ORIGINAL RESEARCH

Surveillance of chronic obstructive pulmonary disease in high-risk individuals by using regional lung cancer mass screening

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Background and objective: Patients with chronic obstructive pulmonary disease (COPD) are at risk for lung cancer; the diseases have common etiologies, including cigarette smoking. We aimed to clarify the effectiveness of COPD detection using a regional mass-screening program for lung cancer.

Materials and methods: A total of 7,067 residents of Togane, Chiba, Japan received lung cancer screening between May and July, 2011. We defined four groups of possible COPD candidates: group A (n=358), positive smoking history, positive chronic respiratory symptoms; group B (n=766), positive smoking history, positive lifestyle-related disease; group C (n=75), passive smoking history, positive chronic respiratory symptoms; and group D (n=301), passive smoking history, positive lifestyle-related disease. Candidates underwent on-site pulmonary function testing (PFT).

Results: The criteria for COPD candidates were fulfilled in 1,686 of 7,067 individuals (23.9%); 1,500 participants underwent PFT (89%), and 171 (11.4%) were diagnosed with COPD. The overall COPD detection rate was 2.4%. The frequency of COPD was significantly higher in groups A and B than in groups C and D (P=0.048); however, the distribution of COPD grades was similar among the groups (P=0.372). Multiple logistic regression analysis identified male sex, age 60 years or greater, and positive smoking history as risk factors for COPD.

Conclusion: COPD screening using a community-based lung cancer-screening program may be effective for disease detection. Individuals who are 60 years of age or older with a positive smoking history should undergo PFT to detect COPD.

Keywords: chronic obstructive pulmonary disease, lung neoplasms, mass screening, respiratory function tests

Introduction

Chronic obstructive pulmonary disease (COPD), although a rapidly growing health problem worldwide, is substantially underdiagnosed[1,2] and frequently misdiagnosed.[3] Soriano et al[2] reported that 72%–93% of COPD patients are not properly diagnosed. The Nippon COPD Epidemiology study reported that the prevalence of airflow limitation, defined as a ratio of forced expiratory volume in 1 second (FEV_1) to forced vital capacity (FVC) less than 70%, was 10.9%, but only 9.4% of patients with airflow limitation had actually been diagnosed with COPD.[4] Although the gold standard for diagnosis is spirometry, the technique is used for only 30%–50% of new cases in general practice.[5,6] Therefore, it is very difficult to detect COPD at the early stages, which would allow for smoking-cessation counseling and prevention of disease progression.

Both COPD and cigarette smoking induce systemic inflammatory changes that result from localized chronic inflammation in the lung. COPD is not only a pulmonary

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disease but also a systemic inflammatory disease that leads to various comorbidities, including coronary artery disease, congestive heart disease, lung cancer, osteoporosis, and neurological disease.[7,8] Patients with COPD have an average of 3.7 chronic comorbidities, while those without COPD have only 1.8.[8] Chatila et al determined that lifestyle-related diseases, including hypertension, angina pectoris, diabetes mellitus, dyslipidemia, and osteoporosis, are common in COPD patients.[9] This suggests that it may be possible to detect COPD by performing pulmonary function testing (PFT) in patients with lifestyle-related disease.

Approximately 30% of Japanese individuals over 40 years of age receive annual community-based mass screening for lung cancer using chest radiography. Several questionnaires are utilized during this screening that may determine patients' risk levels for lung cancer and COPD. The aim of this study was to clarify the effectiveness of regional mass screening for lung cancer in detecting early stage COPD in a Japanese population.

Materials and methods
Ethics
The study protocol was approved by the Togane Ethics Committee in the Chiba Administrative Agency and by the Institutional Review Board Committee of the Chiba Foundation for Health Promotion and Disease Prevention. Each participant provided written informed consent for participation.

