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## Original

# Prevalence of Hypertension, Diabetes Mellitus, and Dyslipidemia in Patients with Chronic Obstructive Pulmonary Disease

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**Abstract** : Recent studies have shown that chronic obstructive pulmonary disease (COPD) causes various extrapulmonary comorbidities. In addition, cardiovascular disease, the pathogenesis of which involves atherosclerosis, has been emphasized as a cause of mortality in patients with COPD. In the present study, we investigated the presence of classical risk factors for atherosclerosis in 183 patients with COPD. The prevalence of comorbidities (hypertension, diabetes mellitus [DM], and dyslipidemia) was investigated and compared with that in a general population. In patients with COPD, the prevalence of hypertension, DM, and dyslipidemia was 43.2%, 15.8%, and 25.7%, respectively, with the prevalence of DM and dyslipidemia significantly higher in patients than in the general population. Furthermore, there were significant differences in the prevalence of the three disorders in patients with COPD. For example, the prevalence of hypertension was significantly higher than that of diabetes mellitus in patients aged 60–69 years and higher than the prevalence of DM and dyslipidemia in patients aged  $\geq 70$  years. Regardless of age, hypertension was noted in the greatest number of patients. In conclusion, a high proportion of patients with COPD were found to have the classical risk factors for atherosclerosis. In particular, the prevalence of DM and dyslipidemia was significantly higher in COPD patients than in the general population.

**Key words** : chronic obstructive pulmonary disease, comorbidity, prevalence, risk factors for atherosclerosis, general population

## Introduction

Chronic obstructive pulmonary disease (COPD) is an inflammatory lung disease related to the long-term inhalation of noxious substances, including tobacco smoke. COPD is characterized by progressive airflow obstruction, which may not return to normal on respiratory function tests, exertional dyspnea, and chronic cough/sputum<sup>1</sup>. In 2000, COPD was reported to be the fourth most common cause of mortality worldwide<sup>2</sup>.

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Table 1. Characteristics of patients with COPD

|                       |                       |                                   |
|-----------------------|-----------------------|-----------------------------------|
| Number of patients    | 183                   |                                   |
| Male / Female, number | 165 / 18              |                                   |
| Mean age (SD), years  | 74.2 (8.1)            |                                   |
| Age-groups, number    |                       |                                   |
| 50–59ys               | 6                     |                                   |
| 60–69ys               | 51                    |                                   |
| 70ys–                 | 126                   |                                   |
| Stage of COPD, number | (Age-groups : number) |                                   |
| I                     | 43                    | (50–59 : 0, 60–69 : 11, 70– : 32) |
| II                    | 78                    | (50–59 : 4, 60–69 : 24, 70– : 50) |
| III                   | 41                    | (50–59 : 2, 60–69 : 13, 70– : 26) |
| IV                    | 21                    | (50–59 : 0, 60–69 : 3, 70– : 18)  |

Recent studies have shown that COPD causes various extrapulmonary comorbidities. Thus, it is important to recognize COPD not only as a respiratory disease, but also as a systemic disease<sup>3)</sup>. Cardiovascular disease, the pathogenesis of which involves atherosclerosis, has been reported to be responsible for approximately 30% of deaths in patients with COPD<sup>4,5)</sup>. Furthermore, hypertension, diabetes mellitus (DM), and dyslipidemia, classical risk factors for atherosclerosis, have been detected in a high proportion of COPD patients<sup>6-8)</sup>. However, few studies have reported on comorbidities of COPD in Japan. In the present study, we focused on hypertension, DM, and dyslipidemia as comorbidities of COPD and determined their prevalence in patients with COPD compared with that in a general population.

## Methods

### Subjects

The COPD group in the present retrospective study consisted of 183 patients who had periodically consulted the outpatient clinic of the Division of Respiratory and Allergy, Department of Internal Medicine, Showa University School of Medicine, or the Department of Internal Medicine, Showa University Toyosu Hospital for the treatment of COPD between April 2008 and March 2009 (165 males, 18 females; mean age  $74.2 \pm 8.1$  years [range 52–93 years]; Table 1). The general population used for comparisons was made up of people over 50 years of age who were selected based on data on hypertension, DM, and dyslipidemia from the National Health and Nutrition Survey (2006) published by the Ministry of Health, Labour and Welfare<sup>9)</sup> (Table 2).

