Risk factors for nicotine dependence in Chinese patients with lung cancer

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Abstract

Objective: Smoking is a poor prognostic factor for lung cancer. Nicotine dependence remains the major cause of failure of smoking cessation. We investigated the risk factors for nicotine dependence in patients with lung cancer.

Methods: Eligible patients were identified from November 2014 to February 2015. Age, marital status, educational level, annual household income, occupation, histology of lung cancer, tumor stage, smoking status, neuron-specific enolase (NSE) level, drive gene mutations, sleep quality, and patient personality were assessed. Physical nicotine dependence was assessed by the Fagerstrom Test for Nicotine Dependence (FTND).

Results: In total, 202 smokers were included in this study. Univariate analysis showed that marital status and pain were significantly correlated with nicotine dependence. Pearson's correlation analysis showed that age at the initiation of smoking, attempts to quit, NSE level, and sleep quality were significantly correlated with FTND scores.

Conclusions: Pain, more attempts to quit, and poorer sleep quality were significantly associated with nicotine dependence. These risk factors could help to prevent smoking in Chinese patients with lung cancer.

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Introduction

Lung cancer is one of the most common cancers worldwide.[1–3] Smoking is a major risk factor for lung cancer.[4] Smoking cessation could improve patients' quality of life and decrease the recurrence of early-stage non-small cell lung cancer.[5–7] Although cigarette smoking has a negative impact on the prognosis, many patients with lung cancer have nicotine dependence.[8,9] About 50% of patients with lung cancer reportedly persist in cigarette smoking after the diagnosis.[8]

Nicotine dependence is a primary issue in patients with a smoking history and lung cancer,[10] but its risk factors remain undetermined. Investigation of the risk factors for nicotine dependence in patients with lung cancer and a smoking history is therefore important. In this study, we investigated the risk factors for nicotine dependence in patients with lung cancer.

Methods

Patients and data collection

We retrospectively identified patients with lung cancer who were hospitalized in our center from November 2014 to February 2015. Patients with impaired cognitive function, secondary tumors, or heart, cerebral, or renal failure were excluded from this study. All patients were histologically diagnosed with lung cancer. Tumor stages were categorized according to the 7th edition of the International Association for the Study of Lung Cancer TNM staging system. All patients provided written informed consent, and the study was approved by the ethics committee of the Shanghai Pulmonary Hospital (No. k16-121).

The following baseline information was collected: age, marital status, education level, annual household income, occupation, lung cancer pathology, lung cancer stage, and smoking status. Smoking status included the number of smoking years, age at initiation of smoking, attempts to quit, and length of the smoking cessation phase. Attempts to quit were the cumulative number of times that patients quit smoking for >24 hours at a time from the time the patient started smoking to the time before the survey. When smokers had not smoked for >1 year, smoking cessation was considered successful. The length of the smoking cessation phase was the duration of the last cessation.

The laboratory examination included measurement of the neuron-specific enolase (NSE) level at the time of diagnosis and 3 months after the diagnosis. The drive mutation status included the epidermal growth factor receptor and anaplastic lymphoma kinase gene statuses.

Questionnaires

The Fagerstrom Test for Nicotine Dependence (FTND) was used to assess physical nicotine dependence.[11,12] Sleep disturbance was assessed by the Pittsburgh Sleep Quality Index (PSQI) (Chinese Version).[13–15] In the PSQI, the sum of the scores of seven components yields one global score ranging from 0 to 21. Higher scores represent poorer sleep

quality. The Junior Eysenck Personality Questionnaire (JEPQ) was used to detect the correlation between nicotine dependence and personality.[16]

Statistical analysis

Categorical variables were compared using the chi-square test or Fisher's exact test as appropriate. Continuous variables were analyzed by analysis of variance and Tukey's multiple comparison test. A Cox proportional hazards model was used for univariate and multivariate survival analyses to calculate the hazard ratios and corresponding 95% confidence intervals (CIs). All statistical analyses were performed using IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, NY, USA). All statistical values were two-sided, and statistical significance was defined as $p < 0.05$.

Results

Patient characteristics

In total, 505 hospitalized patients with lung cancer were identified. Of these patients, 278 were never-smokers and 25 had benign pulmonary disease. Finally, 202 smokers with lung cancer were enrolled in the present study. None of the patients used nicotine-dependence substitutes. Among the 202 patients, 197 (97.5%) were men and 5 (2.5%) were women. Their median age was 63 years. Twelve patients (5.9%) had stage I disease, 27 (13.4%) had stage II disease, 59 (29.2%) had stage III disease, and 104 (51.5%) had stage IV disease. A total of 140 (69.3%) had non-small cell lung cancer and 62 (30.7%) had small cell lung cancer (Table 1). A total of 186 (92.1%) patients had tried to quit smoking when they were diagnosed with lung cancer, and 54 patients smoked again within 6 months after the diagnosis.

