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PREVALENCE OF AIRFLOW LIMITATION IN PRIMARY CARE CLINICS IN AKITA PREFECTURE

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Abstract

Background : The prevalence of chronic obstructive pulmonary disease (COPD) continues to increase worldwide. However, it is often undiagnosed in primary care clinics due to the insufficient use of spirometry.

Objectives : Screening spirometry of patients who attended primary care clinics was performed to estimate the prevalence of airflow limitation in general clinics in Akita prefecture.

Methods : A total of 1,135 patients 40 years of age and older, who attended general clinics in Akita prefecture, were enrolled in this study. We defined airflow limitation as forced expiratory volume in one second (FEV1) over forced vital capacity (FVC) (FEV1/FVC) < 70% in patients without active pulmonary disease. Patients with possible asthma were excluded according to history of bronchial asthma, symptoms specific to asthma, and answers to a patient characteristic questionnaire.

Results : Of the patients in primary care clinics who were 40 years of age or older, prevalence of airflow limitation was 9.2%, of which 88% were undiagnosed as COPD in Akita prefecture. Thus, the widespread use of spirometry in general clinics and improved hospital and clinic cooperation are warranted to reduce the number of undiagnosed COPD cases. Furthermore, we demonstrated that patients with gastric ulcers had a high prevalence of airflow limitation.

Key words : airflow limitation, COPD, prevalence, NICE study, primary care clinics

Introduction

Chronic obstructive pulmonary disease (COPD) is a common preventable and treatable disease characterized by a persistent airflow limitation, which is usually progressive and associated with an enhanced chronic inflammatory response in the airways and lungs to noxious particles or gases[1)]. The prevalence and mortality rate of COPD have increased worldwide in recent years. According to the World Health Organization, COPD is predicted to be the third most common cause of death worldwide by 2030[2)]. The Nippon COPD Epidemiology (NICE) study[3)], performed in 2004, determined that 8.6% of individuals in Japan aged ≥ 40 years had COPD, which is equal to approximately 5.3 million patients. However, only 220,000 patients are actually treated for COPD in primary care clinics and hospitals nationwide. One of the reasons underlying this level of underdiagnosis is that spirometry, which is indispensable for COPD diagno-

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sis, is not widely available.

Akita prefecture is one of the region with the highest aging rate in Japan. The prevalence of COPD in Akita prefecture, where spirometry is not commonly performed in primary care clinics, remains unclear[4]. The specific aims of this study were to determine the prevalence of airflow limitation using spirometry among patients attending primary care clinics in Akita prefecture ; and to determine any common underlying diseases in patients with airflow limitations in primary care clinics. We also compared standardized prevalence of airflow limitation in Akita prefecture with that presented in the NICE study. This is the first spirometry-based epidemiological study to examine the prevalence of airflow limitation in primary clinics in Akita prefecture.

Methods

Study participants

This study was conducted in patients who visited 1 of 16 primary care clinics in Akita prefecture, Japan, from September 2007 to March 2008. All doctors were trained cardiologists. Inclusion criteria were ≥ 40 years of age, patients able to undergo spirometry, and patients able to provide informed consent. Technicians were allocated to each clinic for 5 days per clinic to assess spirometry and assist the completion of self-reported questionnaires on age, sex, smoking status, pulmonary past history, underlying diseases and treatment, respiratory symptoms (cough, sputum, shortness of breath on exertion, and wheeze), and risk of dust inhalation. Exclusion criteria were previous treatment for COPD or bronchial asthma, presence of bloody sputum, diagnosed pneumothorax, previous cardiac problems (e.g., arrhythmia and angina), history of surgery to the thorax or stomach in the past year, and active pulmonary disease including tuberculosis. This study was approved by the Ethics Committee of Akita University Graduate School of Medicine (No. 430 ; May 30, 2007).

