

ORIGINAL ARTICLE

Smoking Status and Postoperative Survival in NSCLC: Insights from A Single-center Retrospective Study

Küçük Hücreli Dışı Akciğer Kanserinde Sigara Kullanımı ve Postoperatif Sağkalım: Tek Merkezli Retrospektif Çalışma Bulguları

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How to cite ?

Uysal S., Kumbasar U., Dikmen E., Demircin M., Doğan R., Smoking Status and Postoperative Survival in NSCLC: Insights from A Single-center Retrospective Study, Genel Tıp Derg. 2025;35(4):667-672

ABSTRACT

Aim: The present study aimed to evaluate both the frequency of non-smoking patients and the impact of smoking status on the long-term survival of patients operated for NSCLC in our institutional cohort. Although tobacco smoking is one of the major causes of lung cancer, the correlation between smoking status and the survival of patients is uncertain.

Methods: Medical records of 249 patients who underwent pulmonary resection for NSCLC were retrospectively reviewed. Patients were divided into smokers and never-smokers. Annual frequency, demographic and clinical characteristics, and overall survival were compared between the groups.

Results: The annual frequency of never-smokers between the years 2002 and 2012 was 33.2, 24, 37.5, 25, 34.3, 35.4, 29.4, 22.7, 22.2, 35.7, and 28.5%, respectively. There were no statistically significant differences in terms of the distribution of age ($p=0.993$), the first second (FEV1) measurements ($p=0.476$), the type of resection performed ($p=0.564$), and tumor histology ($p=0.920$) between the groups. The median survival time was similar in both groups (72 vs 76 months, smokers vs. never-smokers (Log-rank test, $p=0.654$). The proportion of never-smokers was approximately 30% in our cohort.

Conclusions: Data obtained from our study show that smoking does not affect the total survival of patients undergoing resection due to NSCLC.

Keywords: Non-small cell lung cancer, survival, tobacco smoking

ÖZ

Amaç: Bu çalışmanın amacı küçük hücreli dışı akciğer kanseri (KHDAK) nedeniyle akciğer rezeksiyonu uygulanan hastalarda sigara kullanmayan hastaların sıklığının ve sigara kullanımının mortalite üzerine olan etkisini araştırmaktır. Sigara kullanımı akciğer kanserinin en önemli nedenlerinden biri iken sigara içimi ile sağkalım arasındaki ilişki belirsizdir.

Gereç ve Yöntemler: KHDAK nedeniyle akciğer rezeksiyonu uygulanan 249 hastanın dosya verileri incelendi. Hastalar sigara içmiş olanlar ve hiç sigara içmemiş olanlar olmak üzere iki gruba ayrıldı ve gruplar sigara içmeyen hastaların yıllık oranı, demografik, klinik özellikler ve uzun dönem sağkalım açısından karşılaştırıldı.

Bulgular: Sigara içmeyen hastaların 2002-2012 yılları arasındaki oranları sırası ile %33.2, 24, 37.5, 25, 34.3, 35.4, 29.4, 22.7, 22.2, 35.7 ve 28.5 olarak hesaplandı. Sigara içmeyen grupta kadın hastaların oranı daha yüksek bulundu ($p=0.022$). Sigara içmeyen ve içen hasta gruplarında yaş ($p=0.993$), zorlu ekspirasyonun birinci saniyesinde atılan volümler ($p=0.476$), uygulanan cerrahi rezeksiyonlar ($p=0.564$) ve tümörün histolojik tipi ($p=0.920$) açısından istatistiksel olarak farklılık saptanmadı. Ortanca sağkalım sigara içmeyen grupta 76 ay, sigara içen grupta ise 72 ay olarak hesaplandı ($p=0.654$). Sigara içmeyen hastalar kohortumuzun %30'unu oluşturmaktadır.

Sonuçlar: Çalışmamızdan elde edilen veriler, KHDAK nedeniyle rezeksiyon uygulanan hasta grubunda sigara kullanımının hastaların total sağkalımı üzerine etkisi olmadığını göstermektedir.

Anahtar Kelimeler: Küçük hücreli dışı akciğer kanseri, sağkalım, sigara kullanımı

INTRODUCTION

Lung cancer is the leading cause of cancer-related death worldwide, accounting for about 1.6 million deaths per year (1). Although there is a clear association between tobacco smoking and non-small cell lung cancer (NSCLC), 10 – 15% of all lung cancers arise in never smokers (1,2). In addition, many studies showed that the incidence of lung cancer in never-smokers is increasing globally (2-4). There is also little information available about the impact of smoking status on the survival of patients with NSCLC, and the results of the studies are conflicting (5-9). Moreover, little is currently known about the proportion of never-smokers among NSCLC patients in Turkey.

In this present study, we aimed to evaluate both the frequency of non-smoking patients and the impact of smoking status on the long-term survival of patients operated for NSCLC in our institutional cohort.

