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Associations of lifelong cigarette consumption and hypertension with airflow limitation in primary care clinic outpatients in Japan

Harue Utsugi, M.D.[a], *Hidetoshi Nakamura, M.D., Ph.D.*[a,*], *Tomoko Suzuki, M.D., Ph.D.*[b], *Toshitaka Maeno, M.D., Ph.D.*[c], *Makoto Nagata, M.D., Ph.D.*[a], *Minoru Kanazawa, M.D., Ph.D.*[a]

[a]*Department of Respiratory Medicine, Saitama Medical University, 38 Morohongo, Moroyama-machi, Iruma-gun, Saitama 350-0495, Japan*
[b]*Department of Respiratory Medicine, Aizu Medical Center, Fukushima Medical University, 21-2 Kawato-machi, Yazawa aza Maeda, Aizuwakamatsu, Fukushima 969-3492, Japan*
[c]*Department of Respiratory Medicine, Gunma University Graduate School of Medicine, 3-39-15 Showa-machi, Maebashi, Gunma 371-8511, Japan*

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ABSTRACT

Background: Underdiagnosis is a critical problem in the management of chronic obstructive pulmonary disease (COPD). It is important to screen patients at risk for COPD among those with lifestyle-related diseases such as hypertension, diabetes mellitus, and dyslipidemia, since these diseases promote the development of cardiovascular diseases closely associated with increased COPD mortality.

Methods: Thirteen primary care clinics in a suburb of Tokyo participated in the current study. A total of 950 patients from these clinics were enrolled in the study between 2010 and 2012; the patients ranged in age from 40 to 79 years, and they had no diagnosed respiratory diseases at the time of enrollment. Patients fulfilling the selection criteria were recruited to undergo spirometry and then completed a self-report questionnaire about comorbid diseases and smoking habits. Spirometry was performed 15 min after inhalation of 200 μg of salbutamol sulfate.

Results: The prevalence of airflow limitation was 12.7% in the 950 primary care clinic patients. Lifelong cigarette consumption was the most significant risk factor for airflow limitation, e.g., patients who smoked 60 pack-years or more had a 40% likelihood of airflow limitation. Among common lifestyle-related diseases, hypertension was associated with the severity of airflow limitation ($p=0.03$), whereas dyslipidemia appeared to be inversely correlated with the severity of airflow limitation ($p=0.004$) on multiple regression analysis including lifelong cigarette consumption as a factor.

Conclusions: Undiagnosed airflow limitation was detected in 12.7% of outpatients at the primary care clinics. Since most patients with lifestyle-related diseases are treated by primary care physicians, it is essential for the physicians to obtain an accurate history of smoking and comorbid diseases to screen patients for COPD.

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1. Introduction

Chronic obstructive pulmonary disease (COPD) is caused mainly by cigarette smoking and characterized by progressive airflow limitation, and it is among the leading causes of mortality worldwide [1]. Patients with COPD also manifest systemic inflammation related to various comorbidities including cardiovascular disease, diabetes mellitus, osteoporosis, and weight loss [2], which potentially diminish their quality of life and increase their mortality [3,4]. Among the various comorbidities in patients with COPD, cardiovascular disease is of key importance, since the coexistence of COPD in patients with cardiovascular disease is known to increase symptoms, hospitalizations, and mortality [5]. Cardiovascular disease is also among the major causes of death in patients with COPD [6]. As underlying lifestyle disorders, hypertension, diabetes mellitus, and dyslipidemia are the most prevalent and have potent effects on the development of cardiovascular disease [7]. In Japan, these lifestyle diseases are usually treated in outpatient clinics by primary care physicians.

