

# COPD is frequent in conditions of comorbidity in patients treated with various diseases in a university hospital

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**Background:** Chronic obstructive pulmonary disease (COPD) is one of the leading causes of death and loss of disability-adjusted life-years. However, many COPD patients are not diagnosed because of underrecognition or underdiagnosis of this disease among many patients and physicians. One possible reason is underrecognition of spirometry. In this study, we examined the prevalence of airflow limitation and underlying disease in patients with airflow limitation.

**Methodology:** From April 2006 to March 2008, patients who had spirometry performed were examined. The original disease of patients, pulmonary function tests, smoking status, and respiratory symptoms were surveyed from their medical records.

**Results:** Of all patients who had spirometry performed, 15.8% showed airflow limitation ( $FEV_1/FVC < 0.7$ ). A variety of diseases were observed in patients with airflow limitation. Among all diseases, cardiovascular disease was the highest and gastrointestinal malignant disease had the second highest prevalence in patients with airflow limitation.

**Conclusion:** COPD might be frequent in conditions of comorbidity in patients treated for various diseases. Attention should be paid to the possibility of co-existence of COPD and the influence of COPD on these patients.

**Keywords:** airflow limitation, chronic obstructive pulmonary disease, comorbidity, spirometry, prevalence

## Introduction

The prevalence of chronic obstructive pulmonary disease (COPD) is about 10% worldwide.<sup>1,2</sup> COPD was the fourth leading cause of death<sup>3</sup> and will become the third leading cause of death by 2020.<sup>4</sup> The Nippon COPD Epidemiology (NICE) study showed that the prevalence of airflow limitation was 8.6% in Japan.<sup>5</sup> Although there are about 5.3 million COPD patients in Japan estimated from this prevalence, only 220,000 patients are actually treated for COPD in primary care and hospitals. The discrepancy between the estimate in the NICE study and actual COPD patients is derived from underdiagnosis of COPD among physicians and underrecognition of COPD among patients. Furthermore, spirometry is not commonly used in primary care clinics.<sup>6</sup> In primary care settings, the prevalence of COPD diagnosed by spirometry is 9.3% in Poland,<sup>7</sup> 4.6% in the UK,<sup>8</sup> and 10.3% in Japan.<sup>9</sup> However, even with spirometry used in a general setting for screening of COPD, 63.2% of patients who had airflow limitation were not diagnosed with COPD.<sup>8</sup> Therefore, underrecognition of COPD among general physicians might be one of the bigger problems for accurate diagnosis of COPD.

In general hospital settings, spirometry is usually performed in patients with nonrespiratory diseases. Minakata et al reported that the prevalence of COPD was

10.2% in nonrespiratory diseases and its prevalence was higher in patients with liver diseases,<sup>9</sup> whereas the patients who undergo operations using general anesthesia are likely to have spirometry performed. A variety of diseases which are closely connected to cigarette smoking are involved in these cases, such as esophageal cancer, laryngeal cancer, lung cancer, and bladder cancer. However, the prevalence of COPD patients in university hospitals who have spirometry performed for nonrespiratory diseases has not been well studied. Furthermore, it is not well known which diseases are commonly observed among patients with COPD.<sup>10</sup> Since Tottori University Hospital is one of the largest core hospitals in our area, we carried out this study to investigate: 1) the prevalence of airflow limitation in patients who had spirometry performed; and 2) the underlying diseases in patients who had airflow limitation in a university hospital setting.

## Methodology

### Data collection

From April 2006 to March 2008, patients who had spirometry performed were analyzed using their medical records at Tottori University Hospital. Spirometry was performed with a Chestac 33 spirometer (Chest Co, Tokyo, Japan). 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 one second (FEV<sub>1</sub>) values were recorded. The medical records were reviewed to collect the following data: age, gender, FVC, FEV<sub>1</sub>, the original diseases, smoking status, and respiratory symptoms such as dyspnea on exertion, cough, and sputum.

In this study, patients who were diagnosed with COPD as a primary disease, bronchial asthma, old pulmonary tuberculosis, or congestive heart failure were excluded from

the analysis. Patients who had had thoracic surgery were also excluded from the analysis. Airflow limitation was defined as FEV<sub>1</sub>/FVC (%FEV<sub>1</sub>) < 0.7 (70%). This study was approved by the local institutional review board.