Study design
The use of chest radiography for community-based lung cancer screening in Japan is well established,[10,11] and has been supported by the national government under the Health and Medical Services Law for the Aged since 1987. Japanese individuals 40 years of age and older consult with public health nurses and provide their health habits and past and current medical histories on a lifestyle questionnaire. Individuals then undergo annual chest radiography. All holders of National Health Insurance and family members of individuals with employment-related health insurance are eligible for this screening; holders of employment-related health insurance are screened by their companies under a different system. Individuals suspected of having lung cancer based on the results of chest radiography or sputum cytology undergo a secondary evaluation and examination to confirm the diagnosis.

Togane in Chiba Prefecture is 60 km east of Tokyo and is in a typical rural area, with main industries of agriculture and construction. In 2012, the population of Togane

was 59,250. The study subjects were residents of Togane who had received lung cancer screening between May and July, 2011. The individuals underwent screening in a public assembly hall, where they filled out detailed questionnaires about their occupation, alcohol intake, smoking status, past and current medical history, and any chronic symptoms. For the purposes of this study, we paid particular attention to the questions about smoking history, passive smoking history, chronic respiratory symptoms, and lifestyle-related diseases, including hypertension, angina pectoris/myocardial infarction, diabetes mellitus, dyslipidemia, and osteoporosis. We defined two criteria to identify possible COPD candidates: 1) individuals with a positive smoking history, either current or past, or a passive smoking history, either at home or in the workplace; and 2) individuals with chronic respiratory symptoms or lifestyle-related disease. When residents fulfilled both criteria, they were considered COPD candidates and advised to undergo PFT. Two certified medical laboratory technicians administered this testing. No bronchodilators were used, and the best result of three was used as the test result. The functional diagnosis of COPD was defined as forced expiratory volume in 1 second (FEV_1)/forced vital capacity (FVC) less than 70%. The classification of COPD stage was based on GOLD (Global initiative for chronic Obstructive Lung Disease) staging: mild COPD, percentage predicted FEV_1 >80%; moderate COPD, percentage predicted FEV_1 <80% but >50%; severe COPD, percentage predicted FEV_1 <50% but >30%; very severe COPD, percentage predicted FEV_1 <30%.[12] Individuals who refused to undergo PFT and those who could not perform PFT well were excluded from analysis.

We divided COPD candidates into the following four groups (Figure 1): group A, positive smoking history and positive chronic respiratory symptoms, including cough, cough producing sputum, and dyspnea on effort; group B, positive smoking history, no chronic respiratory symptoms, and positive lifestyle-related disease; group C, passive smoking history and positive chronic respiratory symptoms; group D, passive smoking history, no chronic respiratory symptoms, and positive lifestyle-related disease.

Once participants were diagnosed with COPD, they were instructed to receive chest computed tomography to identify radiological emphysema, the severity of which was visually assessed by two independent pulmonary specialists, in a blinded fashion, according to the modified Goddard scoring system.[13,14] Three lung slices, with right and left lungs evaluated separately for a total of six images, were analyzed for each participant. Each image was classified and scored:
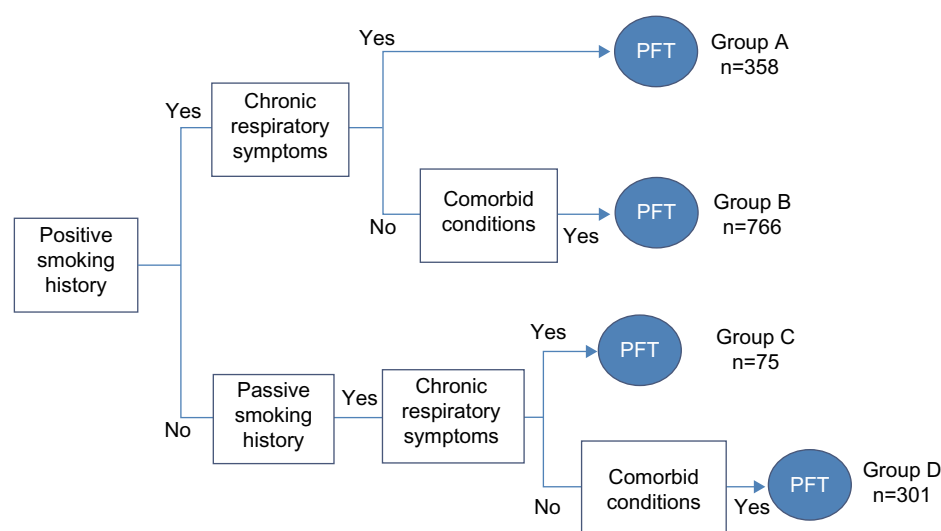
Figure 1 Algorithm of screening for chronic obstructive pulmonary disease (COPD).
Notes: We divided COPD candidates into the following four groups: group A, positive smoking history and positive chronic respiratory symptoms including cough, cough producing sputum, and dyspnea on effort; group B, positive smoking history, no chronic respiratory symptoms, and positive lifestyle-related disease; group C, passive smoking history and positive chronic respiratory symptoms; group D, passive smoking history, no chronic respiratory symptoms, and positive lifestyle-related disease. Comorbid conditions – lifestyle-related disease: hypertension, angina pectoris/myocardial infarction, diabetes mellitus, dyslipidemia, and osteoporosis.
Abbreviation: PFT, pulmonary function test.

