Prevalence of Airflow Limitation in Patients Diagnosed and Treated for Symptoms of Chronic Bronchitis by General Practitioners in Tochigi Prefecture, Japan

Kazuyuki Chibana¹, Yoshiki Ishii¹, Yukitaka Anraku² and Takeshi Fukuda¹

Abstract

Objective Physicians have provided care to only 0.2 million of the 5.3 million Japanese over the age of 40 years old who have chronic obstructive pulmonary disease (COPD). Among such individuals, many patients with respiratory symptoms diagnosed as chronic bronchitis (CB) are prescribed mainly expectorants. To determine the current status of COPD subjects diagnosed with and treated for CB, we investigated the prevalence of airflow limitation (AFL) in CB patients diagnosed by general practitioners (GPs) and the therapies administered to them.

Methods Patients receiving treatment by GPs as CB completed a questionnaire and the FEV₁/FEV₆ ratio was measured by their GPs with a Piko-6. The prevalence of AFL (FEV₁/FEV₆ < 73%) and the correlation between FEV₁/FEV₆ and FEV₁/FVC were examined. Prescription behavior and comorbid lifestyle diseases were also examined.

Results Data from 197 patients with CB were analyzed. Among those who underwent spirometry, the correlation between FEV₁/FVC and FEV₁/FEV₆ was $r^2=0.38$ (p<0.0001), and the sensitivity and specificity of the Piko-6 were 85.7% and 61.1%, respectively. The prevalence of AFL was 47.2% and increased to 54.1% among patients aged 70-79 years. Expectorants were prescribed for 39.8% of CB patients with AFL, but inhaled bronchodilators were prescribed for only 22.6%. Smoking history and age were significantly higher in the group with AFL than in those without AFL (p<0.05). The prevalence of comorbid lifestyle diseases was 73.1% in patients with AFL.

Conclusion AFL was prevalent among patients with CB. Therefore, GPs should test pulmonary function in CB patients to ensure that the appropriate therapy is administered.

Key words: chronic bronchitis, airflow, pulmonary function

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Introduction

Chronic obstructive pulmonary disease (COPD) is an inflammatory disease of the lungs that occurs as a result of long-term exposure to inhaled noxious agents, primarily tabacco smoke. The NICE study estimated that 5.3 million Japanese over 40 years of age have COPD; the prevalence of COPD is 10.9% in the general population and 8.6% if asthma is excluded (1). However, a statistical survey conducted by the Ministry of Health, Labour, and Welfare (MHLW) of Japan indicated that only 223,000 COPD patients were actually treated or under the care of a physician (2). According to a survey of prescription behavior for respiratory diseases, chronic bronchitis (CB), emphysema, and COPD (ICD-10 J42, J43, and J44), outside Japan COPD and emphysema patients accounted for 50% of the patients receiving prescriptions, while CB patients accounted for less than 20%. In Japan, however, the corresponding percentages were 20% and 60% (Copyright 2011 IMS Japan K.

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Table 1. Questionnaire

1). I have had a chronic cough for 3 months.
2). I have had chronic sputum for over 3 months.
3). My common cold symptoms are usually prolonged. I am taking medicine to cough up sputum.
4). I am taking medicine to cough up sputum.
5). I have been diagnosed with chronic bronchitis before.
6). I feel an increased shortness of breath, when I go up stairs or when I walk at the same speed with people of the same age.

K. Based on MDI 2007 Dec MAT. Used with Permission). Recently, Murata et al identified 3,219 patients with CB, emphysema, and COPD from a large-scale insurance billing database (about 330,000 registered patients) in Japan (3). Their study revealed noteworthy findings: CB was diagnosed in 2,440 patients, accounting for 75.8% of all patients included in the analysis, but only 7.4% of the CB patients had actually undergone a pulmonary function test. Of all medications prescribed for these CB patients, expectorants accounted for 46.6%. As for bronchodilators, xanthenes (13.0%) were the most frequently prescribed medication, followed by β,-agonists, including transdermal formulations (18.0%). Long-acting inhaled β,-agonists accounted for only 2.3% and inhaled anticholinergics a mere 1.1%. The most likely reasons for such low rates of testing for pulmonary function and prescription of bronchodilators are that spirometry is not widely performed by general practitioners (GPs) in Japan and patients do not seek medical attention because of mild symptoms. Moreover, the prevalence of air-flow limitation (AFL) in patients diagnosed with CB by GPs remains unclear.

