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Respiratory function in healthy ever-smokers is impaired by smoking habits in a dose-dependent manner

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ABSTRACT

Background: There is limited information about the respiratory function of ever-smokers without lung disorders. We sought to assess the effects of smoking habits on respiratory function in subjects without lung disorders.

Methods: Subjects were recruited from among patients without any evidence of respiratory disorders who visited rural primary care clinics. Each participant was asked to answer a questionnaire that included questions smoking history. Their forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) were measured.

Results: We analyzed 802 subjects (364 men and 438 women). The means of the lambda-mu-sigma method derived z-score of FEV1 (zFEV1) both in current-smokers and ex-smokers were lower than that in never-smokers. The mean zFEV1 in the ever-smokers with more than 30 pack-years of smoking history were lower than that in the ever-smokers with less smoking history. Univariate analysis showed that there were significant negative correlations between pack-years and zFEV1 both in the ex-smokers and current-smokers. There was no significant correlation between the duration of smoking cessation and zFEV1 in the ex-smokers.

Conclusions: Our data suggests that respiratory function in healthy ever-smokers is decreased based on smoking habits in a dose-dependent manner. Even after a long period of smoking cessation, the decreased respiratory function seems to be maintained in ex-smokers.

Abbreviations: FVC, forced vital capacity; FEV1, forced expiratory volume in one second; LMS, lambda-mu-sigma; zFEV1, LMS method derived z-score of FEV1; zFVC, LMS method derived z-score of FVC; zFEV1/FVC, LMS method derived z-score of FEV1/FVC; %FEV1, the percent predicted FEV; COPD, chronic obstructive pulmonary disease

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1. Introduction

Studies have shown that cigarette smoking is associated with impairment of respiratory function [1,2] and that smoking cessation reduces the decline in respiratory function [3–5]. Accordingly, the effects of smoking cessation on lung health have been emphasized.

Although a majority of smokers have chronic respiratory symptoms including chronic cough and sputum production, smoking habits may lead to clinically recognized chronic obstructive pulmonary disease (COPD) only in 15–20% of smokers [1,6]. Since many smokers have normal respiratory function throughout their lifetime, there are fewer studies on the lung health of apparently healthy ever-smokers. There is limited information on the respiratory function of asymptomatic ever-smokers with preserved pulmonary function assessed via spirometry; however, a recent study pointed out that there is potential risk of lung disorders in this group of patients [7]. Our understanding about the effects of smoking habits are still limited. The main aim of present study is to estimate the effects of the smoking habits on the respiratory function in subjects without lung disorders.

Recently, z-scores of spirometric values as calculated using the lambda-mu-sigma (LMS) method have emerged as a scientific tool for the diagnosis of lung disorders [8–10]. In 2014, the Clinical Pulmonary Functions Committee of the Japanese Respiratory Society updated the Japanese spirometric reference values using the LMS method [11]. In the present study, we used the LMS-derived z-score of forced expiratory volume in one second (FEV1) to estimate respiratory function.

2. Patients and methods

Subjects were recruited from among patients without any evidence of respiratory disorders who visited rural primary care clinics. Each subject was asked to answer a questionnaire that included questions to assess present health condition and smoking history. The subjects were selected based on their answers in the questionnaire and their medical records. The inclusion criteria for subjects were as follows: ambulant subjects with no underlying respiratory diseases and no respiratory symptoms within a month before the examination. The exclusion criteria were as follows: subjects with diseases potentially affecting respiratory function including cardiovascular diseases other than hypertension, motor-neuron diseases, chest-wall disorders, severe renal or liver dysfunction, and dementia or psychiatric disorders.

Ex-smokers were defined as subjects who had quit smoking at least 12 months prior to the study. Current-smokers were subjects who reported current smoking or quit smoking within 12 months. Ever-smokers refer to either ex-smokers or current-smokers. To evaluate the dose dependence of smoking, the ever-smokers were divided into three groups based on self-reported pack-years (low pack-years group: less than 10, mid pack-years group: greater than or equal to 10 but less than 30, high pack-years group: greater than or equal to 30).

Forced vital capacity (FVC) and FEV1 were measured in all subjects using a spirometer (Chestac Jr. 101, Chest, Tokyo) by standard methods [12]. We calculated LMS method derived z-scores for FEV1 (zFEV1), z-scores for FVC (zFVC) and z-score for FEV1/FVC (zFEV1/FVC) as: [(measured/median predicted) \widehat lambda-1] / (lambda X sigma). In the calculation, we used a public spreadsheet file for reference values for spirometry in Japanese adults [11]. In the present study, if participants had either zFVC or zFEV1/FVC less than -1.645, their data were excluded [9]. In addition, the percent predicted FEV1 (%FEV1) was used as a standard indicator of airflow limitation.

2.1. *Statistical analysis*

All statistical analyses were conducted using R version 3.3.2. Results are presented as mean ± standard deviation (SD). Differences in proportions were analyzed using the chi-square test or Fisher's exact test. Mean values were compared between two groups using Welch's t-test. Mean values were compared between more than two groups using one-way analysis of variance. Multiple comparisons were made when the F-test had statistically significant results. P values were adjusted for multiple comparisons using Tukey's honest significant difference method. Each correlation was estimated using univariate analyses. Analysis of covariance (ANCOVA) was used to assess the difference between regression lines. A two-sided P value <0.05 was the criterion for statistical significance.

The present study was approved by the Ethical Board of Asahikawa Medical University (Dec. 2, 2008, approval number 471) and were performed in accordance with the Declaration of Helsinki, 1964. Written informed consent was obtained from each participant.

3. Results

A total of 1021 subjects were initially enrolled, but 219 participants (117 men and 102 women) were excluded because at least one of their z-scores for FVC or FEV1/FVC was less than -1.645. Then, the data from 802 subjects (364 men and 438 women) were analyzed. The most frequent underlying diseases were hypertension (52.0%), diabetes mellitus (17.0%), and hyperlipidemia (16.4%). There was no significant difference in the prevalence of each disease among the groups. The characteristics of analyzed subjects are summarized in Table 1.

The current-smokers had longer smoking duration compared to the ex-smokers in both sexes (Table 2). There was no difference in pack-years between the current-smokers and the ex-smokers in both sexes. Both the mean duration of smoking and the mean pack-years in the male ever-smokers were significantly higher than those in the female groups. In the ex-smoker group, the mean duration after smoking cessation was 15.1 ± 12.5 years.

The mean %FEV1 in the current-smokers was lowest among the three groups. There was no significant difference in %FEV1 between the ex-smokers and the never-smokers (Fig. 1, upper panel). However, zFEV1 in the current-smokers

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