High-Resolution Computed Tomography Findings in Healthy Heavy Smokers and Correlation with Pulmonary Function Tests

Ağır Sigara İçicilerde Yüksek Çözünürlüklü Bilgisayarlı Tomografi Bulguları ve Solunum Fonksiyon Testleri ile Korelasyonu

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ABSTRACT

Introduction: Chest radiographs and pulmonary function tests (PFTs), may show the adverse effects of smoking on the lungs, but in some cases these methods are inadequate and interpreted as normal. High-resolution computed tomography (HRCT) provides more sensitive and specific imaging features to identify parenchymal-interstitial abnormalities in the early stages of the disease related with smoking. The purpose of this study is to recognize lung HRCT findings of smoking in cigarette smokers and non-smokers and investigate whether there is a relationship with airway obstruction on PFTs.

Methods: A total of 155 subjects (110 heavy smokers, 45 non-smokers) who performed both HRCT and PFTs were included in the study. Two radiologists independently evaluated the CT findings for the following characteristics: bronchiectasis, bronchial wall thickening, emphysema, atelectasis, interstitial patterns, and fibrotic changes. Afterwards, the relationship between the HRCT findings and PFTs of the heavy smokers and non-smokers was presented statistically.

Results: There were statistically significant differences regarding emphysema and bronchial wall thickening between the heavy smokers and non-smokers (p = 0.001 and p = 0.000, respectively) on HRCT. Emphysema and bronchial wall thickening were more common in patients who had obstructive PFTs. Fibrotic changes, atelectasis, bronchial wall thickening, and emphysema were the most common imaging findings although normal PFTs.

Conclusion: It is crucial to recognize the common imaging findings on HRCT of heavy smokers for diagnosis and treatment of smoking related lung disease. HRCT is vital in detecting the early stages of parenchymal-interstitial abnormalities of the lungs due to smoking, despite normal chest radiograms and PFTs.

Key words: Thorax HRCT, pulmonary function test, smoker, emphysema

ÖZET

Giriş: Göğüs radyografileri ve solunum fonksiyon testleri (SFT), sigaranın akciğerler üzerindeki olumsuz etkilerini gösterebilir, ancak bazı durumlarda bu yöntemler yetersiz kalır ve tetkikler normal olarak yorumlanır. Yüksek çözünürlüklü bilgisayarlı tomografi (YRBT), sigaraya bağlı akciğer hastalıklarının erken evrelerinde parankimal-interstisyel anormallikleri belirlemek için daha hassas ve spesifik görüntüleme özellikleri sağlar. Bu çalışmanın amacı, sigara içen ve içmeyenlerde akciğer YRBT bulgularını tanımak ve SFT'lerinde tanımlanan hava yolu obstrüksiyonu ile bir ilişkisi olup olmadığını araştırmaktır.

Yöntemler: Çalışmaya hem toraks YÇBT hem SFT tetkikleri mevcut 155 olgu (110 ağır sigara içicisi, 45 sigara içmeyen) dahil edildi. Toraks YÇBT incelemesi, nodüller, bronşektazi, bronşiyal duvar kalınlaşması, amfizem, atelektazi, buzlu cam alanları, interstisyel paternler ve fibrotik değişiklikler açısından, iki deneyimli radyolog tarafından bağımsız olarak değerlendirildi. Daha sonra ağır sigara içicilerin ve sigara içmeyenlerin YÇBT bulguları ile SFT arasındaki ilişki istatistiksel olarak sunuldu.

Bulgular: Ağır sigara içenler ve içmeyenler arasında amfizem ve bronşiyal duvar kalınlaşması açısından YRBT'de istatistiksel olarak anlamlı farklar vardı (sırasıyla p = 0,001 ve p = 0,000). Amfizem ve bronşiyal duvar kalınlaşması, obstrüktif SFT değerlerine sahip hastalarda daha sık görülüyordu. Fibrotik değişiklikler, atelektazi, bronşiyal duvar kalınlaşması ve amfizem normal SFT değerlerine rağmen en sık görülen görüntüleme bulgularıydı.