The objective of this study was to investigate the prevalence of AFL in patients diagnosed with CB by GPs, by asking GPs to use a simple device to test pulmonary function, the Piko-6 peak flow meter, (Ferraris Co., London, UK). To ensure patients receive the most appropriate therapy for their disease, the ultimate goal is to use the data from this study to make GPs aware of the necessity to differentiate COPD from CB at diagnosis.

Materials and Methods

This was a multi-center collaborative study conducted from December 2008 to June 2009 that involved mainly GPs who were members of the Tochigi Prefecture Shimotsugagun City Medical Association. Data collected from the study were analyzed by the Department of Pulmonary Medicine and Clinical Immunology of Dokkyo Medical University School of Medicine. The study protocol was approved by the Ethics Committee of Dokkyo University School of Medicine and the Administrative Board of Shimotsugagun City Medical Association before commencing the study.

Inclusion criteria were as follows: 1) age over 40 years, 2) provision of written informed consent, and 3) meeting the following criteria for simple pulmonary function testing with a Piko-6 peak flow meter: (i) diagnosis of CB confirmed based on information provided in the patient self-report questionnaire and the physician’s judgment and (ii) ability to undergo the pulmonary function test. Exclusion criteria were as follows: 1) hemoptysis, 2) history of pneumothorax, 3) symptomatic heart disease, 4) nausea, 5) cyanosis or severe breathlessness, 6) acute exacerbation of respiratory disease, 7) history of aneurysm in the lungs or brain, 8) history of ocular surgery (cataract) in the previous year, 9) history of chest or stomach surgery in the previous year, 10) tuberculosis (active) or apparent sequelae of tuberculosis, 11) history of lung cancer, 12) history of lung resection, 13) cystic fibrosis or history of other types of pulmonary fibrosis, or 14) unsuitability for pulmonary function testing as judged by the attending physician.

In this study, patients who satisfied any of the following criteria, based on information provided in the questionnaire, were confirmed to be diagnosed with CB: 1) chronic cough lasting for at least 3 months, 2) chronic sputum production lasting for at least 3 months, 3) persistence of symptoms after catching a cold, 4) use of expectorants, 5) suspected of having previous CB or 6) diagnosed with CB by a physician.

The patients were asked to complete a questionnaire and FEV1/FEV6 was measured with the Piko-6 by their GP. The questionnaire was conducted in Japanese, however it was translated into English and is shown in Table 1. The prevalence of AFL (FEV1/FEV6 ratio <73%) in this study population was then determined. Spirometry was performed at clinics where this test could be carried out, and the correlation between the results of the Piko-6 test and those of spirometry were analyzed to determine the sensitivity and specificity of the Piko-6 test. Furthermore, the frequency of the use of expectorants and bronchodilators was determined to clarify the type of therapies provided, while smoking history and age were compared between groups with and without AFL.

In addition, the prevalence of comorbid lifestyle diseases was determined for all CB patients and for the subgroup with AFL.

Statistical analysis was performed with Excel 2008 and JMP 8.0 to obtain Pearson’s correlation coefficients. Mean values were compared between the two groups by analysis of variance (ANOVA), and differences with a p value of <0.05 were considered to be statistically significant.

Results

Study population

The selection process of the study population in which 251 patients from 34 clinics were administered the questionnaire is shown in Fig. 1. Four patients less than 40 years of age, patients of unknown age, and those who did not have Piko-6 data were excluded from the analysis. Also excluded were patients for whom apparent technical errors in Piko-6 measurement were suspected because both FEV1 and FEV6 values were ≤1 L or the FEV6 value was as high as 9.9 L.
had no symptoms nor AFL and their Piko-6 data were analyzed. Ultimately, a total of 197 patients met the diagnostic criteria for CB in this study and their Piko-6 data were analyzed. If the Piko-6 values of 2 consecutive patients were exactly the same (it was suspected that the data for the second patient was mistakenly duplicated from that of the first patient), the second patient’s data were excluded from analysis. Ultimately, a total of 197 patients met the diagnostic criteria for CB in this study and their Piko-6 data were analyzed.