### Methodology

Information was obtained regarding the patients' age, gender, stage of COPD, and the

Table 2. Raw data of characteristics of the control group (National Health and Nutrition Survey 2006)

| Age-groups, y    |                | 50–59         | 60–69         | 70–           | total |
|------------------|----------------|---------------|---------------|---------------|-------|
| Object of survey |                | male / female | male / female | male / female |       |
| Hypertension     | object (n)     | 363 / 544     | 411 / 561     | 504 / 631     | 3014  |
|                  | prevalence (n) | 76 / 78       | 130 / 170     | 232 / 305     | 991   |
|                  | prevalence (%) | 20.9 / 14.3   | 31.6 / 30.3   | 46.0 / 48.3   | 32.9  |
| Dyslipidemia     | object (n)     | 351 / 525     | 390 / 527     | 474 / 582     | 2849  |
|                  | prevalence (n) | 31 / 68       | 38 / 101      | 49 / 140      | 427   |
|                  | prevalence (%) | 8.8 / 13.0    | 9.7 / 19.2    | 10.3 / 24.1   | 15.0  |
| Diabetes         | object (n)     | 350 / 525     | 389 / 523     | 472 / 580     | 2839  |
|                  | prevalence (n) | 17 / 12       | 28 / 36       | 56 / 49       | 198   |
|                  | prevalence (%) | 4.9 / 2.3     | 7.2 / 6.9     | 11.9 / 8.4    | 7.0   |

presence or absence of comorbidities (hypertension, DM, and dyslipidemia). The number of COPD patients with these comorbidities as a proportion of all patients was determined, as was the prevalence of the comorbidities with respect to age and stage of disease. The prevalence of hypertension, DM, and dyslipidemia was compared between the COPD patients and the general population. A diagnosis of COPD was made with stage assessment according to the Guidelines for the Diagnosis and Treatment of COPD (Chronic Obstructive Pulmonary Disease) issued by the Japanese Respiratory Society<sup>10</sup>. Patients were determined to have hypertension, DM, or dyslipidemia if they were receiving drug therapy for that disease. Similarly, in the general population, any result reported as “person taking a drug” in the National Health and Nutrition Survey was taken as an indication that that person had the disease.

### Statistical analysis

When comparing the prevalence of hypertension, DM, and dyslipidemia between COPD patients and the general population, data obtained from the National Health and Nutrition Survey for the “general population” in the present study were adjusted for age and gender in the COPD group using direct standardization methods. The Chi-squared test was used to compare percentages.  $P < 0.05$  was considered significant.

### Results

Significant differences were noted in the prevalence of three comorbidities in COPD patients: 79 patients (43.2%) had hypertension, 47 (25.7%) had dyslipidemia, and 29 (15.8%) had DM (Table 3). Overall, 105 patients (57.4%) were found to have at least one of the three comorbidities.

The prevalence of hypertension, DM, and dyslipidemia in patients aged 50–59 years was

Table 3. Prevalence of comorbidities among patients with COPD (n = 183)

| Comorbidity       | Number | %    |
|-------------------|--------|------|
| Hypertension      | 79     | 43.2 |
| Dyslipidemia      | 47     | 25.7 |
| Diabetes mellitus | 29     | 15.8 |

\* : P &lt; 0.05, \*\* : P &lt; 0.001

Table 4. Prevalence of comorbidities among patients with COPD according to each age group

| Age-groups | Comorbidity, % (number) |              |                   |
|------------|-------------------------|--------------|-------------------|
|            | Hypertension            | Dyslipidemia | Diabetes mellitus |
| 50-59      | 33.3 (2)                | 16.6 (1)     | 16.6 (1)          |
| 60-69      | 37.3 (19)               | 31.4 (16)    | 19.6 (10)         |
| 70-        | 46.0 (58)               | 23.8 (30)    | 14.3 (18)         |

