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Clinical differences in the Global Initiative for Chronic Obstructive Lung Disease Stage 0

Kenji Tsushima[a,b,*], Shusuke Sone[a], Sumiko Yoshikawa[b], Shino Furuya[b], Masanori Yasuo[b], Toshirou Suzuki[b], Yoshitaka Yamazaki[c], Tomonobu Koizumi[a], Keisaku Fujimoto[b], Keishi Kubo[b]

[a]*Azumi General Hospital, 3207-1 Ikeda-machi, Kitaazumi-gun 399-8695, Japan*
[b]*First Department of Internal Medicine, Shinshu University School of Medicine, 3-1-1 Asahi, Matsumoto 390-8621, Japan*
[c]*Division of Endoscopy, Shinshu University School of Medicine, 3-1-1 Asahi, Matsumoto 390-8621, Japan*

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Summary This study was to examine the clinical differences between Stage 0 and normal subjects, using low-dose chest computed tomography (CT) and pulmonary function tests. Enrolled subjects performed as a health check for lung cancer screening including low-dose CT and pulmonary function tests. Subjects were divided into Stage 0, chronic obstructive pulmonary disease according to pulmonary function tests, and normal subjects. The severity of emphysema (visual score) was calculated on three low-dose CT slices. Low-dose CT and pulmonary function tests were performed in 1359 men and 888 women. The numbers and percentages of men and women smokers were 1076 (79.2%), and 107 (12.0%), respectively. A total of 722 individuals had one or more respiratory symptoms, such as cough (69.8%), sputum (75.8%), or shortness of breathing (0.83%). Of the 722 subjects, 71 (9.8%) individuals satisfied the criteria of chronic respiratory symptoms. Among the normal subjects, smoking caused differences in airflow limitation as a result of pulmonary function tests. The proportion of smokers and the visual score were significantly higher in Stage 0 than those in the normal subjects. The percentages of the maximal mid-expiratory flow (%MMF) and of the peak expiratory flow rate were significantly lower in Stage 0 than in the normal subjects. %MMF and the proportion of visual score were significantly lower in the smoking Stage 0 than in the nonsmoking Stage 0 subjects. Smoking would indicate early signs of emphysematous change between Stage 0 and normal subjects in comparison of pulmonary function tests and visual score of low-dose CT.

*Corresponding author. Azumi General Hospital, 3207-1 Ikeda-machi, Kitaazumi-gun 399-8695, Japan. Tel.: +81 263 37 2631; fax: +81 263 36 3722.
E-mail address: tsushima@hsp.md.shinshu-u.ac.jp (K. Tsushima).

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Introduction

Chronic obstructive pulmonary disease (COPD) has been forecast to be the third leading cause of death in the world by 2020 because of the global increase in smoking.[1] Recently, a Japanese epidemiological study indicated that over 5,300,000 Japanese people (approximately 8.5% of the total population) may suffer from COPD.[2] However, the number of patients receiving treatment for COPD was only approximately 210,000. Many people who develop COPD are smokers, and their pulmonary function decreases more rapidly than that of nonsmokers.[3,4] COPD is normally diagnosed by pulmonary function tests, which are often used for the initial diagnosis and assessment of severity of emphysema. However, COPD is an insidious disease, with many years intervening between the development of pulmonary dysfunction and the onset of serious respiratory symptoms, such as severe breathlessness.

Many studies have indicated that smoking is the major environmental factor contributing to the decrease in pulmonary function. Passive exposure to cigarette smoke may also contribute to respiratory symptoms and COPD by increasing the lung's total burden of inhaled particulates and gases.[5] Cessation of cigarette smoking does not necessarily result in the recovery of the level of pulmonary function but it is associated with slower rates of decline in pulmonary function.[6,7] Moreover, cessation of cigarette smoking can improve the survival prospects of middle-aged smokers over the entire range of pulmonary function.[8] Smoking reduction meaning a reduction in the number of cigarettes smoked per day; however, this is associated with a small increase in risk as compared with sustained heavy smokers.[9]

Cigarette smoke has direct toxic effects on bronchial epithelial cells and alveoli, and the pathological changes include mucus hypersecretion, ciliary dysfunction and airflow limitation. Mucus hypersecretion and ciliary dysfunction are related to chronic cough and sputum production. These symptoms are often present for many years before the development of other more serious symptoms (shortness of breath, dyspnea) or pathological abnormalities. The classification of severity based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) includes Stage 0, which includes subjects at risk of developing COPD late in life.[10] Subjects in the Stage 0 group complain of chronic cough and sputum production but have no airflow obstruction, as defined by a decrease in forced expiratory volume in 1 s (FEV_1). Active smoking is strongly associated with chronic cough and sputum production. Therefore, the most effective intervention is to stop smoking, preferably at an early stage, such as of Stage 0.[3]

Screening the general population for the respiratory symptoms of Stage 0 is effective but not feasible in the daily routine of a general practice. However, Stage 0 includes patients with other respiratory diseases, such as bronchial asthma, chronic bronchitis, etc. As a result, many individuals who have other underlying diseases are included in Stage 0. It is necessary to promote the cessation of smoking as a means of early intervention in Stage 0 subjects. The present study was performed to examine the clinical differences between Stage 0 subjects, i.e., those defined as "at risk" of COPD and normal subjects, using clinical information, low-dose chest computed tomography (CT) scan and pulmonary function tests.

Materials and methods

Our research protocol, including the use of low-dose CT and pulmonary function tests, was approved by the human ethics committee of Azumi General Hospital.

Subjects

During our health-screening program for the detection of lung cancer (February 1, 2003, to January 31, 2004), enrolled individuals, who participated after lung cancer screening was publicized in our community, received a general health check including a low-dose chest CT scan and pulmonary function tests. They were also representative of the general population in that they included a highly motivated group of individuals who had some reason to worry about lung cancer. The enrolled individuals were from the general population of the Azumi or Kouhoku area around Azumi General Hospital, or belonged to an agricultural cooperative association in Nagano Prefecture. There were no selection criteria such as age, smoking history, occupation or symptoms. Low-dose chest CT scan was performed to detect lung cancer. All individuals gave their informed consent at presentation for chest CT scan and pulmonary function tests. They first underwent a low-dose chest CT and pulmonary function tests were performed. The subjects filled out a questionnaire about lifestyle, respiratory symptoms, smoking history, past histories and demographic data as of the health-screening program. The information was entered into a database. Questions about respiratory