## Stages of COPD

The severity of airflow limitation was classified according to GOLD (Global Initiative for Chronic Obstructive Lung Diseases)<sup>11</sup> criteria as follows:

Stage I: Mild COPD characterized by mild airflow limitation (FEV<sub>1</sub>/FVC < 0.70; %FEV<sub>1</sub> ≥ 80%);

Stage II: Moderate COPD characterized by worsening airflow limitation (FEV<sub>1</sub>/FVC < 0.70; 50% ≤ %FEV<sub>1</sub> < 80%);

Stage III: Severe COPD characterized by further worsening of airflow limitation (FEV<sub>1</sub>/FVC < 0.70; 30% ≤ %FEV<sub>1</sub> < 50%);

Stage IV: Very severe COPD characterized by severe airflow limitation (FEV<sub>1</sub>/FVC < 0.70; %FEV<sub>1</sub> < 30%).

## Statistical analysis

All data are expressed as mean ± standard deviation. The Mann–Whitney *U*-test or chi-square test was used to analyze the difference between data from the group with airflow limitation and data from the group without airflow limitation. All statistical analysis was performed using Graph-Pad Prism 4.0 (GraphPad Software Inc., San Diego, CA). Differences were considered to be statistically significant at *P* < 0.05.

## Results

### Characteristics of the patients

A total of 3,855 cases were analyzed. The average age, gender, and smoking status are shown in Table 1. The average age of all patients was 65.7 years. Females accounted for

**Table 1** Patient characteristics

	All	Patients with airflow limitation (%FEV <sub>1</sub> < 70%)	Patients without airflow limitation (%FEV <sub>1</sub> ≥ 70%)
Number of patients (%)	3855	608 (15.8%)	3247 (84.2%)
Age (years)	65.7 ± 12.0	72.3 ± 8.61	63.4 ± 12.0*
Gender (%)			
Male	1968 (51.1%)	462 (76.0%)	1506 (46.4%)**
Female	1887 (48.9%)	146 (24.0%)	1742 (53.6%)
Smoking status (%)			
Current smoker	1571 (40.8%)	357 (58.7%)	1214 (37.4%)***
Ex smoker	221 (5.7%)	114 (18.8%)	107 (3.3%)***
Nonsmoker	2063 (53.5%)	137 (22.5%)	1926 (59.3%)

**Notes:** \* = significantly different to the age of the patients with airflow limitation (*P* < 0.001); \*\* = significantly different compared to the percentage of males among patients with airflow limitation (*P* < 0.01); \*\*\* = significantly different compared to the percentages of current and past smokers among patients with airflow limitation (*P* < 0.01).

**Abbreviation:** %FEV<sub>1</sub>, ratio of forced expiratory volume in one second to forced vital capacity.

48.9% of patients. Among all patients, 40.8% were current smokers; 5.7% were ex smokers, 53.5% were nonsmokers. Among all patients, 608 (15.8%) patients showed airflow limitation ( $FEV_1/FVC < 0.7$ ). Table 1 summarizes characteristics of the subgroups of patients divided according to the presence of airflow limitation. The average age, the percentage of male, and the percentage of current or past smokers was significantly higher in patients with airflow limitation (Table 1).

The severity of airflow limitation was classified according to GOLD criteria.<sup>11</sup> The percentage of patients with mild airflow limitation ( $\%FEV_1 \geq 80\%$ ) was 72%; the percentage with moderate airflow limitation ( $50\% \leq \%FEV_1 < 80\%$ ) was 25.5%; the percentage with severe airflow limitation ( $30\% \leq \%FEV_1 < 50\%$ ) was 2.5%; and the percentage with very severe airflow limitation ( $\%FEV_1 < 30\%$ ) was 0.2% (Table 2).