Sonuç: Sigaraya bağlı akciğer hastalığının tanı ve tedavisi için ağır sigara içicilerinin toraks YÇBT'lerinde en sık görülen görüntüleme bulgularının tanınması çok önemlidir. HRCT, normal göğüs radyogramları ve normal SFT değerlerine rağmen, sigaraya bağlı akciğerlerde görülebilecek parankimal-interstisyel anormallikleri erken evrede yakalamada hayati öneme sahiptir.

Anahtar Kelimeler: Toraks YÇBT, solunum fonksiyon testi, sigara içicisi, amfizem

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Eskisehir Med. J. 2022; 3(2):176-183.
Received date:21.03.2022 Accepted date:20.06.2022
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INTRODUCTION

Since cigarette contains more than 4000 harmful substances, smoking is responsible for deaths which result from lung cancer, chronic bronchitis, emphysema and coronary heart disease. (1). Even though many important changes in the lungs as a result of smoking can be evaluated by clinical examination, pulmonary function tests (PFTs), and chest radiography, the general opinion is that these studies provide limited information on the early pathologic changes considered as subclinical abnormalities (2-5). Further evaluation is required in the absence of airflow limitation in substantial lung pathologies, such as emphysema (6). Multislice computed tomography (MSCT) is a high-resolution fast cross-sectional imaging method that is the most commonly used method after direct X-ray screening in thoracic examinations. Computed tomography (CT) imaging performed with the routine thorax protocol may be inadequate to detect pathologies (emphysema, bronchiectasis, etc.) related to the cigarette accurately. However, high-resolution computed tomography (HRCT) can determine parenchymal pathologies, such as emphysema and bronchiectasis, which cause airflow obstruction on PFTs (7, 8).

Therefore, radiologic evaluation with HRCT is critical in the early diagnosis of subclinical abnormalities. In the literature, a few studies have been reported about the imaging findings of smokers on CT and their correlation with PFTs (9-11).

In this study, we aimed to review the imaging findings of healthy heavy smokers and non-smokers on lung HRCT and evaluate the correlation with PFTs. We hypothesized that many imaging features on HRCT can be seen in smokers, even if there are no early parenchymal or interstitial abnormalities on the PFTs or direct roentgenogram. For this purpose, the HRCT imaging findings of healthy smokers and non-smokers were compared and the correlation with PFTs was evaluated retrospectively.

METHODS

The current study received institutional review board approval from our university ethical committee (KA 14/285). This study was planned retrospectively (January to April 2016). The electronic archives of the Chest Department searched for patients who were admitted to our hospital with complaints of dyspnea, cough, and purulent or mucopurulent sputum. Patients who performed both PFT and HRCT examinations were included in the study. There was no gender discrimination between the patients. Patients who had lung operation, pulmonary infection, right heart failure, parenchymal scar or non-specific infiltration, or peripheral allergen and dust exposure history, diffuse parenchymal lung disease, interstitial lung disease, rheumatoid arthritis, Sjogren's syndrome, or Scleroderma diseases were excluded from the study.

A total of 155 patients, comprising 110 heavy smokers and 45 non-smokers, were included in this study. Verbal informed consent was obtained from participants before the study. Heavy smoking was defined as smoking cigarettes 25 cigarettes/day or 20 packs/year, according to the International Environmental Research and Public Health and National Health Survey database (12). A total of 110 heavy smokers were divided into two groups: 41 current smokers (consumption of 1 cigarette/day) and 69 ex-smokers (not having smoked for more than 1 year). As a control group, 45 non-smoker healthy subjects were included in the study.