normal, score 0; ≤5% affected, score 0.5; ≤25% affected, score 1; ≤50% affected, score 2; ≤75% affected, score 3; and >75% affected, score 4. The mean score of the six images was considered to be representative of emphysema severity. The participants were then classified into three groups based on the severity of emphysema: 1) no/mild emphysema (emphysema score <1, average percentage low-attenuation area in the assessed lung <12.5%); 2) moderate emphysema (emphysema score 1–2.5, average percentage low-attenuation area in the assessed lung <50%); and 3) severe emphysema (emphysema score ≥2.5, average percentage low-attenuation area in the assessed lung ≥50%).

Statistical analysis

Data were analyzed using SPSS version 19 (IBM, Armonk, NY, USA). The χ^2 test was used to analyze categorical variables, and the Kruskal–Wallis test was used for continuous variables. The relation between two quantitative variables was examined using the Spearman rank correlation test. Possible predictor variables, including patient sex, age, smoking status, and the presence of lifestyle-related disease, were assessed as risk factors for COPD using multiple regression analysis. A significance level of 5% was adopted, and the significance of predictor variables was tested using the likelihood-ratio test.

Results

Of the 7,067 total participants (2,720 male and 4,347 female), COPD candidate criteria were fulfilled in 1,686 (23.9%), and 1,500 of these underwent PFT. We excluded from analysis 153 individuals who refused to undergo PFT and 23 who could not perform PFT well; a total of 1,500 participants (21.2%) were included in the study.

Of those who underwent PFT, 171 (11.4%) were diagnosed with COPD, yielding a COPD detection rate of 2.4% (171 of 7,067). Table 1 shows the characteristics of the possible COPD candidates according to group: group A consisted of 358 subjects, group B had 766 subjects, group C had 75 subjects, and group D had 301 subjects. In groups A and B, there was a significantly higher proportion of male patients than in groups C and D ($P<0.001$). Age, smoking status, and lifestyle-related disease distribution were also significantly different among the four groups ($P<0.001$). Table 2 shows the distribution of COPD severity and PFT results. The frequency of COPD was significantly higher in groups A and B than in groups C and D ($P=0.048$); however, the distribution of COPD grades was similar in the four groups ($P=0.372$). Although the values for FEV_1/FVC were similar across all groups ($P=0.185$), the mean value in groups A and B was significantly lower than in groups C and D ($P=0.003$). The percentage predicted FEV_1 was significantly worse in groups A and B than in groups C and D ($P<0.001$). Table 3 shows the characteristics of participants who were diagnosed with COPD. Male sex and higher age were significantly more common in groups A and B than in groups C and D ($P<0.001$).