Underdiagnosis is a critical problem in the management of COPD. In a previous Japanese epidemiological study, the Nippon COPD Epidemiology (NICE) Study, it was reported that the prevalence of airflow limitation was 10.9% in subjects aged ≥ 40 years, while only 9.4% of subjects with airflow limitation had been diagnosed as having COPD [8]. In the presence of coexisting COPD, patients with lifestyle diseases may develop cardiovascular diseases, such as coronary artery disease, chronic heart failure, and arrhythmia, with higher mortality, as reported previously [9]. In addition, patients with these diseases treated by primary care physicians would be more likely to be referred to pulmonologists if risk factors for the presence of airflow limitation were clarified. In the present study, the prevalence of airflow limitation was evaluated in outpatients in whom no respiratory diseases had been diagnosed in primary care clinics, and the risk factors were examined.

2. Patients and methods

2.1. Study populations

Thirteen primary care clinics in the cities of Tsurugashima, Sakado, and Hidaka, located about 30 miles northwest of downtown Tokyo, participated in this study. Inclusion criteria were: (1) age range 40–79 years; (2) outpatients regularly treated by physicians; (3) absence of respiratory diseases including COPD, bronchial asthma, and lung cancer, as judged by the physicians and self-report questionnaires described below; and (4) willingness to undergo spirometry. A total of 969 patients were initially recruited into the study from 2010 to 2012. The study protocol was approved by the Institutional Review Board of Saitama Medical University Hospital (No. 10-014-1, June 15, 2010), and written informed consent was obtained from each participant. This study was registered with UMIN (UMIN000003718, July 1, 2010).

2.2. Spirometry and questionnaires

Spirometry was performed at the primary care clinics with the patient in a stable condition, 15 min after inhalation of 200 μg of salbutamol sulfate by the patient. The procedure was performed by expert technicians according to the American Thoracic Society protocols [10], using an electronic spirometer (Chestgraph HI-105, Chest MI Inc., Tokyo, Japan). Airflow limitation was defined as FEV_1 (forced expiratory volume in 1 s)/FVC (forced vital capacity) <0.70 after bronchodilation. The severity of airflow limitation was classified into grades I ($\%FEV_1 \geq 80$), II ($50 \leq \%FEV_1 < 80$), III ($30 \leq \%FEV_1 < 50$), and IV ($\%FEV_1 < 30$) in the presence of airflow limitation as reported in the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines [11]. Predicted values were derived from the guidelines for pulmonary function tests issued by the Japanese Respiratory Society [12]. Consecutive patients who had visited the clinics and fulfilled the study inclusion criteria described above were recruited by the physicians, underwent spirometry, and completed self-report questionnaires at the clinics including information on diseases under treatment and smoking histories ($n=969$). Nineteen patients were excluded due to comorbid respiratory diseases reported in the questionnaires, resulting in a final study population consisting of the remaining 950 patients. To further confirm the diagnoses of comorbid diseases and obtain accurate smoking histories, a second detailed self-report questionnaire including medications was distributed to all participants in 2013.

2.3. Statistical analysis

Data are presented as means ± standard deviations, unless otherwise stated. Between-group comparisons were made using the unpaired *t*-test. Differences between four or five groups were tested with analysis of variance followed by Scheffe's test. Frequencies between two groups were compared by the χ^2-test. Frequencies between four or five groups were compared by the Kruskal–Wallis test followed by the Mann–Whitney *U* test with the Bonferroni correction. Multivariate logistic regression analysis was conducted to examine independent contributions of factors to the presence of airflow limitation or grade II/III severities. Multiple regression analyses were performed to examine covariates, including age, lifelong cigarette consumption, and the presence of

Abbreviations: COPD, chronic obstructive pulmonary disease; NICE, Nippon COPD Epidemiology; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; GERD, gastroesophageal reflux disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein

*Corresponding author. Tel./fax: +81 49 276 1319.
E-mail addresses: uharue@saitama-med.ac.jp (H. Utsugi), hnakamur@saitama-med.ac.jp (H. Nakamura), suzukito@fmu.ac.jp (T. Suzuki), mutoyu03@gunma-u.ac.jp (T. Maeno), favre4mn@saitama-med.ac.jp (M. Nagata), mkanazaw@saitama-med.ac.jp (M. Kanazawa).