MATERIALS and METHODS

Between January 2002 and December 2012, 249 patients who underwent complete pulmonary resection for NSCLC at our institutions were retrospectively analyzed from a prospectively collected database. Data were compiled from individual patient notes, electronic patient records, and pathology reports. The study was approved by the ethical committee of Hacettepe University School of Medicine. Patients were evaluated after approval was obtained Ethics Committee (Decision No: GO17/472-39). The study was conducted under the principles of the Declaration of Helsinki. Survival status was determined from the date of last follow-up. Mortality status was documented from patient records and the

National Health Service database.

Histological type of tumors was determined according to the World Health Organization's classification. Patients' data were collected, including the following variables: sex, age, forced expiratory volume in the first second (FEV1), tumour histologic subtype, type of resection, preoperative comorbidities, and postoperative early complications. Never-smokers were defined as patients who did not ever smoke any tobacco in their lifetime. Smokers were defined as patients who continued smoking upon diagnosis or had stopped smoking at least one month before admission for operation and had smoked more than 100 cigarettes during their lifetime. Preoperative comorbidities included hypertension, diabetes mellitus, coronary artery disease, and chronic obstructive pulmonary disease. Postoperative early complications were defined as prolonged air leak, postoperative ventilatory support, rhythm disturbances, and surgical site infections. Patients were divided into smokers and never-smokers. Annual frequency, demographic and clinical characteristics, and overall survival were compared between the groups.

Statistical analysis

Statistical analyses were performed with SPSS 19.0 software (SPSS Inc., Chicago, IL, USA). Distribution of data was determined by the Shapiro-Wilk test. Continuous variables were expressed as mean±standard deviation (SD), and categorical variables as frequency and percent. Continuous variables were compared with the independent sample t-test or the Mann-Whitney U test for two groups. Categorical variables were compared using the chi-square test. Survival was estimated by

using the Kaplan-Meier method. Survival distribution was compared by the log-rank test. A p-value of less than 0.05 was considered statistically significant for all tests.

RESULTS

Of the 249 patients included, 208 (83.5%) were male and 41 (16.5%) were female. The median age at admission was 60.8 years (range, 35 to 81). Among them, 75 patients (30.1%) were never-smokers. The patient characteristics are summarized in Table 1. The annual frequency of never-smokers between the years 2002 and 2012 was 33.2, 24, 37.5, 25, 34.3, 35.4, 29.4, 22.7, 22.2, 35.7, and 28.5%, respectively. Never smokers were more likely to be female, 46.3% vs. 26.9% male ($p=0.022$). No statistically significant difference existed in the distribution of age ($p=0.993$), FEV1 measurement ($p=0.476$), type of resection performed ($p=0.564$), and tumor histology ($p=0.920$) between the groups (Table 2).

Out of 249 patients, 146 (58.6%) died and 103 (41.4%) survived during the study period. The median survival time was 72 months in smokers and 76 months in never-smokers (log-rank test; $p=0.654$). The Kaplan-Meier estimates of the overall survival functions of the groups are shown in Figure 1.

DISCUSSION

Lung cancer is classified as a preventable cancer since tobacco smoking is considered to be the major cause of lung cancer. Although there is a decline in the incidence of lung cancer, the question of whether the number of never-smoking patients with NSCLC is increasing is very difficult to address

due to poorly recorded smoking histories in the past and demographic factors that may affect the actual percentage of the population (10). However, a vast amount of studies highlighted an increase in the proportion of never-smoking patients with NSCLC (3,11-13).

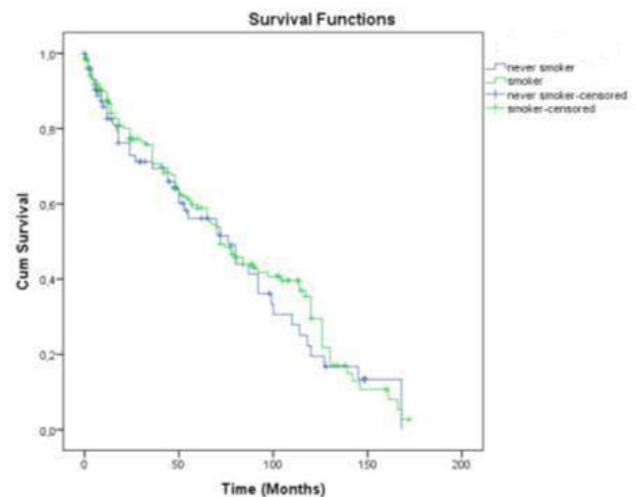


Figure 1. Overall survival of patients with non-small cell lung cancer according to smoking status

According to global statistics, the proportion of never-smokers among NSCLC patients is around 10%-15% in Western countries and approximately 32% in the Asian region (14,15). In our cohort, the proportion of never-smoker patients undergoing surgery for lung cancer was 30.1% which is parallel to the Asian population, and we also pointed out that the annual percentage did not change considerably in the 10 years. This latter conflicting observation may be explained by demographic diversity and the lack of previous data regarding this issue.