\* : p &lt; 0.05, \*\* : P &lt; 0.001

Table 5. Prevalence of comorbidities among patients with COPD according to each COPD stage

| COPD stage |        | Comorbidity, % (number) |              |                   |
|------------|--------|-------------------------|--------------|-------------------|
|            |        | Hypertension            | Dyslipidemia | Diabetes mellitus |
| I          | n = 43 | 46.5 (20)               | 34.9 (15)    | 16.3 (7)          |
| II         | n = 78 | 46.2 (36)               | 25.6 (20)    | 17.9 (14)         |
| III        | n = 41 | 39.0 (16)               | 17.1 (7)     | 14.6 (6)          |
| IV         | n = 21 | 33.3 (7)                | 23.8 (5)     | 9.5 (2)           |

n.s. : not significant

33.3%, 16.6%, and 16.6%, respectively; in the 60-69 years age group, the prevalence of the three comorbidities was 37.3%, 19.6%, and 31.4%, respectively; whereas in patients  $\geq 70$  years of age, the prevalence was 46.0%, 14.3%, and 23.8%, respectively. There was a significant difference between the prevalence of hypertension and DM in subjects aged 60-69 years. Similarly, significant differences were found between the prevalence of hypertension and dyslipidemia / DM in patients aged  $\geq 70$  years. The proportion of patients with hypertension was the highest, regardless of age (Table 4). There were no significant differences in the prevalence of these comorbidities in patients with different stages of the disease (Table 5).

To enable comparisons with COPD patients, a "general population" was created by age and gender adjustment of results from the National Health and Nutrition Survey.

Table 6. Adjusted data of characteristics of the control group

| Age-groups, y    |                | 50–59         | 60–69         | 70–           | total |
|------------------|----------------|---------------|---------------|---------------|-------|
| Object of survey |                |               |               |               |       |
|                  |                | male / female | male / female | male / female |       |
| Hypertension     | object (n)     | 38 / 97       | 349 / 578     | 891 / 1061    | 3014  |
|                  | prevalence (n) | 8 / 14        | 110 / 178     | 409 / 523     | 1242  |
|                  | prevalence (%) | 21.0 / 14.4   | 31.5 / 30.8   | 45.9 / 49.3   | 41.2  |
| Dyslipidemia     | object (n)     | 37 / 91       | 331 / 545     | 847 / 998     | 2849  |
|                  | prevalence (n) | 4 / 6         | 36 / 54       | 97 / 124      | 321   |
|                  | prevalence (%) | 10.8 / 6.6    | 10.9 / 9.9    | 11.5 / 12.4   | 11.3  |
| Diabetes         | object (n)     | 37 / 90       | 330 / 543     | 844 / 995     | 2839  |
|                  | prevalence (n) | 2 / 3         | 23 / 50       | 98 / 111      | 287   |
|                  | prevalence (%) | 5.4 / 3.3     | 7.0 / 9.2     | 11.6 / 11.2   | 10.1  |