Table 1 Characteristics of COPD candidates

	Group A (n=358)	Group B (n=766)	Group C (n=75)	Group D (n=301)	Total	*P*-value
Male/female	277/81	613/153	9/66	27/274	926/574	<0.001
Male %	77.4%	80.0%	12.0%	9.0%		
Age (years)						<0.001
40–49	61 (17.0%)	30 (3.9%)	17 (22.7%)	2 (0.7%)	110	
50–59	60 (16.8%)	76 (9.9%)	16 (21.3%)	44 (14.6%)	196	
60–69	125 (34.9%)	301 (39.3%)	31 (41.3%)	144 (47.8%)	601	
70–79	95 (26.5%)	269 (35.1%)	10 (13.3%)	85 (28.3%)	459	
80+	17 (4.8%)	90 (11.8%)	1 (1.4%)	26 (8.6%)	134	
Mean ± standard deviation	62.6±11.2	68.5±9.2	59.2±10.5	67.2±8.0	66.4±10.0	<0.001
Median	64.0	69.0	61.0	66.0	67.0	
Smoking status						<0.001
Current	204 (57.0%)	194 (25.3%)	0	0	398	
Past	154 (43.0%)	572 (74.7%)	0	0	726	
Passive	0	0	75	301	376	
Smoking index (pack-years)	33.6±20.6	31.0±22.3	0	0		<0.001
Positive respiratory symptoms*	358	0	75	0	433	<0.001
Lifestyle-related disease						
Hypertension	93 (26.0%)	564 (73.6%)	15 (20.0%)	232 (77.1%)	904	<0.001
AP/MI	14 (3.9%)	64 (8.4%)	1 (1.3%)	6 (2.0%)	85	<0.001
Diabetes mellitus	19 (5.3%)	141 (18.4%)	5 (6.7%)	28 (9.3%)	193	<0.001
Dyslipidemia	30 (8.4%)	143 (18.7%)	9 (12.0%)	99 (32.9%)	281	<0.001
Osteoporosis	1 (0.3%)	22 (2.9%)	1 (1.3%)	36 (12.0%)	60	<0.001

Notes: *Positive respiratory symptoms include cough, cough producing sputum, and dyspnea on effort. Group A, positive smoking history, positive chronic respiratory symptoms; group B, no chronic respiratory symptoms, positive lifestyle-related disease; group C, passive smoking history, positive chronic respiratory symptoms; group D, passive smoking history, no chronic respiratory symptoms, positive lifestyle-related disease.
Abbreviations: COPD, chronic obstructive pulmonary disease; AP, angina pectoris; MI, myocardial infarction.

Table 2 COPD classification and pulmonary function testing results

	Group A (n=358)	Group B (n=766)	Group C (n=75)	Group D (n=301)	Total	*P*-value
COPD (FEV$_1$/FVC <70%), n (%)	47 (13.1)	96 (12.5)	5 (6.7)	23 (7.6)	171	0.048
Mild COPD	8 (17.0)	28 (29.2)	3 (60.0)	8 (34.8)	47 (27.0)	
Moderate COPD	31 (66.0)	58 (60.4)	2 (40.0)	14 (60.9)	105 (61.4)	0.0372
Severe COPD	7 (14.9)	10 (10.4)	0	1 (4.3)	18 (10.5)	
Very severe COPD	1 (2.1)	0	0	0	1 (0.6)	
FEV$_1$/FVC, n (%)						0.185
>70	311 (86.9)	670 (87.5)	70 (93.3)	278 (92.4)	1,329 (88.6)	
50–70	45 (12.6)	92 (12.0)	5 (6.7)	23 (7.6)	165 (11.0)	
30–50	2 (0.6)	4 (0.5)	0	0	6 (0.4)	
<30	0	0	0	0	0	
Mean ± standard deviation	78.3±8.8	78.0±8.5	80.4±6.9	79.5±7.3	78.5±8.3	0.003
Median	78.9	78.4	80.5	80.2	79.2	
% predicted FEV$_1$, n (%)						<0.001
>80	245 (68.4)	542 (70.8)	64 (85.3)	258 (85.7)	1,109 (73.9)	
50–80	105 (29.3)	212 (27.7)	11 (14.7)	41 (13.6)	369 (24.6)	
30–50	7 (2.0)	12 (1.6)	0	2 (0.7)	21 (1.4)	
<30	1 (0.3)	0	0	0	1 (0.1)	
Mean ± standard deviation	87.1±17.3	88.0±16.3	96.0±17.3	97.0±17.5	90.0±17.3	<0.001
Median	87.3	88.5	96.6	97.7	90.6	