We next asked whether patients experienced respiratory symptoms (Table 3). In patients with airflow limitation, 259 patients (42.3%) experienced at least one respiratory symptom, such as dyspnea on exertion, cough, or sputum. Eighty-eight patients (14.3%) experienced dyspnea on exertion, 144 patients (23.5%) experienced cough, and 155 patients (25.3%) experienced sputum. However, 353 patients (57.7%) experienced no respiratory symptoms.

We next examined the original diseases in patients with airflow limitation. In all, 289 patients (47.8%) had malignant diseases and 319 patients (52.8%) had benign diseases (Tables 4 and 5). Among patients with malignant disease, the percentage of patients with gastrointestinal malignancy was highest (71 cases; 10.5%), the percentage of otolaryngeal, head, and neck cancer was the second highest (64 cases; 10.5%), and the percentage of lung and mediastinal malignancy was the third highest (53 cases; 8.7%) (Table 4). Among patients with benign tumor, the most frequent prevalent diseases were cardiovascular diseases (72 cases; 11.8%). The second most frequent diseases were orthopedic diseases (66 cases; 10.9%) and the third most frequent diseases were otolaryngeal diseases (60 cases; 9.9%) (Table 5).

**Table 2** Breakdown of patients by severity of airflow limitation

Stage I	$80 \leq \%FEV_1$	437 (71.9%)
Stage II	$50 \leq \%FEV_1 < 80$	155 (25.5%)
Stage III	$30 \leq \%FEV_1 < 50$	15 (2.5%)
Stage IV	$30 > \%FEV_1$	1 (0.2%)
Total		608 (100%)

**Abbreviation:**  $\%FEV_1$ , ratio of forced expiratory volume in one second to forced vital capacity.

**Table 3** Symptoms of patients with airflow limitation

No respiratory symptoms	351 (57.7%)
Some respiratory symptoms	257 (42.3%)
Dyspnea on exertion	88 (14.3%)
Cough	144 (23.5%)
Sputum	155 (25.3%)

## Discussion

### Prevalence of airflow limitation

In this study, we investigated the prevalence of patients with airway limitation among patients who had had spirometry performed. We showed that 15.8% of patients had airflow limitation. In primary care settings, the prevalence of airflow limitation was 11.4% in Japan<sup>9</sup> and 9.3% in Poland.<sup>7</sup> In these three studies, the prevalence of patients with airflow limitation was studied with a post-bronchodilator. The authors reported that airflow limitation was demonstrated in 15% of patients without a bronchodilator and in 11% with a bronchodilator.<sup>7</sup> Therefore, our study might overestimate the prevalence of patients with airflow limitation. Furthermore, the patients' background might influence the prevalence of patients with airflow limitation. In the NICE,<sup>5</sup> PLATINO,<sup>2</sup> and BOLD (Burden of Lung Disease)<sup>1</sup> studies, healthy people were surveyed for the prevalence of COPD.<sup>2,5,7</sup> In primary care clinic settings, the participants suffered from some diseases, such as hypertension, diabetes mellitus, hyperlipemia, or liver disease.<sup>9</sup> In our study, patients had some comorbidity (Tables 4 and 5), and in

**Table 4** Comorbidity in patients with airflow limitation (benign disease)

Cardiovascular diseases (thoracic and abdominal aortic aneurysm, ischemic heart diseases, arteriosclerosis, etc)	72 (22.6%)
Orthopedic diseases (fractures, osteoarthritis, spondylosis, etc)	66 (20.1%)
Otolaryngeal diseases (chronic sinusitis, tympanitis, cyst of upper and lower jaw, etc)	60 (18.8%)
Neurological diseases (brain infarction, Parkinson's disease, depression, etc)	26 (8.9%)
Urologic diseases (benign prostatic hypertrophy, urinary stones, etc)	20 (6.3%)
Gynecological diseases	15 (4.7%)
Dermatological diseases	13 (4.1%)
Inguinal and ventral hernia	11 (3.4%)
Liver and gall bladder diseases	9 (2.8%)
Ophthalmologic diseases	9 (2.8%)
Lung and mediastinal diseases	8 (2.5%)
Collagen vascular diseases	7 (2.2%)
Gastrointestinal diseases	3 (0.9%)
Total	319 (100%)