Table 2. Characteristics of Eligible Patients

<table>
<thead>
<tr>
<th>M/F (N)</th>
<th>150/47</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65.7 ± 12.6</td>
</tr>
<tr>
<td>40-49</td>
<td>30 (15.2%)</td>
</tr>
<tr>
<td>50-59</td>
<td>36 (18.3%)</td>
</tr>
<tr>
<td>60-69</td>
<td>42 (21.3%)</td>
</tr>
<tr>
<td>70-79</td>
<td>61 (31.0%)</td>
</tr>
<tr>
<td>80+</td>
<td>28 (14.2%)</td>
</tr>
</tbody>
</table>

Smoking history
- Never: 43 (21.3%)
- Ex: 77 (39.1%)
- Current: 74 (37.5%)

Table 3. Sensitivity and Specificity of Piko-6

<table>
<thead>
<tr>
<th>Spirometry &lt; 70</th>
<th>sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ 18 21 39 0.857</td>
<td></td>
</tr>
<tr>
<td>Piko-6 &lt; 73 -3 33 36 Specificity</td>
<td></td>
</tr>
<tr>
<td>21 54 75 0.611</td>
<td></td>
</tr>
</tbody>
</table>

Figure 3. Prevalence of AFL in CB patients of the 197 CB patients, 93 had AFL (FEV/FVC <73%).

Correlation between results of the simple pulmonary function test (Piko-6) and those of spirometry

Spirometry was performed simultaneously with the simple pulmonary function test in 75 of the 197 patients to verify the reliability of the simple pulmonary function test. There was a good correlation between FEV/FVC measured by spirometry and FEV/FVC measured by the Piko-6 ($r^2=0.38$, p<0.0001; Fig. 2). With reference to spirometry, the sensitivity and specificity of the Piko-6 were 85.7% and 61.1%, respectively (Table 3).

Figure 1. Selection process of the study population. Of the 251 patients from 34 clinics enrolled in the study, 197 had a diagnosis of CB. *1: Age unknown, no Piko-6 data, both FEV$_1$ and FEV$_{50} <1$ L, FEV$_1$ too high (9.9 L), or possible display of the previous patient’s values. *2: In this study, CB was diagnosed if patients met any of the following criteria based on the information obtained by questionnaire: chronic cough for at least 3 months, chronic sputum production for at least 3 months, persistent symptoms of a cold, use of expectorants, previously suspected of having CB, or previous diagnosis of CB by a physician. *3: Impossible to diagnose CB in the absence of symptoms and prescription. *4: AFL defined as FEV$_1$/FEV$_{50} <73\%$, as determined with the Piko-6.

Figure 2. Correlation between Piko-6 data and those obtained by spirometry. Among the 75 patients available for simultaneous measurements with the Piko-6 and spirometry, the correlation between FEV$_1$/FEV$_{50}$ measured with the Piko-6 and FEV$_1$/FVC measured by spirometry was determined.

If the Piko-6 values of 2 consecutive patients were exactly the same (it was suspected that the data for the second patient was mistakenly duplicated from that of the first patient), the second patient’s data were excluded from analysis. Ultimately, a total of 197 patients met the diagnostic criteria for CB in this study and their Piko-6 data were analyzed. The characteristics of these 197 patients (150 men, 47 women; mean age 65.7±12.6 years) are presented in Table 2. Among them were 74 current smokers (37.5%), 77 former smokers (39.1%), and 43 nonsmokers, with 76.7% having smoking experience.

Correlation between results of the simple pulmonary function test (Piko-6) and those of spirometry

Spirometry was performed simultaneously with the simple pulmonary function test in 75 of the 197 patients to verify the reliability of the simple pulmonary function test. There was a good correlation between FEV$_1$/FVC measured by spirometry and FEV$_1$/FEV$_{50}$ measured by the Piko-6 ($r^2=0.38$, p<0.0001; Fig. 2). With reference to spirometry, the sensitivity and specificity of the Piko-6 were 85.7% and 61.1%, respectively (Table 3).
AFL in patients with CB