NSCLC in newer smokers could be described as a distinct disease due to its differences from NSCLC in ever-smokers in terms of epidemiologic, clinical, and molecular characteristics, and high

Table 1. The characteristics of patients

Variables	Mean (SD) (Min-Max)
Age (years)	60.8 (9.1) (35-81)
Male (%)	208 (83.5)
FEV1 (l)	2.39 (0.6) (1.1-3.9)
Preoperative Comorbidity (%)	132 (53.0)
Type of Operation	
Pneumectomy (%)	66 (26.6)
Lobectomy (%)	177 (71.0)
Segmentectomy (%)	6 (2.4)
Tumor Histology	
Adenocarcinoma	93 (37.3)
Squamous-cell Carcinoma	114 (45.8)
Large-cell Carcinoma	21 (8.4)
Others	21 (8.4)
Postoperative Complications	156 (62.6)
Hospital Stay (days)	9.9 (7.9) (4-60)

FEV1: Forced expiratory volume in the first second, SD: Standard deviation

Table 2. Baseline characteristics of the study population

Variables	Smoker (n=174)	Non-smoker (n=75)	p-value
Age (years) (SD)	60.82±9.2	60.83±9.0	0.993
Gender (%)			0.022
Female	22 (12.6)	19 (25.3)	
Male	152 (87.4)	56 (74.7)	
FEV1 (l)	2.38±0.68	2.41±0.6	0.476
Type of Resection (%)			0.564
Pneumectomy	55 (25.8)	21 (26)	
Lobectomy	125 (71.9)	52 (69.3)	
Segmentectomy	4 (2.3)	2 (2.7)	
Postoperative Complication (%)			
Tumor Histology (%)			
Adenocarcinoma	65 (37.4)	28 (37.3)	
Squamous-cell Carcinoma	77 (44.3)	37 (49.3)	
Large-cell Carcinoma	16 (9.2)	5 (6.7)	
Mixed	8 (4.6)	2 (2.7)	
Others	8 (4.6)	3 (4)	

FEV1: Forced expiratory volume in the first second, SD: Standard deviation

occurrence in the female population and with adenocarcinoma histology (12,15). In our study, the proportion of female patients among non-smokers was higher, which is in line with the previous studies. However, the major histologic type in the never-smoker group was squamous cell carcinoma, which is inconsistent with the literature.

As far as smoking cessation improves the survival of patients with lung cancer, there is a debate whether smoking status at the time of diagnosis has an impact on the overall survival of patients with lung cancer (16-18). Some studies described smoking as a predictor of poor prognosis in patients with lung cancer (8,9,19-21). Recently, Cho et al. analysed 1860 patients who were newly diagnosed with NSCLC in Korea and emphasised that never-smoker patients had a longer overall survival compared with ever-smokers due to their different clinical characteristics and major driver mutations (13). Nia et al. evaluated the role of smoking specifically in patients operated for NSCLC and demonstrated that smoking at the time of admission for operation is associated with poor prognosis (7). More recently, Cufari et al. reported that the 5-year survival was lower for ex-smokers than never-smokers in patients operated for NSCLC at a tertiary care hospital in the United Kingdom (3). In contrast, other studies reported no difference in survival between ever-smokers and never-smokers and put forward smoking status as an insignificant prognostic factor (6,22-25). Correspondingly, the results of our study demonstrate similar overall survival among never-smokers compared to smokers (median survival 76 and 72 months, respectively; $P=0.654$).

CONCLUSION

We acknowledge that our observations are limited as we are a single institution. We are also not certain if our cohort is representative of the country as a whole; however, as one of the largest tertiary institutions for lung cancer resections, we have a significant proportion of the cross-sectional cohort for early lung cancer in Turkey.

This study had limitations that should be addressed. First of all, it is a retrospective study and cause specific mortality could not be evaluated. Secondly, the sample size was relatively small. Thirdly, information about exposure to other risk factors and passive cigarette smoking status was unavailable. We also acknowledge that our observations are limited to a single institution.

To sum up, according to our study, virtually 30% of Turkish patients operated for NSCLC were never-smokers. This percentage remains reasonably stable between the years 2002 and 2012. In a long follow-up, never-smokers had similar survival rates compared to smokers. However, our data deserve further verification with multi-centre and larger-scale prospective trials.

Conflict of interest: The Authors declare that there is no conflict of interest.

Financial support: The authors declared that they did not receive any financial support during the research and writing process of this article.

This study was presented as an oral presentation at the 8th National Lung Cancer Congress, entitled "The effect of smoking on long-term survival in patients diagnosed with non-small cell lung cancer

undergoing surgery" between October 4th and 7th, 2018, in Bodrum, Türkiye.

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