Spirometry

Spirometry was performed with a portable spirometer (CHESTGRAPH HI-101®, Chest MI, Inc., Tokyo, Japan), which was also used in the NICE study. All patients were asked to perform a forced vital capacity (FVC) test at least three times, and the highest FVC and forced expiratory volume in 1 s (FEV1) values were recorded. In this study, airflow limitation was defined as airflow limitation (FEV1/FVC) < 70%. The severity of airflow limitation was classified according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) severity criteria[5]. Patients with possible asthma were excluded according to previous history of bronchial asthma, symptoms particular to asthma (paroxysmal breathing difficulty and wheezing at night), and responses to the patient characteristic questionnaire.

Statistical analyses

The results are expressed as means ± standard deviations (SDs). Associations between underlying diseases

Table 1. Comparison of patient characteristics between the NICE study and the survey of subjects

		NICE	Akita
Number of patients		2,343	1,135
Sex	male	1,218 (52.0%)	514 (45.3%)
	female	1,125 (48.0%)	621 (54.7%)
Age(years)		58	66.6 ± 11.1
	40-49	660 (28.2%)	94 (8.3%)
	50-59	675 (28.8%)	221 (19.5%)
	60-69	599 (25.6%)	293 (25.8%)
	70+	409 (17.5%)	527 (46.4%)
Smoking status			
	current smoker	707 (30.2%)	158 (14.0%)
	ex-smoker	533 (22.7%)	308 (27.1%)
	never smoker	1,103 (47.1%)	669 (58.9%)
Pack-years			
	0-24	1,633 (69.7%)	858 (75.6%)
	25-49	493 (21.1%)	179 (15.8%)
	59+	217 (9.2%)	98 (8.6%)
airflow limitation		256 (10.9%)	138 (*9.2%)
diagnosed		10%	12%
undiagnosed		90%	88%

*Standardized according to age and sex based on the 2005 census. NICE study, the Nippon COPD Epidemiology study

and airflow limitation were examined using logistic regression analyses, and odds ratios (ORs) and 95% confidence intervals (95% CIs) for the prevalence of airflow limitation were calculated. A P value < 0.05 was considered statistically significant. Differences of prevalence ratio between our study and NICE study were examined using chi test. The prevalence of airflow limitation was standardized according to age and sex based on 2005 census data.

Results

A total of 1,135 subjects were enrolled. The mean age of the subjects was 66.6 ± 11.1 years. The patient characteristics are shown in Table 1. Of the 1,135 subjects surveyed, 138 (12.2%) were confirmed to have airflow limitations. When standardized according to age and sex based on 2005 census data, the prevalence of COPD was 9.2%.

The details of prevalence of airflow limitation and its odds ratio analyzed for age, gender, smoking status or pack-years are shown in Table 2. The proportion of patients with airflow limitations increased with age (3.1% in subjects aged 40-49 years vs 16.3% in subjects over 70 years). The prevalence of airflow limitation was much higher in males than females (12.9% vs 6.0%, respectively). The distribution patterns of prevalence of airflow limitation by age and gender were similar between this study and NICE study (Fig. 1, Fig. 2, Table 2).

On the other hand, the prevalence of airflow limitation by smoking status was different between this study and NICE study. In this study, the prevalence in current smokers, ex-smokers and never smokers was 21.3%, 9.3% and 4.7%, respectively, whereas that in NICE study was 15.4%, 15.6% and 6.1% (Fig. 3, Table 2). The prevalence of airflow limitation in this study compared to that in NICE study was significantly higher in current smokers with OR of 1.55 (95% CI : 1.01-2.37, P=0.04), and significantly lower in ex-smokers with OR of 0.56 (95% CI : 0.36-0.89, P=0.01) (Fig. 4, Table 2). Furthermore, according to analysis by smoking index, a rapid increase in the prevalence rate was observed in this study espe-