A total of 93 CB patients (47.2%) had FEV$_1$/FEV$_6$ <73% (Fig. 3). In terms of age, the group of patients aged 70-79 years accounted for the largest number of CB patients: 61 (31.0%) patients (Fig. 4). The proportion of patients with AFL (black column) increased with age, from 16.7% (5/30) of the patients aged 40-49 years to 82.1% (23/36) of the patients aged 80-89 years, although the number was the highest among those aged 70-79 years, at 54.1% (33/61). In terms of gender, men accounted for 78.5% (73 patients) of the patients with AFL, and the patients aged 70-79 years constituted the largest age group for both men and women, namely 22 men (31.0%) and 10 women (50.0%) (data not shown). Among men, the prevalence of AFL tended to increase with age; among women, the prevalence increased rapidly among those aged 70-79 years.

When the relationship between AFL and smoking history was assessed, AFL was detected in 32.1% of the patients with less than 30 pack-years, but the detection rate increased to more than 50% for patients with 30 or more pack-years. When smoking history (pack-years) and age were compared between the groups with and without AFL, both pack-years and age were significantly higher in the group with AFL (p<0.05) (Fig. 5).

Therapy and comorbidity

Overall, 85 CB patients (43.1%) used either expectorants or bronchodilators (Fig. 6). Expectorants were the most frequently prescribed medications, used by 62 patients, while oral and inhaled bronchodilators were prescribed to 45 and 33 patients, respectively. AFL was detected in 57 of the patients prescribed medications and in 37, 35, and 21 of the patients prescribed expectorants, oral bronchodilators, and...
inhaled bronchodilators, respectively. Even in patients in whom no AFL was detected, expectorants and oral and inhaled bronchodilators were prescribed for 25, 10, and 12 patients, respectively. Overall, medications were prescribed to 57 (61.3%) of the 93 patients with AFL: expectorants were prescribed to 37 patients (39.8%), oral bronchodilators to 35 (37.6%), and inhaled bronchodilators to 21 (22.5%) (data not shown).

The prevalence of comorbid lifestyle diseases was investigated in all CB patients and in the subgroup of patients with AFL. Overall, 130 of the 197 patients confirmed to have CB (66.0%) had hypertension, diabetes mellitus, or hyperlipidemia. The prevalence of comorbid lifestyle diseases in the subgroup of 93 patients with AFL was much higher, occurring in 68 (73.1%), compared to 62 of the 104 patients without AFL (data not shown).

### Discussion

This study aimed to determine the current status of diagnosis and treatment of COPD among the subjects diagnosed with CB by GPs. The ultimate goal is to use the obtained information to make GPs aware of the need to accurately distinguish COPD from CB at diagnosis to ensure that patients receive the most appropriate therapy for their disease. To this end, we investigated the prevalence of AFL, as determined with the Piko-6 peak flow meter, in 197 patients who met the study’s diagnostic criteria of CB. The original diagnosis of CB had been made by GPs, who were not necessarily respiratory specialists, on the basis of symptoms and prescription history. Although there have been several previous reports on screening for COPD by performing simple pulmonary function tests (4, 5) the unique characteristic of the present study is that we investigated the prevalence of AFL in symptomatic patients who had already been diagnosed with and treated for CB. We found that the prevalence of AFL among patients with a diagnosis as CB was 47.2%, which is much higher than the prevalence of 8.6% reported in the general population aged 40 years and above (NICE study) (1). These data confirm the importance of screening for AFL among patients with symptoms of CB in Japan.

One factor that may impede screening for AFL among patients with respiratory symptoms is the limited access of GPs to spirometers. As a result, a diagnosis of CB is often made by GPs on the basis of clinical symptoms alone. In this study, we demonstrated that there was a good correlation between the results of spirometry and those obtained with the Piko-6 ($r^2=0.38$, $p<0.0001$). With reference to spirometry and with AFL defined as FEV₁/FEV₆ $<73\%$, the sensitivity and specificity of the Piko-6 were 85.7% and 61.1%, respectively, among CB patients. Thus, Piko-6 might serve as an effective screening tool for GPs to identify patients whose disease warrants management by both GPs and specialists in respiratory diseases.