Analysis of risk factors for nicotine dependence

We found that marital status ($p = 0.036$) and pain ($p = 0.017$) were significantly correlated with nicotine dependence in the univariate analysis (Table 1). We then conducted Pearson's correlation analysis to investigate the association between the FTND score and the smoking status, NSE level, PSQI score, and JEPQ score. The results showed that the age at initiation of smoking ($p = 0.040$), attempts to quit ($p = 0.003$), NSE level at the time of diagnosis ($p = 0.019$) and 3 months after diagnosis ($p = 0.031$), and sleep quality ($p = 0.045$) were significantly associated with the FTND score (Table 2). In the multivariate analysis, pain ($p = 0.001$; 95% CI, 0.158–0.338), attempts to quit ($p = 0.034$; 95% CI, 0.182–3.563), and sleep quality ($p = 0.010$; 95% CI, 0.151–0.832) were significantly correlated with the FTND score (Table 3).

Discussion

Smoking cessation can improve patients' quality of life and long-term survival.[5] Nicotine dependence is an invitation to propose adequate treatment. In the current study, we found that the risk factors for nicotine dependence were pain, cigarette consumption, attempts to quit, and sleep quality. These factors were significantly correlated with the FTND score, which could predict the probability of nicotine dependence.

Nicotine dependence is common in smokers with lung cancer. A previous study showed that nearly half of patients with lung cancer who had quit smoking would fail at quitting.[17] Interestingly, the male/female ratio was very high in this study. In China, it is not widely acceptable for women to smoke. However, a small number of women still had a smoking

Table 1. Correlations with nicotine dependence by univariate analysis.

Variable	n (%)	FTND (mean ± SD)	F/t	p
Sex			0.879[2]	0.414
Female	5 (2.5)	4.40 ± 0.89		
Male	197 (97.5)	4.79 ± 2.57		
Age, years			0.621[2]	0.535
≤70	174 (86.1)	4.82 ± 2.56		
>70	28 (13.9)	4.50 ± 2.43		
Household income, yuan			0.975[1]	0.406
<1000	26 (12.9)	4.69 ± 2.84		
1000–2999	87 (43.1)	4.48 ± 2.53		
3000–4999	57 (28.2)	4.96 ± 2.52		
≥5000	32 (15.8)	5.31 ± 2.35		
Employed			0.494[2]	0.622
No	116 (57.4)	4.85 ± 2.50		
Yes	86 (42.6)	4.67 ± 2.61		
Education level			1.102[1]	0.349
Elementary school	51 (25.2)	5.20 ± 2.33		
Junior high school	98 (48.5)	4.58 ± 2.62		
Senior high school	37 (18.3)	5.00 ± 2.53		
College and higher	16 (8.0)	4.13 ± 2.68		
Marital status			2.110[2]	0.036
Married/partnered	192 (95.0)	4.70 ± 2.57		
Single	10 (5.0)	6.63 ± 0.92		
Pain score			−2.409[2]	0.017
0	144 (71.3)	4.51 ± 2.42		
≥1	58 (28.7)	5.45 ± 2.74		
Lung cancer type			−1.132[2]	0.259
Non-small cell lung cancer	140 (69.3)	4.64 ± 2.44		
Small cell lung cancer	62 (30.7)	5.08 ± 2.78		
Cancer stage			0.746[1]	0.526
I	12 (5.9)	4.55 ± 2.58		
II	27 (13.4)	4.23 ± 2.70		
III	59 (29.2)	5.09 ± 2.40		
IV	104 (51.5)	4.67 ± 2.58		
Gene mutation			0.598[1]	0.551
None	178 (88.1)	4.84 ± 2.53		
EGFR	16 (7.9)	4.13 ± 2.73		
ALK	8 (4.0)	4.63 ± 2.56		

[1]F value, [2]t value.
FTND, Fagerstrom Test for Nicotine Dependence; SD, standard deviation; EGFR, epidermal growth factor receptor; ALK, anaplastic lymphoma kinase.

history. Thus, the male/female ratio was relatively high. According to the Shanghai adult tobacco epidemic monitoring data of 2015, the smoking rate of adults aged 15 to 69 years was 23.3%, among which the smoking rate of men was 46.8% and that of women was 2.0%.[18] In our hospital, physicians and nurses perform smoking cessation education for every patient. Previous studies have demonstrated that smoking

Table 2. Correlation between FTND score and smoking status, NSE level, PSQI score, and JEPQ score.