Table 2. Prevalence of airflow limitation and odds ratios

	No of Pt	No of AFL	*Prevalence of AFL (95%CI)	Odds ratio	95%CI
	1,135	138	9.2% (7.6, 10.9)		
Age(years)					
40-49	94	3	3.1% (0.0, 6.7)	ref	ref
50-59	221	12	5.4% (2.5, 8.3)	1.74	0.14-9.83
60-69	293	34	11.8% (8.1, 15.5)	3.98	1.20-20.70
70＋	527	89	16.3% (13.2, 19.3)	6.16	1.97-31.07
Sex					
Male	514	92	12.9% (10.0, 15.7)	2.73	1.85-4.06
Female	621	46	6.0% (4.2, 7.8)	ref	ref
Smoking status					
current smoker	158	41	21.3% (13.1, 29.5)	4.75	2.89-7.74
ex-smoker	308	51	9.3% (4.1, 14.6)	2.69	1.72-4.20
never smoker	699	46	4.7% (3.0, 6.4)	ref	ref
Pack-years					
0-24	858	62	5.3% (3.9, 6.8)	ref	ref
25-49	179	41	23.1% (8.8, 3.41)	3.81	2.40-6.00
50＋	98	35	60.2% (54.5, 65.9)	7.31	4.22-11.89

*Standardized according to age and sex based on the 2005 census. AFL, airflow limitation 95% CI, 95% confidence interval

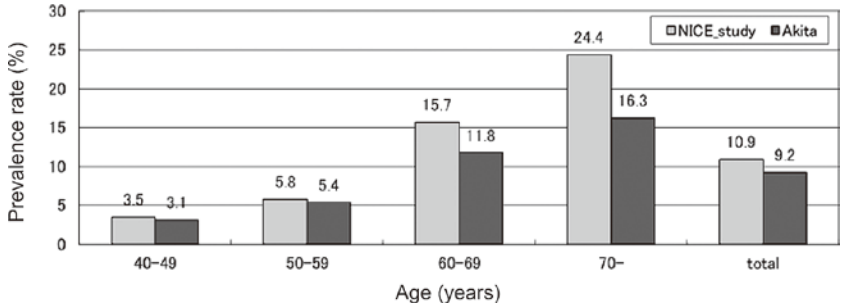

Fig. 1. Prevalence of airflow limitation according to age (comparison with the NICE study).
NICE study, the Nippon COPD Epidemiology study

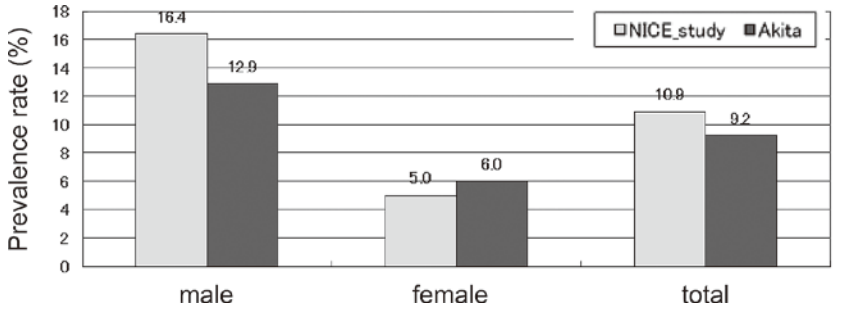

Fig. 2. Prevalence of airflow limitation according to sex (comparison with the NICE study).
NICE study, the Nippon COPD Epidemiology study

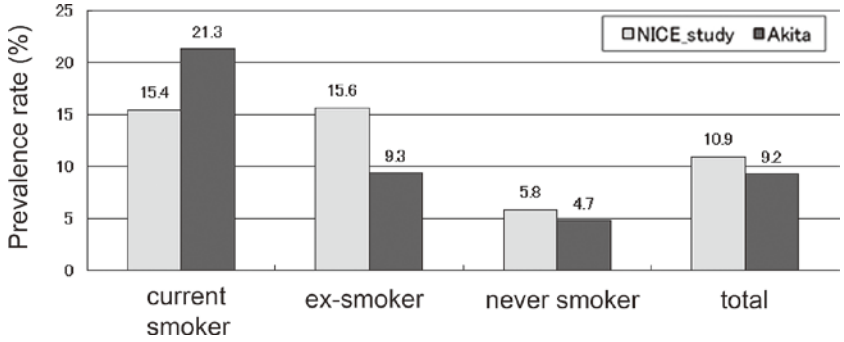

Fig. 3. Prevalence of airflow limitation according to smoking status (comparison with the NICE study).
NICE study, the Nippon COPD Epidemiology study

cially with a 50 pack-years or more, which showed significant increase compared to that in NICE study with OR of 3.32 (95% CI : 2.04-5.39, $P<0.0001$).