The HRCT examinations of 110 heavy smokers and 45 non-smokers were evaluated independently and retrospectively by two radiologists, who had at least 10 years of experience in thoracic CT reporting, for the following characteristics: micronodules, bronchiectasis, bronchial wall thickening, emphysema, branched tubular structures, atelectasis, ground-glass pattern,

interstitial pattern, and fibrotic changes. In addition, the CT findings were divided into four groups to assess the significance of the HRCT-detected lesions of the heavy smokers and non-smokers; category 0: normal HRCT, category 1: the presence of an HRCT finding, category 2: the presence of 2 HRCT findings, and category 3: the presence of 3 or more HRCT findings. In order to determine the distribution of parenchymal abnormalities, the lungs were divided into 3 zones: the zone above the carina level (upper zone), the zone between the carina level and the inferior pulmonary vein (middle zone), and the zone below the inferior pulmonary vein level (lower zone). A post-bronchodilator PFT, which was performed at a time close to the HRCT examination for each patient, was also evaluated by two pulmonologists retrospectively. The forced vital capacity and forced expiratory volume in one second (FEV1/ FVC) ratios were recorded on the PFTs. Patients were divided into Group A (those with simple chronic bronchitis or were normal) with normal PFTs with a FEV1/FVC ratio >70% and Group B (those with chronic obstructive bronchitis) with obstructive PFTs with a FEV1/FVC ratio <70%.

IBM SPSS Statistics for Windows 21.0 (IBM Corp., Armonk, NY, USA) was used for all of the statistical analyses. In the evaluation of the obtained data, the mean ± standard deviation, median, minimum, and maximum values were used for numerical measurements of the descriptive statistics, while number and percentage (%) were used for the qualitative data. The Fisher Exact and Mann-Whitney U tests were applied in the statistical analyses. Odds ratios (OR), significance values (p-value), and 95% confidence intervals (95% CI) were used to present the results of the logistic regression analyses. P <0.05 was accepted as statistically significant. Interobserver compliance was more than 80% for each parameter.