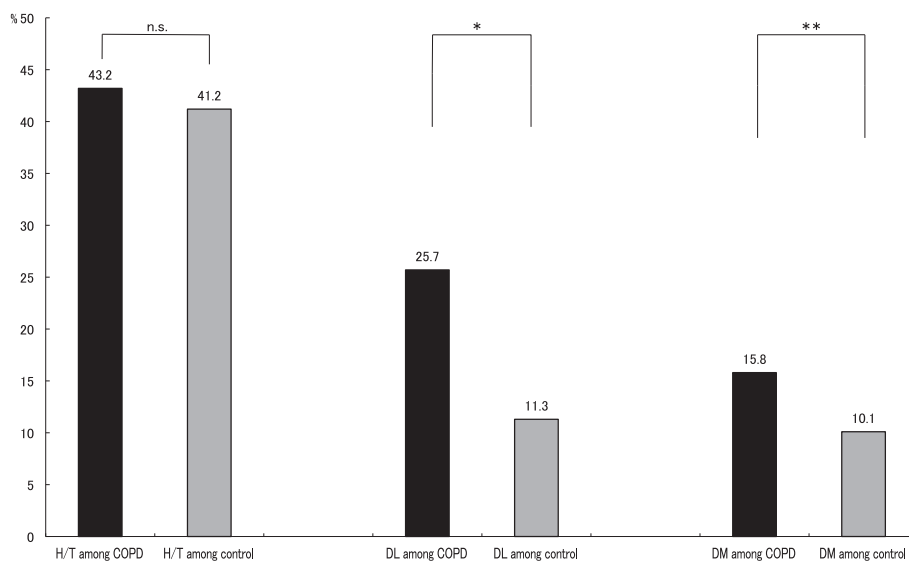


Fig. 1. Comparison of prevalence of comorbidities between COPD and control groups

The prevalence of hypertension was not significantly different between COPD and control groups. The prevalence of dyslipidemia and diabetes mellitus in the COPD group was significantly higher than in the control group.

H/T: hypertension, DL: dyslipidemia, DM: diabetes mellitus, n.s.: not significant, \*:  $p < 0.001$ , \*\*:  $p < 0.05$

Following adjustment, 1242 of 3014 people (41.2%) of the general population were found to have hypertension, 321 of 2849 (11.3%) had dyslipidemia, and 287 of 2839 (10.1%) had DM (Table 6). Comparison of the prevalence of these conditions between the general population and the COPD patients revealed that the prevalence of DM and dyslipidemia was significantly higher in patients with COPD. There was no significant difference in the prevalence of hypertension between the two groups (Fig. 1).

## Discussion

COPD has been reported to cause various extrapulmonary comorbidities and the importance of recognizing COPD as a systemic disease has been emphasized<sup>3)</sup>. As a comorbidity of COPD, cardiovascular disease in particular has been investigated as a cause of mortality in patients with COPD<sup>4,11,12)</sup>.

Of the three comorbidities evaluated in the present study, namely hypertension, DM, and dyslipidemia, all of which are classical risk factors for atherosclerosis, hypertension was the most prevalent in patients with COPD, as reported previously<sup>6-8)</sup>. The second most frequent comorbidity was dyslipidemia, followed by DM. The prevalence of DM and dyslipidemia was significantly higher in COPD patients than in the general population. The prevalence of hypertension increased with age, showing significant differences compared with the other comorbidities. However, there was no significant difference in the prevalence of hypertension between COPD patients and the general population, suggesting the influence of age.

Recent studies have revealed the presence of systemic inflammation in patients with COPD<sup>13-15)</sup>. Because various chronic comorbidities related to systemic inflammation have been observed, “chronic systemic inflammatory syndrome” has been introduced as a disease entity<sup>16)</sup>. Therefore, in the present study, it may be that COPD-specific systemic inflammation contributed to a significant increase in impaired glucose / lipid metabolism in patients with COPD. However, this requires further investigation, with the precise etiology and mechanisms underlying the dyslipidemia and DM in COPD patients yet to be determined.

The pathogenesis of cardiovascular disease in the presence of COPD is unclear. A recent study reported that inflammation was involved in the onset and deterioration of atherosclerosis, and so atherosclerosis has been recognized as an inflammatory disease<sup>17)</sup>, as has COPD. In addition, many studies have suggested that systemic inflammation in COPD patients contributes to the development of cardiovascular disease<sup>18-25)</sup>. Taking these findings into consideration, the development of cardiovascular disease in the presence of COPD may be due to an additive / synergistic effect of systemic inflammation and classical risk factors for atherosclerosis.

In the present study, approximately 60% of COPD patients had classical risk factors for atherosclerosis. In particular, the prevalence of DM and dyslipidemia was significantly higher in COPD patients than in the general population. Thus, controlling atherosclerosis in COPD patients may prevent the development of cardiovascular disease, subsequently improving the prognosis for these patients. Therefore, in the clinical management of COPD, screening for and the treatment of any classical risk factors for atherosclerosis may prove to be important, recognizing COPD as a systemic disorder.

## Acknowledgment

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