Variable	Mean ± SD	Correlation coefficient	p
Years of smoking	36.16 ± 10.15	0.122	0.086
Age at initiation of smoking, years	20.64 ± 4.30	−0.146	0.040
Number of attempts to quit	1.49 ± 1.10	0.227	0.003
Length of smoking cessation phase, months	17.70 ± 1.93	−0.144	0.052
NSE at time of diagnosis, ng/mL	26.38 ± 25.07	0.166	0.019
NSE 3 months after diagnosis, ng/mL	23.69 ± 21.62	0.164	0.031
Sleep quality	5.92 ± 3.45	0.129	0.045
Psychoticism	51.15 ± 7.30	0.05	0.481
Extraversion	55.24 ± 8.43	−0.11	0.123
Neuroticism	50.82 ± 9.16	0.138	0.052
Lie	51.5 ± 9.41	−0.052	0.464

FTND, Fagerstrom Test for Nicotine Dependence; NSE, neuron-specific enolase; PSQI, Pittsburgh Sleep Quality Index; JEPQ, Junior Eysenck Personality Questionnaire; SD, standard deviation.

Table 3. Multivariate analysis of nicotine dependence in patients with lung cancer.

	Non-standardized coefficient		Standardized coefficient			β Coefficient (95% CI)	
	B	Standard error	Trial version	t	p	Lower limit	Upper limit
Constant	8.373	9.301		0.900	0.391	−12.667	29.413
Marital status	−0.492	1.447	−0.047	−0.340	0.742	−3.764	2.781
Pain	0.248	0.040	1.178	6.264	0.001	0.158	0.338
NSE at time of diagnosis	0.137	0.063	0.475	2.198	0.055	−0.004	0.279
NSE 3 months after diagnosis	0.008	0.036	0.037	0.211	0.838	−0.075	0.090
Age at initiation of smoking	0.000	0.139	0.001	0.003	0.998	−0.314	0.315
Attempts to quit	1.872	0.747	0.608	2.506	0.034	0.182	3.563
Sleep quality	0.492	0.150	0.611	3.270	0.010	0.151	0.832

$R = 0.835$, $R^2 = 0.697$, adjusted $R^2 = 0.621$.

cessation is more likely to be successful under the guidance of nurses.[19,20] In the present study, 29.0% of patients with lung cancer smoked again within 6 months after the initial diagnosis. This rate is lower than that in previous publications.

There are several risk factors for nicotine dependence.[17] In patients with early-stage lung cancer, these risk factors include low household income, exposure to environmental tobacco smoking at home, and depression.[17] In addition, people who work long hours tend to have nicotine dependence.[21] In the present study, patients with pain, more attempts to quit, and poorer sleep quality more readily developed nicotine dependence. One study showed that nicotine dependence was associated with pain in

patients with chronic non-malignant disease.[22] However, another study showed no correlation between chronic pain and cigarette dependence.[23] In the present study, we found a positive correlation between pain and nicotine dependence in patients with lung cancer. Patients who smoke high numbers of cigarettes per day are reportedly at greater risk of developing smoking-related illnesses and have more difficultly quitting.[24] We obtained similar results in the present study. The number of attempts to quit was a protective factor against nicotine dependence, which has not been previously reported. We also found that more attempts to quit was associated with smoking relapse. The positive correlation between nicotine dependence and the PSQI score suggested that poor sleep quality can induce nicotine dependence. Our results are consistent with a previous study of normal young adults.[15] To our knowledge, this study is the first to investigate the correlation between nicotine dependence and sleep quality in patients with lung cancer. We also analyzed the correlation between gene mutations and nicotine dependence. Patients with driver mutations receive targeted therapies, which have fewer adverse effects than chemotherapy. We found no significant association between gene mutations and nicotine dependence.

This study has two main limitations. First, the sample size was relatively small. The findings of this study should be interpreted with caution and validated in larger populations. Second, the patients' survival data were missing. A prospective comparison of nicotine dependence and patient survival in a large-scale study would be informative.

In summary, we found that pain, more attempts to quit, and poorer sleep quality were positively correlated with nicotine dependence in patients with lung cancer. Future research is needed to investigate how to reduce pain and improve quality of sleep so that we can increase the success rate of smoking cessation in patients with lung cancer.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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