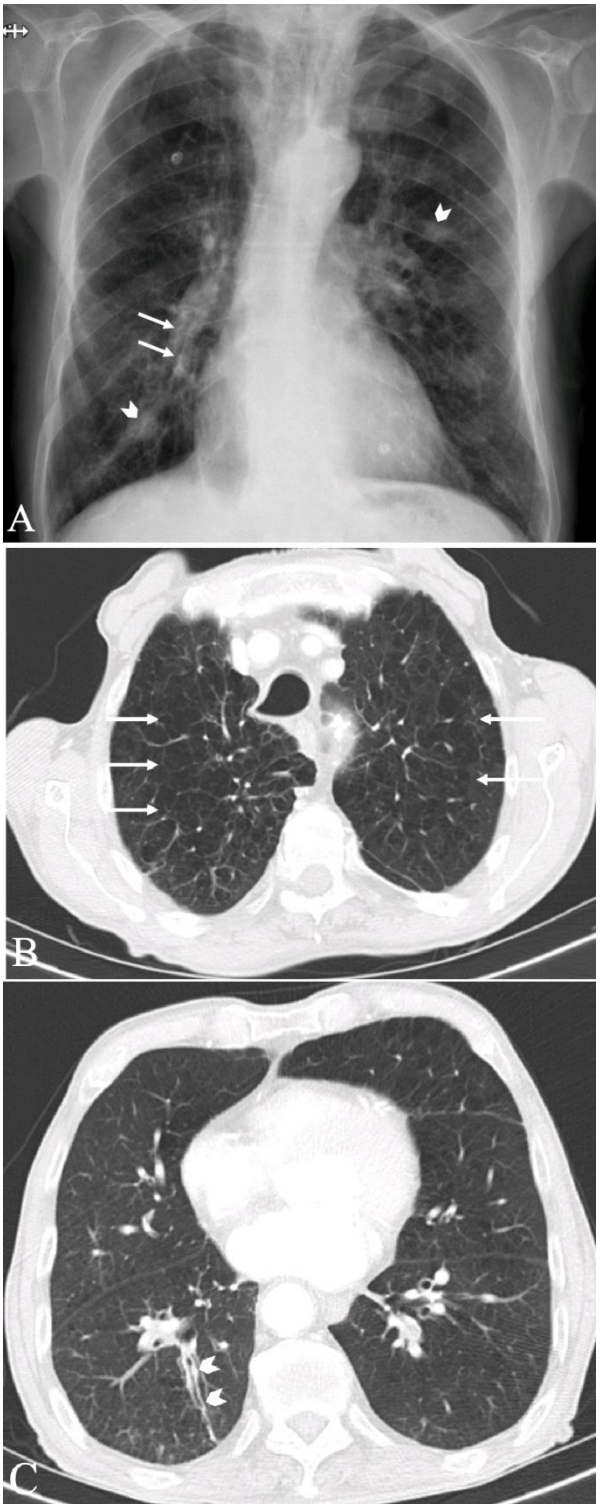

Figure 1. A 71-year-old male heavy-smoker with a normal PFT. PA chest X-ray shows bronchial wall thickening (*arrows,* **A**) and nodular opacities (arrow heads, **A**). Axial contrast-enhanced thorax CT images show centrilobular emphysema dominantly in the upper lobes of the bilateral lungs (*arrows*, **B**) and bronchial wall thickening (arrow heads, **C**).

RESULTS

A total of 155 patients were included in the study. The demographic characteristics are summarized in Table 1. There was no statistically significant difference in terms of cigarette consumption between the current smokers and ex-smokers (p= 0.344).

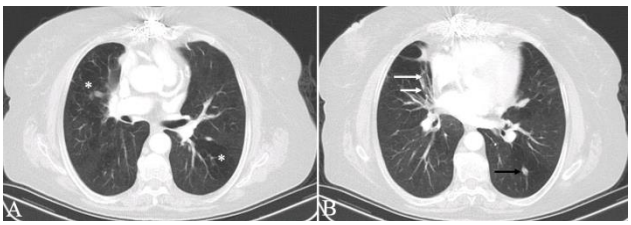

Figure 2. A 63-year-old male heavy-smoker with an obstructive PFT. Axial contrast-enhanced thorax CT images show mosaic attenuation pattern in bilateral lungs (asterisks, **A**) and bronchial wall thickening in the middle lobe of the right lung (*arrows*, **B**). Note that a micronodule in the lower lobe of the left lung (*black arrow*, **B**).

For the PFTs, 127 of 155 patients (81.9%) had normal PFTs with a FEV1/FVC ratio >70%, without airflow obstruction findings, and 28 of 155 patients (18.1%) had obstructive PFTs with a FEV1/FVC ratio <70%. The mean values of the PFTs were calculated as 82.10 ± 16.05% in active smoker group, 80.01 ± 15.53% in ex-smoker group, and 85.13 ± 13.93% in non-smoker group, and they were within normal limits. There was no statistically significant difference between smokers and non-smokers in terms of FEV1 and FEV1/FVC ratio values (p = 0.676 and p = 0.373, respectively). Cigarette consumption was 23.59 ± 22.79 packs/year in 23 patients with obstructive PFTs and 87.9 ± 21.71 packs/year in 87 patients with normal PFTs. There was no statistically significant difference between the groups in terms of PFTs and cigarette consumption (p = 0.098).

HRCT findings of the current smokers, ex-smokers, and non-smokers are shown in Table 2. There was a statistically significant difference (p = 0.001 and p = 0.000, respectively) with regards to emphysema and bronchial wall thickening between the current smokers, ex-smokers, and non-smokers. There were no statistically significant differences in terms of atelectasis, fibrotic change, nodule, or presence of obstructive PFTs.

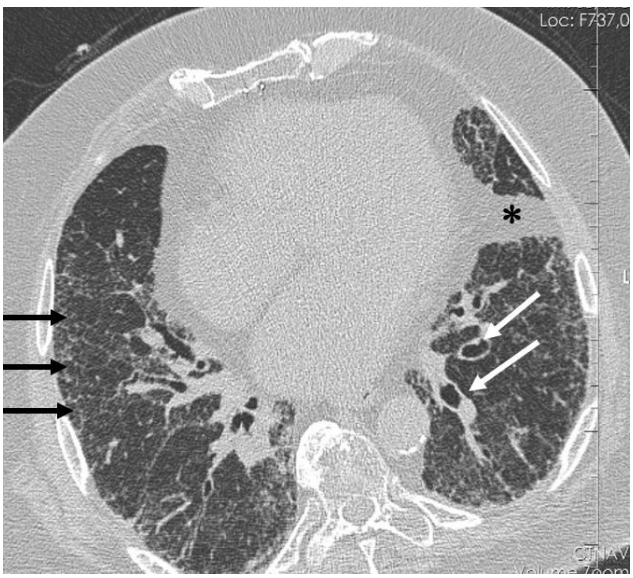

Figure 3. A 49-year-old female ex-smoker with a normal PFT. Axial contrast-enhanced thorax CT image shows bronchial wall thickening and bronchiectasis in the left lung (*white arrows*). Note the dominantly peripheral interlobular septal thickening in bilateral lungs (*black arrows*) and subsegmental atelectasis (asterisk).