**Table 5** Comorbidity in patients with airflow limitation (malignant disease)

Gastrointestinal diseases (gastric cancer, esophageal cancer, colon cancer, etc)	71 (24.6%)
Otolaryngeal, head and neck diseases (laryngeal or pharyngeal cancer, thyroid cancer)	64 (22.1%)
Lung and mediastinal diseases (lung cancer, thymoma, etc)	53 (18.3%)
Urological diseases (bladder cancer, renal pelvic cancer, etc)	42 (14.5%)
Dermatologic diseases (basal cell carcinoma, malignant melanoma, etc)	17 (5.9%)
Hepatocellular and cholangiocellular carcinoma	14 (4.8%)
Breast cancer	11 (3.8%)
Hematological malignancy	8 (2.8%)
Gynecological malignancy	6 (2.1%)
Pancreas cancer	3 (1.0%)
Total	289 (100%)

many cases, spirometry was performed before an operation. Although the method of spirometry and the background of the patients affect the prevalence of airflow limitation, substantial numbers of patients with potent COPD might be underdiagnosed in university hospitals.

## Comorbidities of COPD

Comorbidities of COPD affect symptoms and mortality of patients with COPD. Mapel et al reported that COPD patients were more likely to be admitted to the hospital and had a longer average length of stay than patients without COPD.<sup>12</sup> They also reported that COPD patients had a higher prevalence of smoking-related comorbidities, such as heart disease, cancer, neurologic injuries, and gastritis. In this study, we surveyed which diseases are underlying in patients with airflow limitation. There were many diseases which had possible COPD as comorbidity and most diseases were smoking-related.

Cardiovascular disease had the highest prevalence and malignant disease of the gastrointestinal area had the second highest prevalence in this study. Soriano et al reported that COPD patients were at increased risk of pneumonia, osteoporosis, respiratory infection, myocardial infarction, angina, fracture, and glaucoma.<sup>10</sup> On the other hand, an epidemiological study showed that the leading causes of smoking-attributed deaths were cancer, ischemic heart diseases, stroke, COPD, and pneumonia.<sup>13</sup> Among the tobacco-related cancer sites, the lung, cervix uteri, lip/oral cavity, esophagus, urinary tract, pancreas, and stomach exhibited a high hazard ratio compared with nonsmokers. Among cardiovascular diseases (ischemic heart diseases, aortic aneurysm, and dissection), abdominal aortic aneurysm

exhibited a high hazard ratio compared with nonsmokers.<sup>13</sup> Furthermore, Young et al reported that COPD is an important independent risk factor in lung cancer.<sup>14</sup> Therefore, smoking-related diseases such as cancer and cardiovascular diseases are closely related to COPD. While Minakata et al reported that the prevalence of COPD was different among the background diseases and patients with liver disease had high prevalence of COPD in a primary care setting,<sup>9</sup> in our study, we did not check pre- and/or post-bronchodilator spirometry in each underlying disease. It is therefore a limitation of this study that we could not calculate precise prevalence of COPD in each underlying disease in all the patients in our hospital. However, COPD might be an underlying disease with high prevalence, especially among patients who have smoking-related diseases.

## Respiratory symptoms of the patients

In this study, we asked the patients with airflow limitation whether they had respiratory symptoms such as cough, sputum, and dyspnea on exertion. Yawn et al reported that evaluation of spirometry in patients with smoking history and chronic bronchitis symptoms might help for diagnosis of COPD patients in general practice.<sup>15</sup> Since the use of spirometry are not practical in primary care settings, Price et al showed the usefulness of a symptoms-based questionnaire to detect COPD in patients with a smoking history.<sup>16,17</sup> However, Akamatsu et al reported that symptoms such as dyspnea on exertion, cough, and sputum are less sensitive in detecting early COPD.<sup>18</sup> In our study, 57.7% of patients with airflow limitation had no respiratory symptoms. Therefore, spirometry should be used to identify COPD, even though patients have no respiratory symptoms.

