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Original Article

An analysis of cigarette smoking in thoracic surgery patients

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ABSTRACT

Background: Cigarette smoke (CS) is a long-term risk factor for several disorders of the respiratory and cardiovascular systems. In this study, we aimed to analyze the current effects of cigarette smoke on patients who underwent thoracic surgery. In line with this purpose, we analyzed patients who were admitted to a thoracic surgery clinic recently and their smoking history.

Materials and Methods: We reviewed patients who underwent thoracic surgery ($n = 867$) and were admitted to our clinic between January 2018 and December 2018. The patients were categorized into seven groups comprising the most common types of thoracic pathology as, lung carcinoma ($n = 338$), pneumothorax ($n = 219$), pleural effusion ($n = 131$), mediastinal lymphadenopathy ($n = 77$), pneumomediastinum ($n = 22$), bronchiectasis ($n = 30$), and hydatid cyst ($n = 10$). Cases were reviewed in detail for demographics, smoking history in terms of pack-years, thoracic pathology, and hospitalization duration (days).

Results: Statistical analysis revealed that smoking is still a significant factor contributing to lung cancer. Cigarette smoke did not appear to be a factor in mediastinal lymphadenopathy, bronchiectasis, pleural effusion or hydatid cyst cases. Additionally, hospitalization duration was significantly longer in the smoker group.

Conclusions: The data reviewed are compatible with the current knowledge on the mechanisms of cigarette smoke-related pathologies. Cigarette smoke is still associated with common thoracic surgery pathologies such as lung carcinoma, pneumothorax, and pneumomediastinum. This may be rephrased thus, the absence of cigarette smoke would greatly decrease the prevalence of thoracic surgery cases.

Keywords: cigarette smoking, lung neoplasms, pneumothorax, pleural effusion, lymphadenopathy, mediastinum, COPD, thoracic surgery

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Introduction

Cigarette smoke (CS) is a hazardous mixture of multiple chemical compounds that cause a variety of pulmonary and systemic effects in humans [1]. CS is a long-term risk factor for several disorders of the respiratory and cardiovascular systems. Tobacco is consumed in the form of CS by nearly one-fifth of the world's population [2].

Smoking is the most significant cause of chronic respiratory bronchitis, pulmonary emphysema, and bronchial carcinoma [3]. In addition, studies have revealed that cigarette smoking is the major cause of both obstructive pulmonary diseases and chronic respiratory symptoms such as cough, wheezing, and dyspnea. CS is the main known cause of cancer-related deaths worldwide [4].

Chest radiography studies demonstrated that pulmonary micronodules and lobular opacities were mostly due to changes induced by pathological CS substrates [5]. Moreover, CS-related *in vitro* studies revealed induction of DNA strand breaks, formation of DNA adducts, and mutagenic cytogenetic effects [6].

In this study, we aimed to analyze the current effects of CS on patients who underwent thoracic surgery. In line with this purpose, we analyzed patients who were admitted to a thoracic surgery clinic recently and their smoking history.

Material and Methods

This retrospective study was approved by the local ethics committee (2020-64, December 2020). All participants provided informed consent prior to their inclusion in the study. We reviewed patients who underwent thoracic surgery ($n = 867$) and were admitted to our clinic between January and December 2018. We excluded patients ($n = 40$) who were exposed to toxic substances, or had pectus deformities, traumatic hemothorax, rib fracture, and traumatic pneumothorax. Subsequently, the remaining 827 patients were included in the study.

The patients were categorized into seven groups comprising the most common types of thoracic pathology: lung carcinoma ($n = 338$), pneumothorax ($n = 219$), pleural effusion ($n = 131$), mediastinal lymphadenopathy ($n = 77$), pneumomediastinum ($n = 22$), bronchiectasis ($n = 30$), and hydatid cyst ($n = 10$). Lung cancer patients with mediastinal lymphadenopathy or pleural effusion were included in the lung cancer group. We analyzed the studied cases in two groups depending on their classification as smokers or non-smokers.

Cases were reviewed in detail for demographics, smoking history in terms of pack-years, thoracic pathology, and hospitalization duration (days). Twenty cigarettes smoked every day for one year was referred to as "a pack-year." Lymph node enlargement was defined as a size of more than 7-11 mm on the short axis depending on the regional nodal station [7].

Statistical Analysis

All statistical analyses were performed using SPSS version 21.0 software (SPSS, Inc., Chicago, IL, USA). Descriptive statistics are summarized as counts and percentages for categorical variables; mean and standard deviations and median (minimum and maximum) for others. The differences between two groups in terms of categorical variables were compared by using Chi-Square test or Fisher's exact test, where applicable. Differences between two groups for non-normally distributed continuous variables were evaluated by Mann Whitney U test. P value less than 0.05 was considered significant.

Results

Our retrospective study recruited 827 patients, including 669 men (80.1%) and 158 women (19.1%). The mean age was 48.8 ± 16.7 (range 16-90) years, and the mean hospitalization duration was 3.9 ± 5.8 (range 1-26) days. Of the 827 patients, 554 (67.1%) underwent surgery due to related thoracic pathology. The smoker group comprised 72% ($n = 595$) of the cohort. The mean value of consumption was 24.6 ± 14.3 (range 3-90) pack-years in the smoker group.