Of the 41 current smokers, 37 (90%) had centrilobular emphysema, 6 (14%) had bullous emphysema, 7 (17%) had paraseptal emphysema. There was a statistically significant difference in terms of centrilobular emphysema between the current smokers and non-smokers (p = 0.02). The emphysema was mainly in the upper lobe of lungs in 41 (37%) of the 110 heavy smokers, and 4 (9%) of the 45 non-smokers (Fig. 1).

Bronchial wall thickening was detected in 60 (54.5%) of the 110 heavy smokers and 8 (17.7%) of the 45 non-smokers (Fig. 2). There was a statistically significant difference with regards to bronchial wall thickening between current smokers and non-smokers (p = 0.001). Bronchial wall thickening was observed only in the lower lobe of the non-smokers, whereas bronchial wall

thickening was observed in all of the lobes, but predominantly in the lower lobe, of the heavy smokers.

An interstitial pattern was detected in 22 (20%) of the 110 heavy smokers and 7 (15%) of 45 non-smokers. There was no statistically significant difference with regards to interstitial pattern between the current smokers and non-smokers (p = 0.520) (Fig. 3 and 4). On the other hand, there was a statistically significant difference with regards to age and interstitial pattern (p = 0.001). Categories 0 and 1 (11.1% and 24.4%) were more common in the non-smokers, whereas categories 2 and 3 (31.1% and 59.09%) were commonly seen in the smokers. HRCT categories were statistically significant higher in the heavy smokers (p = 0.000).

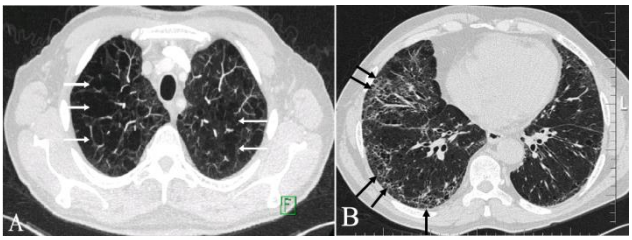

Figure 4. A 58-year-old male heavy-smoker with a normal PFT. Axial contrast-enhanced thorax CT images show bilateral emphysema in upper lobes of the lungs (*white arrows*, **A**) and interlobular septal thickening dominantly in the right lung (*black arrows*, **B**).

The most common HRCT findings were fibrotic changes in 88 (69.3%), atelectasis in 86 (67.7%), bronchial wall thickening in 49 (38.6%), and emphysema in 30 (23.6%) of the 127 patients with normal PFTs. The most common HRCT findings were bronchial wall thickening in 19 (67.9%), atelectasis in 18 (53.6%), emphysema in 15 (53.6%), and fibrotic changes in 15 (53.6%) of the 28 patients with obstructive PFTs (Fig. 5). There was a statistically significant difference with regards to emphysema and bronchial wall thickening between patients with normal and obstructive PFTs (p = 0.002 and p = 0.005, respectively) (Table 3).

Figure 5. A 79-year-old male non-smoker with an obstructive PFT. PA chest X-ray shows bronchovascular thickening (*arrows,* **A**) and subsegmental atelectasis (arrow heads, **A**). Axial contrast-enhanced thorax CT image shows peripheral interlobular septal thickening (black *arrows*, **B**) in the bilateral lungs and subsegmental atelectasis in the left lung (asterisk, **B**). Note that the bronchial wall thickening and bronchiectasis (curve arrow, **B**) in the upper lobe of the left lung.