The severity of airflow limitation was classified according to GOLD criteria, as follows : mild (%FEV1 ≥ 80%), moderate (50% ≤ %FEV1 < 80%), severe (30% ≤ %FEV1 < 50%), and very severe (%FEV1 < 30%)[5]. The percentage of patients with mild, moderate, severe, and very severe airflow limitation was 50%, 42.8%, 7.2%, and 0%, respectively (Fig. 5). The proportion of severity in this study was compatible with that in NICE study (56%, 38%, 5%, and 1%, respectively).

Only 12% (NICE 10%) of subjects with airflow limitations had already been diagnosed with COPD (Fig. 6),

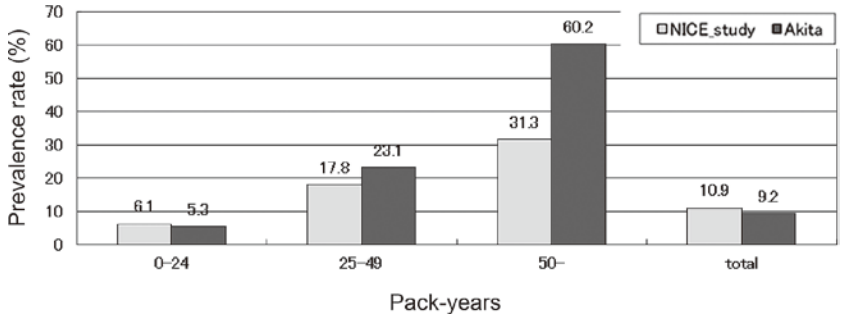

Fig. 4. Prevalence of airflow limitation according to smoking index (comparison with the NICE study).
NICE study, the Nippon COPD Epidemiology study

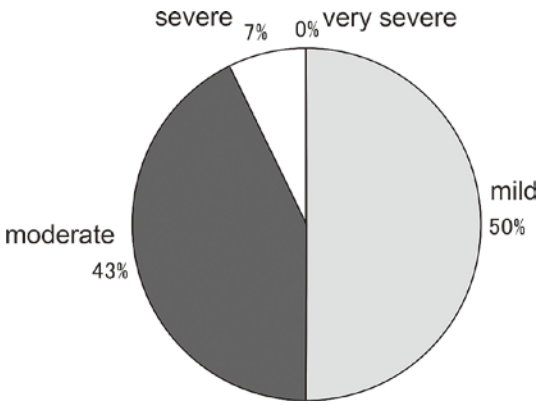

Fig. 5. Airflow limitation severity according to GOLD criteria.
GOLD, Global Initiative for Chronic Obstructive Lung Disease

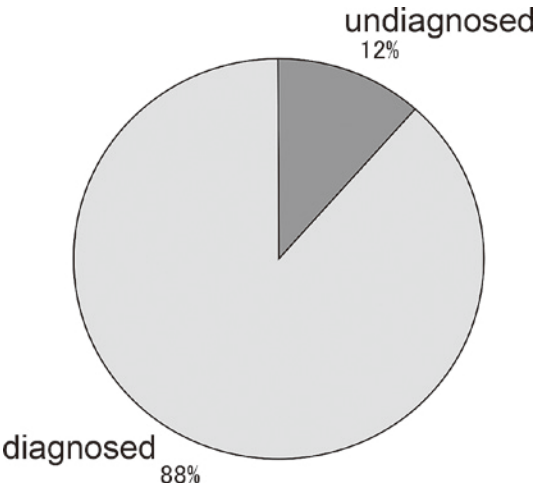

Fig. 6. Percentage of COPD patients who had been previously diagnosed.

yielding a low diagnostic rate, similar to that of the NICE study.

