Analysis of health measures in patients with lung cancer

	N	Mean	SD	1	2	3	4	5	6	7	8
1. Pain	893	3.1	2.7	1.00	.45 [†]	.33 [†]	.25 [†]	.38 [†]	.16 [†]	-.02	-.17 [†]
2. Health status	893	2.6	0.9		1.00	.34 [†]	.32 [†]	.57 [†]	.13 [†]	.06	-.06
3. Problem breathing	893	1.5	0.7			1.00	.19 [†]	.31 [†]	.09 [±]	-.01	-.05
4. Trouble eating	893	1.3	0.6				1.00	.27 [†]	.07 [*]	.07 [*]	-.14 [†]
5. Fatigue	893	2.2	0.9					1.00	.09 [±]	.06	-.05
6. Persistent smoker	893	0.17	0.4						1.00	-.05	-.20 [†]
7. Stage of LC	893	4.0	1.4							1.00	-.03
8. Age	893	63.0	10.0								1.00

Footnote: Correlations reported are Pearson correlations.

* p ≤ .05
± p ≤ .01
† p ≤ .001

Table 3

Patient characteristics by pain level

Patient characteristic	None to mild pain N=530	Moderate to severe pain N=363	P value
	N (%)	N (%)	
Age, mean [SD]	64 [10]	62 [10]	<0.001
Race:			
White	482 (61)	314 (39)	
Black	44 (54)	38 (46)	
Other	4 (33)	8 (67)	0.09
Gender:			
Male	264 (60)	178 (40)	
Female	266 (59)	185 (41)	0.8
Education:			
Less than High School	47 (46)	56 (54)	
High School	151 (55)	122 (45)	
Post High School	332 (64)	185 (36)	<0.001
Health status:			
Poor	43 (30)	101 (70)	
Fair, Good, Excellent	487 (65)	262 (35)	<0.001
Smoking status:			
Persistent smoker	65 (43)	86 (60)	
Non-smoker	465 (63)	277 (37)	<0.001
Stage of disease:			
Ia/b	73 (59)	50 (41)	
IIa/b	31 (65)	17 (35)	
IIIa	27 (57)	20 (43)	
IIIb	107 (55)	89 (45)	
IV	292 (61)	187 (39)	0.56
Time since diagnosis:			
Less than 90 days	146 (58)	106 (42)	
More than 90 days	384 (60)	257 (40)	0.58
Symptoms:			
Fatigue	345 (53)	307 (47)	<0.001
Shortness of breath	177 (45)	214 (55)	<0.001

Patient characteristic	None to mild pain N=530	Moderate to severe pain N=363	P value
	N (%)	N (%)	
Difficulty eating	68 (38)	113 (62)	<0.001

Footnote: Symptoms (fatigue, shortness of breath and difficulty eating) were dichotomized at the median which was 1 for each symptom: values ranged from 1 (not at all) to 4 (very much). Data presented for those above the median (2-4).

Table 4

Logistic regression analysis with pain level as dependent variable (4-10 compared to 0-3)

Patient characteristic	Odds ratio	95% confidence intervals
Age	0.92	0.85-0.99
Persistent smoking	1.6	1.1-2.4
Poor perceived health	3.0	2.0-4.7
High School vs. Less than High School	0.75	.46-1.2
Post High School vs. Less than High School	0.52	.33-.84
Fatigue	1.9	1.3-2.7
Shortness of breath	2.1	1.5-2.8
Trouble eating	1.8	1.2-2.6

Footnote: OR and 95% CI reported for age is based on each 5 year increase in age.