DISCUSSION

To date, many studies have been conducted to detect the adverse effects of smoking on lung health earlier than diseases occur. To the best of our knowledge, this study was the first to present a large number of imaging findings of heavy smokers and non-smokers and evaluate the correlation with PFTs (9-11). The most important finding of this study was that emphysema and bronchial wall thickening were more common in patients with obstructive PFTs than in those with normal PFTs. Moreover, fibrotic changes, atelectasis, bronchial wall thickening, and emphysema were the most common imaging findings in patients with normal PFTs. These imaging findings may serve as an auxiliary criterion in the early parenchymal and interstitial abnormalities of the lungs due to smoking, despite normal chest radiograms and PFTs.

Macroscopic reflections of the pathomorphological changes in the lungs in long-term smokers have a ground-glass appearance, atelectasis, interstitial-reticular pattern, and emphysema areas in lungs on HRCT (13-15). In the current study, thoracic HRCT findings, which could be superior to PFTs at early diagnosis, were investigated in cases of heavy cigarette smoking.

Table 1. Demographic characteristics, smoking status and PFT results of patients

	Patients n (%)	Female (n)	Male (n)	Cigarette Consumption (packs/year)	PFT	
					normal (FEV1 / FVC >70%)	obstructive (FEV1 / FVC <70%)
Current smoker	41 (%26,5)	31	79	40,32±5,2	34	7
Ex-smoker	69 (%44,5)			36,17±19	53	16
Non-smoker	45 (%29)	35	10	-	40	5
Total	155 (%100)	66	89	-	127	28

Abb. PFT: Pulmonary function test, FEV1: Forced expiratory volume in one second, FVC: Forced vital capacity

It has been shown that HRCT may reveal earlier emphysematous areas than radiograms and PFTs (16). Kubo et al. (17) found that there was no difference in the level of emphysema between those who smoked mildly and those who did not but found that the rate of emphysema in severe smokers increased in a similar manner to that in heavy smokers. West et al. (16) emphasized that the destructive effect of smoking in the upper lung zones was due to the high mechanical stress, as well as the densities and temperature, of the cigarette smoke that was inhaled. The emphysema detected in the current study was mostly of centrilobular type and located in the upper zone, which may have been due to physiopathological and mechanical effects that were similar to those mentioned above (18, 19). The results showed that the upper lobes may be regions where destruction primarily begins, without functional abnormalities in the lung becoming apparent. Of the 127 patients with normal PFTs, emphysema was detected in 30 (23.6%) patients, whereas emphysema was detected 15 (53.6%) of the 28 patients with obstructive PFTs. Although the PFT was found to be statistically significant (p = 0.002) in patients with impaired PFTs when compared to normal patients, 30 patients who had emphysematous changes on their HRCT, but were clinically termed as PFT normal, was questioned about the reliability of PFT.

Bronchial wall thickening was reported (9, 20) to occur in 33%–39% of the HRCTs of smokers in the literature. With regards to the thickness of the bronchial wall, Remy-Jardin et al. (9) emphasized that there was no direct relationship between smoking and bronchial thickening. However, in the current study, there was a significant relationship between cigarette smoking and bronchial wall thickening. Bronchial wall thickening was observed herein at the relatively high rate of approximately 54%, which was considered to be primarily due to the selection of heavy smokers and symptomatic patients in the smoker group. Bronchial wall thickening was seen as statistically significantly higher in patients with obstructive PFTs than in patients with normal PFTs (p = 0.005). However, the presence of bronchial wall thickening in the 49 patients with normal PFTs revealed the necessity of HRCT in addition to PFTs.

Even though peripheral thin-septal streaks are usually seen in HRCT, the clear visualization of interlobular septa is abnormal and pathologically interpreted. Studies have shown that these patients have a high likelihood of developing interstitial lung disease (9, 21). In the current results, as in the studies in the literature,

Table 2. Imaging findings of current smokers, ex-smokers, and non-smokers on HRCT.