In patients with airflow limitations, shortness of breath was the most common symptom followed by sputum, wheeze, and cough. The OR for airflow limitation by symptom number was as follows: one symptom, OR=1.44 (95% CI: 0.96–2.16), two symptoms, OR=3.64 (95% CI: 2.37–5.59), three symptoms, OR=4.41 (95% CI: 2.41–8.08), and four symptoms, OR=5.84 (95% CI: 3.27–10.42). Patients with two or more symptoms had a significantly higher risk of acquiring airflow limitation. When the prevalence of airflow limitation was analyzed according to the type of underlying disease present, the only significantly high OR was found for gastric ulcer (OR 4.39, 95% CI: 1.43–12.31) among the following condi-

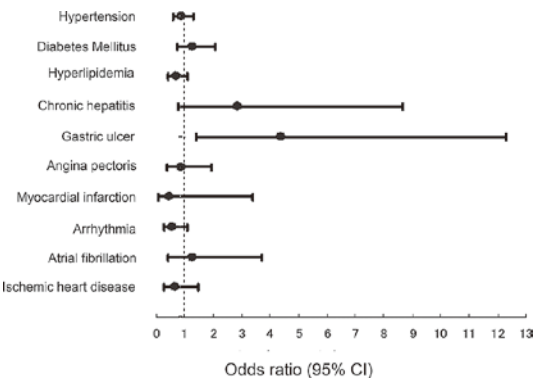

Fig. 7. Odds ratio of underlying diseases in patients with airflow limitation.
95% CI, 95% confidence interval

tions : hypertension, diabetes mellitus, hyperlipidemia, chronic hepatitis, gastric ulcer, angina pectoris, myocardial infarction, arrhythmia, atrial fibrillation, and ischemic heart disease (Fig. 7).

Discussion

This is the first spirometry-based epidemiological study to examine the prevalence of airflow limitation in primary care clinics in Akita prefecture. The prevalence of COPD was 9.2% (standardized according to age and sex based on 2005 census data) in patients from primary care clinics who were 40 years or older in Akita prefecture. This study demonstrated that screening spirometry in a primary care setting can detect undiagnosed cases of airflow limitation. The prevalence of airflow limitation in our study was almost equal to that of the NICE study (unadjusted prevalence of 10.9%)[3]. Moreover, the prevalence of COPD in patients who attended general clinics in Nagasaki prefecture (13.6%)[6] and Wakayama prefecture (10.3%)[7] was similar to that in our study.

Smoking is a major risk factor for COPD, and aging increases its prevalence, which is in line with the results of our study, as the prevalence of airflow limitation increased with age in our participants. The prevalence of COPD in patients > 80 years of age was 16.9%[8], which is higher than that in our study and others[6,7] in patients > 40 years old. This suggests that there might be a high percentage of undiagnosed COPD cases in the elderly population. The prevalence of airflow limitation was higher in heavy smokers, and the prevalence also increased in those with a history greater than 25 pack-years. In current smokers, ex-smokers, and never smokers, the airflow limitation prevalence rate was 21.3% (NICE 15.4%), 9.3% (NICE, 15.6%) and 4.7% (NICE 5.8%), respectively. The OR for airflow limitation by smoking status of this study compared to NICE study was significantly higher in current smokers, and significantly lower in ex-smokers. The fact that airflow limitation prevalence is lower in ex-smokers than in current smokers indicates the potential effects of smoking cessation on COPD. In this study, the prevalence of COPD and OR in current smokers and heavy smokers with a smoking history greater than 50 pack-years was significantly higher than that in the NICE study. It suggests that smokers in this study are more sensitive to cigarette smoke than that in NICE study.