The present data showed that the prevalence of AFL was increased at 54.1% for patients aged 70-79 years, reaching 82.1% for those older than 80 years of age. Although senile lung tissue was not differentiated from COPD in this study, our results suggest that there is a high prevalence of undiagnosed COPD in the elderly. In men, the prevalence of AFL tended to increase with age, while in women, the prevalence reached 70% in those older than 70, although the small number of women makes an accurate assessment difficult. As for smoking history, the prevalence of AFL increased in patients with a smoking history of over 30 pack-years. When we compared groups with and without AFL, the number of pack-years was significantly higher in the patients with AFL. Similarly, the age of patients with AFL was significantly higher. A study conducted outside Japan reported that in a primary care setting, the prevalence of AFL in patients with a smoking history and self-reported symptoms of CB was 26% (6). The mean age of the patients in that study was 52.9 years, and their smoking history was 39.8 pack-years. Compared with the patients in our study, those patients had a similar smoking history but were younger. In the present study, the prevalence of AFL by age was 16.7% in the patients aged 40-49 and 33.3% in those aged 50-59 years, and these figures were lower than the overall preva-
lence. When the study by Yawn et al is considered in regard to age, a similar prevalence of AFL may be suggested in younger individuals in Japan as well (6). According to the report by Guerra et al (7), the hazard rate for survival of individuals younger than 50 years of age with cough and sputum production is 2.2 times higher than for those without these symptoms. Because these symptoms have greater effects on the prognosis of younger individuals than in the elderly, early diagnosis of COPD may be of clinical importance.

Lange et al (8) reported that decreased respiratory function in obstructive pulmonary diseases is strongly associated with prognosis, and that chronic mucus hypersecretion increases the mortality risk. Screening for AFL with attention to symptoms of cough and sputum production may be of great importance because it enables the early detection of AFL, especially in patients with a poor prognosis. Yawn et al also reported that patients generally do not inform physicians about their cough and sputum production (6). Hence, GPs who regularly treat patients for various chronic diseases may play an important role in identifying chronic cough and sputum production and the AFL associated with them.

The association of COPD and lifestyle diseases has already been pointed out (9, 10), and in this study, we investigated the prevalence of hypertension, diabetes mellitus, and hyperlipidemia among all patients diagnosed with CB and in the subgroup of those with AFL. Comorbid lifestyle diseases were observed in 130 patients (66.0%), and in 73.1% of the patients with AFL. Therefore, if AFL is detected in patients with symptoms of CB visiting an outpatient clinic, lifestyle diseases should also be considered.

Ichinose et al (11) reported that the rate of use of inhaled bronchodilators, recommended as the mainstay of drug treatment by the guidelines, is less than 16%, indicating that therapies targeting airflow obstruction in AFL are not widely used, as revealed in this study too. Inhaled bronchodilators were prescribed to 21 patients (63.6%) with AFL, and this high prescription rate was probably because patients with AFL complain of more symptoms. However, inhaled bronchodilators were also inappropriately administered to 12 patients (36.4%) without AFL. We suggest that by performing pulmonary function tests, therapy that targets the appropriate disease can be prescribed more often.

In the present study, antitussives were not included in the questionnaire, and no symptomatic therapies other than expectorants were investigated. In addition, our study classified bronchodilators simply as oral and inhaled formulations, providing no detailed analysis of the prescriptions of transdermal formulations, long-/short-acting medications, and inhaled β-agonists/inhaled anticholinergics. However, because the aim of this study was to provide information to educate non-specialists about the importance of determining appropriate therapy for COPD patients, as determined using a simple pulmonary function testing device, we have attempted to simplify the categories of medications as expectorants (representative of symptomatic therapy) and bronchodilators (representative of therapy targeting airflow obstruction in AFL).

**Conclusion**

We used the Piko-6 to evaluate the pulmonary function in patients who had been diagnosed with CB by GPs in Japan and found that the prevalence of AFL was 47.2%. The prevalence was even higher among older patients and those who smoked. Finally, a high proportion of the patients with AFL had the lifestyle diseases of hypertension, diabetes, and/or hyperlipidemia. The diagnostic performance of the Piko-6 was good, and it is suitable for use in a routine clinical practice. We conclude that the screening of patients with symptoms of CB using the Piko-6 peak flow meter could help GPs distinguish COPD in CB patients during diagnosis and thereby improve the treatment of COPD.

**The authors state that they have no Conflict of Interest (COI).**

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