## Conclusion

In conclusion, a high prevalence of patients with airflow limitation was observed in a university hospital setting. Recent studies have shown that earlier trial of long-acting muscarinic antagonist has beneficial effects for patients with moderate to severe COPD, such as reductions in exacerbations, hospitalizations, risk of all cause mortality, and cardiovascular mortality.<sup>19</sup> Therefore, earlier diagnosis and treatment of COPD as comorbidity with other diseases might be important and beneficial, not only for COPD itself, but also for patients' original diseases to reduce mortality. Further study is needed to find the precise prevalence of COPD in smoking-related diseases and the influence of COPD on the underlying diseases.

## Disclosure

The authors report no conflicts of interest in this work.

## References

- Buist AS, McBurnie MA, Vollmer WM, et al. International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. *Lancet*. 2007;370:741–750.
- Menezes AM, Perez-Padilla R, Jardim JR, et al. Chronic obstructive pulmonary disease in five Latin American cities (the PLATINO study): a prevalence study. *Lancet*. 2005;366:1875–1881.
- Jemal A, Ward E, Hao Y, Thun M. Trends in the leading cause of death in the United States. *JAMA*. 2005;294:1255–1259.
- Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: Global burden of disease study. *Lancet*. 1997;349:1498–1504.
- Fukuchi Y, Nishimura M, Ichinose M, et al. COPD in Japan: the Nippon COPD Epidemiology study. *Respirology*. 2004;9:458–465.
- Takahashi T, Ichinose M, Inoue H, Shirato K, Hattori T, Takishima T. Underdiagnosis and undertreatment of COPD in primary care settings. *Respirology*. 2003;8:504–508.
- Bednarek M, Maciejewski J, Wozniak M, Kuca P, Zielinski J. Prevalence, severity and underdiagnosis of COPD in the primary care setting. *Thorax*. 2008;63:402–407.
- Frank TL, Hazell ML, Linehan MF, Frank PI. The diagnostic accuracies of chronic obstructive pulmonary disease (COPD) in general practice: The results of the MAGIC (Manchester Airways Group Identifying COPD) study. *Prim Care Respir J*. 2006;15:286–293.
- Minakata Y, Sugiura H, Yamagata T, et al. Prevalence of COPD in primary care clinics: correlation with non-respiratory diseases. *Intern Med*. 2008;47:77–82.
- Soriano JB, Visick GT, Muellerova H, Payvandi N, Hansell AL. Patterns of comorbidities in newly diagnosed COPD and asthma in primary care. *Chest*. 2005;128:2099–2107.
- Global Strategy for the Diagnosis, Management, and Prevention of COPD [updated Dec 2009]. Available from: <http://www.goldcopd.org/Guidelineitem.asp?l1=2&l2=1&intId=2003>. Accessed 2010 Aug 13.
- Mapel DW, Picchi MA, Hurley JS, et al. Utilization in COPD: patient characteristics and diagnostic evaluation. *Chest*. 2000;117(5 Suppl 2):S346–S353.
- Katanoda K, Marugame T, Saika K, et al. Population attributable fraction of mortality associated with tobacco smoking in Japan: a pooled analysis of three large-scale cohort studies. *J Epidemiol*. 2008;18:251–264.
- Young RP, Hopkins RJ, Christmas T, Black PN, Metcalf P, Gamble GD. COPD prevalence is increased in lung cancer, independent of age, sex and smoking history. *Eur Respir J*. 2009;34:380–386.
- Yawn B, Mannino D, Littlejohn T, et al. Prevalence of COPD among symptomatic patients in a primary care setting. *Curr Med Res Opin*. 2009;25:2671–2677.
- Price DB, Tinkelman DG, Nordyke RJ, Isonaka S, Halbert RJ. Scoring system and clinical application of COPD diagnostic questionnaires. *Chest*. 2006;129:1531–1539.
- Price DB, Tinkelman DG, Halbert RJ, et al. Symptom-based questionnaire for identifying COPD in smokers. *Respiration*. 2006;73:285–295.
- Akamatsu K, Yamagata T, Kida Y, Tanaka H, Ueda H, Ichinose M. Poor sensitivity of symptoms in early detection of COPD. *COPD*. 2008;5:269–273.
- Tashkin DP. Long-acting anticholinergic use in chronic obstructive pulmonary disease: efficacy and safety. *Curr Opin Pulm Med*. 2010;162:97–105.

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