Systemic inflammation may be involved in the pathogenesis of COPD[9-11]. COPD patients are at increased risk for several comorbidities including myocardial infarction, osteoporosis, depression, and diabetes[1]. However, it is still unclear whether such diseases affect the prevalence of COPD. Therefore, it is important to clarify the correlation between the prevalence of COPD and other diseases. In this study, we demonstrated that patients with gastric ulcers had a high prevalence of airflow limitation. The relationship between emphysema, peptic ulcers, and smoking has previously been highlighted[12]. Indeed, hypoxemia and hypercapnia, which are latent in pulmonary emphysema and chronic bronchitis, may be associated with ulcer formation[13]. It has also been shown that gastric mucosal disorders are induced by hypoxic exposure in rats[14], and that the pH of the gastric mucosa is lowered by inhalation of carbon dioxide in healthy subjects[15]. Thus, respiratory function deterioration and hypoxemia may be related to gastrointestinal mucosal disorders. Moreover, an epidemiological investigation using a questionnaire developed in the Netherlands showed that 21 (7.2%) of 290 patients with chronic airflow limitations had a comorbid peptic ulcer (OR 7.33, 95% CI : 2.41-22.25)[16].

According to the demographic statistics of the Ministry of Health, Labor and Welfare[17], the mortality rate in patients with COPD in Akita prefecture was 11.9 per 100,000 in 2014, which is lower than the national average (12.9 per 100,000). On the other hand, lung cancer mortality was 74.4 per 100,000 in Akita prefecture, which is higher than the national average of 58.5 per 100,000. Smoking is the major risk factor for both lung cancer and COPD, but there is a large difference in the mortality rate of the two diseases, which may potentially be caused by the low rate of COPD diagnosis in Akita prefecture. The screening protocol for lung cancer is well established, including medical checkups and chest X-rays. On the other hand, performing spirometry, which is necessary to diagnose COPD, is difficult in the medical checkup setting, unless it is done as part of a comprehen-

sive health examination[18].

In this study, we performed spirometry on patients already being treated for other diseases at general health clinics. Of these patients, approximately 10% had airflow limitation, of which 88% were undiagnosed as COPD. In addition, GOLD severity was mild in 50% of patients and moderate in 43% of patients, in total approximately 90% of patients are in the early stage of COPD. Patients in the early stage of COPD have few or no respiratory symptom. Therefore, COPD is underdiagnosed by physicians and derecognized by patients. Our results suggest that widespread use of spirometry for primary care clinics in Akita prefecture is necessary, including referral of patients with suspected COPD to hospitals in a model of "hospital and clinic cooperation." In addition, awareness of COPD is needed, focusing on those who are over 40 years old, who have a history of smoking, and who have respiratory symptoms[19]. The Ministry of Health, Labor and Welfare aims to set the recognition level of COPD, which was 25% in 2011, to 80% by 2022. To achieve this goal, respiratory physicians must partake in educating the public through such things as public lectures. Because COPD is thought to be a preventable and treatable disease, early diagnosis promotes early intervention before the burden of COPD on society can become more substantial. Recent publications demonstrate that early interventions can reduce declines in FEV1[20]. Therefore, ensuring earlier diagnosis and interventions may improve the prognosis of COPD and associated comorbidities and reduce the disease burden of COPD on society.

There were some limitations to this study. First, spirometry was only performed in a pre-bronchodilator condition because the inhalation of bronchodilators was not allowed in patients without respiratory diseases at primary care clinics. Therefore, we may have overestimated the prevalence of COPD. Next, the prevalence of bronchial asthma and smoking history was determined using only a self-administered questionnaire. Our inclusion criteria do not completely exclude the possibility that some asthmatic individuals and patients with other obstructive lung diseases, such as diffuse panbronchiolitis, were included in this study.

In conclusion, 9.2% of the patients in Akita prefecture primary care clinics who were 40 years or older had airflow limitation, of which 88% were undiagnosed as COPD. Our results suggest that widespread use of spirometry in primary care clinics as well as cooperation between hospitals and clinics are warranted to reduce the number of undiagnosed COPD cases. Furthermore, we demonstrated that patients with gastric ulcers had a high prevalence of airflow limitation.

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