Of the 827 patients who were referred to our thoracic surgery clinic, 40.9% had lung cancer, among whom 79% were smokers ($n = 267$); 26.5% had pneumothorax, among whom 75.8% were smokers ($n = 166$); 15.8% had pleural effusion, among whom 67.1% were smokers ($n = 88$); 9.3% had mediastinal lymphadenopathy, among whom 46.7% were smokers ($n = 36$); 2.6% had pneumomediastinum, among whom 86.3% were smokers ($n = 19$); 3.6% had bronchiectasis, among whom 56.7% were smokers ($n = 17$), and 1.2% had hydatid cyst, among whom 20% were smokers ($n = 2$). The characteristics and comparative analysis of the smokers and non-smokers are shown in table 1.

Table 1. Characteristics of the studied groups.

Parameter	Smoker (n=595)	Non-smoker (n=232)	P
Gender			
Male	481 (80.8%)	188 (81.1%)	0.949 ^c
Female	114 (19.2%)	44 (19%)	
Age (years)	49.3±16.9	48.6±18.2	0.56 ^m
Smoking (pack year)	-	24.6±14.3	-
Hospitalization (days)	2.4±5.1	4.6±5.7	0.001 ^m
Pathology			
Lung cancer	267 (44.5%)	71 (30.6%)	<0.001 ^c
Pneumothorax	166 (27.9%)	53 (22.8%)	0.139 ^c
Pleural effusion	88 (14.7%)	43 (18.5%)	0.185 ^c
Mediastinal LAP	36 (6.1%)	41 (17.7%)	<0.001 ^c
Pneumomediastinum	19 (3.2%)	3 (1.3%)	0.127 ^c
Bronchiectasis	17 (2.9%)	13 (5.6%)	0.058 ^c
Hydatid cyst	2 (0.3%)	8 (3.4%)	0.001 ^f

c; chi-square test, m; Mann-Whitney U test, f; Fischer's exact test

The parameters were studied to predict the possibility of CS as a factor in related thoracic pathology. Statistical analysis revealed that smoking is a factor contributing to lung cancer, pneumothorax, and pneumomediastinum while it was only significant for lung cancer (Table 1). CS did not appear to be a factor in mediastinal lymphadenopathy, pleural effusion, bronchiectasis, or hydatid cyst cases. Additionally, hospitalization duration was significantly longer in the smoker group (4.6 ± 5.7 , range 1-26 days) than in the non-smoker group (2.4 ± 5.1 , range 1-24 days) ($p = 0.001$).

Discussion

Cigarette smoke causes apoptotic cell death and aging, and damages repair functions performed by lung fibroblasts, which are essential for maintaining the integrity of the alveolar structure by producing extracellular matrix proteins [8]. CS inhibits fibroblast proliferation and migration, and induces DNA damage [9]. CS-induced inhibition of fibroblast activity contributes to the reduction of lung repair following lung injury [10]. In our study, we aimed to demonstrate the current effects of a commonly known toxic substance; CS, in thoracic surgery patients. We mainly analyzed patients with the seven most common groups of thoracic surgery pathologies.

CS is the most important cause of lung cancer [4].

Carcinoma arises from genetic alterations that cause the release of neoplastic cells from homeostatic mechanisms that govern cell proliferation [11]. After the discovery of the significant role of the tumor suppressor gene p53 mutations in human cancer, many studies have revealed a high prevalence of p53 mutations in many types of cancers that were linked to CS exposure. Almost half of all lung cancer cases have been reported to present p53 mutations. Furthermore, the prevalence of mutations in the p53 gene, were higher in lung tumors from smokers as compared to those from non-smokers [12]. In addition, mutations in the KRAS gene occur in approximately one-third of lung cancer patients with adenocarcinoma histology, and these mutations have been found to be associated with smoking [13]. CS has been a known cause of lung carcinoma for decades and continues to be the leading cause of lung carcinoma. In our study, statistical analysis revealed that smoking still had a significant effect on lung carcinoma.

Pneumothorax remains one of the most common pathologies requiring thoracic surgery. As a result of the rupture of subpleural blebs or bullae, primary spontaneous pneumothorax (PSP) typically occurs mostly in tall and young male smokers, with no apparent co-existing lung diseases. The risk of PSP is linked to CS and increases with duration of exposure and daily consumption. CS stimulates bronchiolar remodeling by inducing growth factors in the distal airway wall via increased release of active transforming growth factors [14]. CS induces pathologic changes in the small distal airways, which contributes to the development of local emphysema followed by the consequent formation of bullae. The trapping of air distally due to CS-induced bronchiolar inflammation and respiratory bronchiolitis leading to alveolar overdistension, causes bullae formation and possible rupture [15]. However, the pathophysiologic mechanism of PSP formation due to CS and its clinical correlation are not strictly demonstrated. Controversy still exists around the occurrence of bullae and PSP. In our study, statistical analysis revealed that smoking had an effect on pneumothorax but it was not significant.

