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Visualized changes in respiratory resistance and reactance along a time axis in smokers: A cross-sectional study

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ABSTRACT

Background: Early detection of changes in respiratory function in smokers is important for the prevention of chronic obstructive pulmonary disease (COPD). The objective of this study was to investigate any changes in the respiratory impedance of smokers with normal FEV_1/FVC.
Methods: We assessed and compared the impedance components, respiratory resistance, and reactance in both the inspiratory and expiratory phases of nonsmokers, smokers, and COPD patients.
Results: Approximately 60% of smokers showed elevated resistance and a negative shift in reactance, mainly in the expiratory phase, as observed in COPD patients. Smokers showed an increased gap between the maximum and minimum R5 and X5 values (R5sub, X5sub) in comparison with nonsmokers. Furthermore, R5–R20 was significantly higher in smokers than in nonsmokers. The expiratory–inspiratory gaps in resistance and reactance were also significantly higher in smokers than in nonsmokers. In smokers and COPD patients, the magnitude of expiratory X5 was more negative than that in nonsmokers. In smokers with $\dot{V}50/\dot{V}25 \geq 3$, R5–R20 was significantly higher than those in smokers with $\dot{V}50/\dot{V}25 < 3$.
Conclusions: Approximately 60% of smokers were shown to exhibit apparent impedance changes despite having normal FEV_1/FVC values. Smoking-induced early remodeling of the small airways may be responsible for the observed changes in airway function of smokers. Further studies are necessary to determine if the change in respiratory impedance observed in smokers is an early indicator of COPD.

Abbreviations: COPD, chronic obstructive pulmonary disease; PFT, pulmonary function test; FOT, forced oscillation technique; Zrs, respiratory impedance; Xrs, respiratory reactance; Rrs, respiratory resistance; FEV_1, forced expiratory volume in 1 s; 3D, 3-dimensional; R5, Rrs at 5 Hz; R20, Rrs at 20 Hz; X5, Xrs at 5 Hz; R5sub, difference of R5 between maximum and minimum value; R5–R20 sub, difference of R5 between maximum and minimum value; X5sub, difference of X5 between maximum and minimum value; Fres, frequency of resonance; LABA, long-acting beta-agonist; ICS, inhaled corticosteroids; LAMA, inhaled long-acting muscarinic antagonist

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1. Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of death and disability worldwide [1]. In Japan, there are over 5 million people with COPD, and the high prevalence of smoking coupled with an aging population threatens to further increase the burden of COPD on the health care system, necessitating enhanced early screening efforts and interventions [2]. COPD is associated with an abnormal inflammatory response of the lung to noxious particles and gases, especially tobacco smoking. Airflow limitation in COPD is usually progressive and occurs earlier in smokers than in nonsmokers. Early detection of airway changes and cessation of smoking are indispensable for preventing COPD [3–5]. The internationally recognized gold standard for diagnosing COPD is the pulmonary function test using spirometry (PFT) [6]. However, airway disease is already apparent before FEV_1 levels decrease. Furthermore, PFT does not always reflect the real lung function, as measurement of forced expiratory vital capacity requires effort on the part of the patient.

Forced oscillation technique (FOT) is a non-invasive assessment of lung function that does not require any effort by the patient. It was developed to evaluate respiratory impedance (Zrs), which represents different aspects of the mechanical properties derived from spirometry. Small pressure oscillations are applied at the mouth under usual tidal breathing. The impulse oscillometry system is a modified method that uses FOT to assess respiratory reactance (Xrs) and resistance (Rrs), which together represent respiratory impedance [7]. This method is a very useful tool for examining airway diseases including COPD, as it is capable of evaluating Xrs and Rrs over a wide range of oscillatory frequencies. Previous studies using impulse oscillometry revealed that Xrs is closely related to other pulmonary functions [8]. Kurosawa and colleagues at Tohoku University recently developed a method to analyze the respiratory cycle dependency of Rrs and Xrs and assessed their frequency dependency using a FOT-based method, adding a time axis to the frequency and levels for visualization as a 3-dimensional (3D) graph [9]. This method is being utilized in the evaluation of airway diseases such as COPD and asthma [10].

We hypothesized that our novel approach of analyzing respiratory cycle dependency and frequency dependency in Zrs parameters can distinguish respiratory changes in smokers who do not meet the diagnostic criteria of COPD compared to nonsmokers. To evaluate the changes in airway function in smokers, we analyzed the time-dependent variations in impedance patterns, comparing the gaps in the fluctuations of parameters along the respiratory cycle while simultaneously measuring conventional impedance parameters.

2. Methods and materials

2.1. Subjects

Ninety-two former and current smokers and 16 healthy volunteers with no history of smoking (nonsmokers) were recruited for this study at Kobe University Hospital (Table 1). Of the 92 former and current smokers, 44 were diagnosed with COPD (stage I, $n=12$; stage II, $n=24$; stage III, $n=6$ and stage IV, $n=2$) according to the Global Initiative for Chronic Obstructive Lung Disease criteria [3]. Two subjects with COPD were being treated with long-acting beta-agonists, 14 were using inhaled corticosteroids, 18 were using inhaled long-acting muscarinic antagonist, 1 was using xanthines, and 29 had received no treatment for their COPD during the time of the study. The remaining 48 smokers had $FEV_1/FVC \geq 70\%$ in PFT. All COPD patients had a smoking history of at least 10 pack-years. All subjects were clinically stable and had no history of other lung diseases or lung resection. Subjects with an apparent history of obstructive diseases other than COPD were excluded from the study. All subjects gave written informed consent. The study was approved by The Ethics Committee of Kobe University (Approval period: June 15, 2009-March 31, 2012, IRB# 892).

2.2. Measurements of Rrs and Xrs

Using a commercial device (MostGraph-01; CHEST MI. Inc., Tokyo, Japan), we applied an intermittent hunning impulse signal with a loud speaker and recorded mouth pressure and flow while the subjects were breathing at rest for 30–60 s. The subjects remained in an upright position, wore a nose clip,

Table 1 – Anthropometric and pulmonary function data in nonsmokers, smokers, and COPD patients. Values are presented as means ± SD.

	Nonsmokers ($n=16$)	Smokers ($n=48$)	COPD ($n=44$)
Sex (M/F)	9/7	37/11	40/4
Age (yrs)	47±20	56±13*,**	69±9**,***
Height (cm)	163±11	166±8	164±8
Body weight (kg)	60±15	65±15	59±9
Smoking history (pack-years)	0	43.4±26.3	50.0±26.7
VC (L)	4.06±0.96	3.50±0.77	3.31±0.78
FEV1 (L)	3.27±0.93	2.69±0.57	1.90±0.62*
FEV_1 (%predicted)	97.1±10.9	93.7±12.1	70.2±19.2*
FEV_1/FVC (%)	81.9±2.0	78.0±5.0	58.0±10.0**,***
V50/V25	2.4±0.19	3.49±0.11**	3.70±0.17**

* $p<0.05$ and.
** $p<0.01$ versus nonsmokers.
*** $p<0.01$ versus smokers.