HRCT findings	Current smoker (n=41)	Ex-smoker (n=69)	Non-smoker (n=45)	Total (n=155)	Overall statistics P Value
Emphysema	18 (40%)	23(51.1%)	4(8.9%)	45	**0.001**
Ground-glass areas	2(20%)	2(20%)	6(60%)	10	0.084
Bronchial wall thickening	21(30.9%)	39(57.4%)	8(11.8%)	68	**0.000**
Bronchiectasis					
Atelectasis	8(40%)	9(45%)	3(15%)	20	0.207
Interlobular septal	29(27.9%)	41(39.4%)	34(32.7%)	104	0.170
thickening	5(17.2%)	17(58.6%)	7(24.1%)	29	0.220
Sequel changes					
<7 mm nodule	13(25%)	19(36.5%)	20(38.5%)	52	0.169
≥7 mm nodule	4(40%)	5(50%)	1(10%)	10	0.375
	2(18.2%)	5(45.5%)	4(36.4%)	11	0.858

Abb. HRCT: High resolution computed tomography

it was determined that there was no statistically significant relationship between smoking and interlobular septal thickening. However, Webb et al. (22) emphasized that secondary fibrosis may develop with age progression rather than the interstitial pattern of cigarette smoke consumption.

As the number of cigarettes smoked per day increased, the percentage of abnormalities determined by thoracic HRCT also clearly increased in many studies (9, 20, 23). According to the results found herein, there was no significant difference among the HRCT categories in the non-smokers. However, it was found that as the amount of smoking increased, the pathology categories increased. In the current study, abnormal HRCT findings were observed only in emphysema and bronchial wall thickening with obstructive PFT results. Therefore, it was observed that HRCT and PFT correlated significantly in terms of these 2 findings in smokers. However, other abnormal parenchymal changes observed in HRCT have been found to be significant in cases with normal PFT results.

This study had several limitations. First, this study was performed retrospectively. Second, the evaluation has conducted using the data of only 1 center, and a relatively small study group was evaluated; nevertheless, this was the most extensive review of the imaging findings of heavy smokers, in terms of the number of patients and imaging parameters from a radiological perspective to date.

Table 3. HRCT findings of patients with normal PFTs and obstructive PFTs

HRCT Findings	Normal PFTs (n=127)	Obstructive PFTs (n=28)	Overall statistics P Value
Emphysema	30 (23.6%)	15 (53.6%)	0.002
Ground-glass areas	10 (7.9%)	0	0.210
Bronchial wall thickening	49 (38.6%)	19 (67.9%)	0.005
Bronchiectasis	13 (10.2%)	7 (25%)	0.056
Atelectasis	86 (67.7%)	18 (64.3%)	0.727
Interlobular septal thickening	27 (21.3%)	2 (7.1%)	0.083
Sequel changes	88 (69.3%)	15 (53.6%)	0.111
<7 mm nodule	8 (6.3%)	2 (7.1%)	1.000
≥7 mm nodule	8 (6.3%)	3 (10.7%)	0.419

Abb. HRCT: High resolution computed tomography, PFT: Pulmonary function test

CONCLUSION

In conclusion thoracic HRCT is more sensitive than standard chest radiograms and PFTs in determining the early stages of parenchymal and interstitial abnormalities in the lung due to cigarette smoking. It is possible that smoking cessation treatment can be badly

affected and terminated without significant changes, especially on the PFTs of the patients who applied to smoking cessation clinics. Awareness of the typical imaging findings of heavy smokers on HRCT allows for early diagnosis and initiation of treatment, which includes essential agents, such as bronchodilators or steroids. The results herein confirmed that atelectasis, emphysema, and bronchial wall thickening were the most common imaging findings of heavy smokers. In addition, several imaging findings in smokers were observed that required clinical monitoring on HRCT, even though the chest radiograms and PFTs were normal. Therefore, it is recommended that imaging findings might prove to be an auxiliary tool in the early stages of parenchymal and interstitial abnormalities of the lungs due to smoking, despite normal chest radiograms and PFTs.

Informed Consent: Informed consent was obtained from patients who participated in this study.

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

Financial Disclosure: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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Cite as: Ozkale Yavuz O, Hekimoglu K, Coskun M, et al. High-Resolution Computed Tomography Findings In Healthy Heavy Smokers And Correlation With Pulmonary Function Tests. Eskisehir Med J. 2022;3(2):176-183.