CS interferes with macrophage response to infection by decreasing its phagocytic ability [16]. Thus, smokers tend to contract primary tuberculosis and pneumonia. Patients with latent tuberculosis may develop active disease, leading to increased disease burden in the community due to CS. Smoking is associated with a higher incidence of parapneumonic effusion in patients with community-acquired pneumonia and higher pleural in-

flammatory markers [17]. In our study, the most common causes of pleural effusion were tuberculosis and pneumonia-related pleuritis due to the exclusion of malignant and cardiac pleural effusion. We excluded these cases because elaboration of the CS effect on these patients was not possible due to the apparent cause of pleural effusion. Statistical analysis revealed that smoking did not have a significant effect on pleural effusion.

Enlarged lymph nodes are mostly known as a sign of malignancy, although they are also observed in benign conditions such as sarcoidosis, chronic heart failure, obstructive pulmonary disease, and pneumoconiosis. In addition to exposure to various substances, the deposition of CS itself also results in enlargement of the hilar and mediastinal lymph nodes of smokers. Recent studies have demonstrated that benign enlargement of mediastinal lymph nodes is a common finding in heavy smokers and is more often identified in smokers than in non-smokers. Thus, CS itself is hypothesized to be a cause of enlargement of mediastinal lymph nodes [18]. Nevertheless, in our study, statistical analysis revealed that smoking did not have a significant effect on mediastinal lymphadenopathy.

Spontaneous pneumomediastinum (SPM) is mostly a self-limiting pathology that clinically presents as the presence of free air in the mediastinum without any traumatic cause. SPM is usually observed in young adults with the most common clinical symptoms, including shortness of breath, chest and neck pain, difficulty in swallowing, and swelling of the face and neck. The most common precipitating factor of SPM is bronchial asthma, with alveolar rupture being the main etiology. Other causes include barotrauma including the Valsalva maneuver, and inhalation of various substances such as CS, cocaine, and marijuana. Alveolar rupture leads to air leakage to the broncho-vascular sheath, which consequently results in the release of air that reaches the mediastinum [19]. CS has been well reported in the literature as a risk factor for SPM. In our study, statistical analysis revealed that smoking had an effect on SPM but it was not significant.

Bronchiectasis is a pathological, nonreversible enlargement of the bronchial airways. The diagnosis of this condition is made on the basis of visual identification of an airway whose diameter is greater than that of the adjacent artery on computed tomography (CT) scans or lung tissue [20]. Studies suggest that bronchiolitis is the initial lesion in bronchiectasis. The presence and se-

verity of airflow obstruction, correlated with the intensity of mosaic attenuation detected on high-resolution CT scans, cause bronchiectasis. CS-related chronic bronchitis and bronchiectasis share many common pathological findings. There are three well-known causes of chronic bronchitis: cystic fibrosis and primary ciliary dyskinesia, which are genetically determined, and CS [21]. All three conditions compromise the mucociliary transport apparatus and may lead to bronchiectasis. However, in our study, statistical analysis revealed that smoking did not have an effect on bronchiectasis.

Hydatid cyst disease is a parasitic infection caused by *Echinococcus granulosus*, characterized by cystic lesions in the liver and lungs. In the available literature, there is no established relationship between hydatid cyst of the lung and tobacco exposure. Statistical analysis revealed that smoking had no effect on hydatid cysts in our study.

Lung fibroblasts produce extracellular matrix proteins, including collagen, elastin, and fibronectin, which are required for the attachment, structure, and function of alveolar epithelial cells; thus, they are considered mandatory for the maintenance of the integrity of alveolar structure. CS causes a malfunction in the body's repair mechanism by vitiating fibroblast activity [22]. In our study, we found that smokers also had significantly longer hospital stay compared to non-smokers due to longer recovery time.

In our study, nonsmoker patients' ratio to smoker patients was higher compared to literature. In terms of probable factors, subtle exposure to asbestos which is common in our country or living in limestone houses especially in Anatolian region of the country may be agents of thoracic pathology in nonsmoker patients.

Limitations of the Study

Our study was a retrospective, single-center clinical study. It utilized one year's worth of collected data, which consisted of a limited number of thoracic surgery cases. Our study recapitulates the effect of CS on the studied pathologies using up-to-date data; however, it does not contribute additional knowledge to existing literature

In conclusion, CS initiates damage by causing respiratory bronchiolitis and disrupting the homeostatic mechanisms governing cell proliferation, followed by parenchymal damage. The data reviewed are compatible with the current knowledge on the mechanisms of CS-related pathologies. CS is still associated with common thoracic surgery pathologies such as lung carci-

noma, pneumothorax, and pneumomediastinum. This may be rephrased thus: the absence of CS would greatly decrease the prevalence of thoracic surgery cases.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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Ethics approval

Approval for this retrospective, descriptive, single-center study was obtained from Istanbul Yedikule Chest Disease and Thoracic Surgery Training and Research Center Ethical Comitee (2020-64, December 2020).

Authors' contribution

YS; designed the analysis, wrote the paper, OVY; collected data, performed the analysis, MÖ; collected data, NM; contributed data, LC, MAB; editing.

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