Notes: COPD stage – mild, % predicted FEV$_1$ >80%; moderate, 50%–80%; severe, 30%–50%; very severe, <30%.
Abbreviations: COPD, chronic obstructive pulmonary disease, FEV$_1$, forced expiratory volume in 1 second; FVC, forced vital capacity.

Table 3 Characteristics of COPD patients

	Group A (n=47)	Group B (n=96)	Group C (n=5)	Group D (n=23)	Total	*P*-value
Male/female	44/3	87/9	1/4	2/21	134/37	<0.001
Male %	(93.6)	(90.6)	(20.0)	(8.7)	(78.4)	
Age (years), n (%)						<0.001
40–49	0	1 (1.0)	2 (40.0)	0	3 (1.8)	
50–59	2 (4.3)	2 (2.1)	1 (20.0)	0	5 (2.9)	
60–69	17 (36.2)	20 (20.8)	1 (20.0)	10 (43.5)	58 (33.9)	
70–79	21 (44.7)	41 (42.7)	1 (20.0)	6 (26.1)	69 (40.4)	
80+	7 (14.9)	22 (22.9)	0	7 (30.4)	36 (21.1)	
Mean ± standard deviation	70.0±7.2	72.8±8.2	56.0±12.6	72.7±8.7	71.7±8.6	0.015
Median	70.0	73.5	57.0	71.0	71.0	
Smoking status, n (%)						<0.001
Current smoker	27 (57.4%)	31 (32.3%)	0 (0.0%)	0 (0.0%)	58 (33.9%)	
Past smoker	20 (42.6)	65 (67.7)	0	0	85 (49.7)	
Passive smoker	0	0	5 (100)	23 (100)	28 (16.4)	
Smoking index (pack-years)	48.8±22.1	35.8±23.0	0	0		<0.001
Positive respiratory symptoms*	47	0	5	0	52	<0.001
Lifestyle-related disease, n (%)						
Hypertension	17 (36.2)	76 (79.2)	1 (20.0)	15 (65.2)	109 (63.7)	<0.001
AP/MI	0	9 (9.4)	0	0	9 (5.3)	0.06
Diabetes mellitus	3 (6.4)	15 (15.6)	0	2 (8.7)	20 (11.7)	0.31
Dyslipidemia	3 (6.4)	10 (10.4)	0	9 (39.1)	22 (12.9)	0.001
Osteoporosis	0	0	0	4 (17.4)	4 (2.3)	<0.001

Note: *Positive respiratory symptoms include cough, cough producing sputum, and dyspnea on effort.
Abbreviations: COPD, chronic obstructive pulmonary disease; AP, angina pectoris; MI, myocardial infarction.

Computed tomography data were collected from 152 participants who were diagnosed with COPD and underwent the examination for secondary evaluation. Figure 2 shows the relation between PFT data (percentage predicted FEV_1 and FEV_1/FVC) and the emphysema score (Goddard classification). The emphysema score was not correlated with either the percentage predicted FEV_1 or the FEV_1/FVC value.

Of the 171 patients with COPD, 124 (72.5%) had moderate or worse disease requiring medical treatment. Subjects with a positive smoking history (groups A and B) had a significantly higher COPD detection rate (143 of 1,124, 12.7%) compared with subjects who had a passive smoking history (groups C and D, 28 of 376, 7.4%).

Univariate analysis of risk factors for COPD, according to patient sex and age, identified that a history of pulmonary disease was only a risk factor for COPD in patients younger than 60 years. In patients 60 years of age or older, a smoking index greater than 30 pack-years was a risk factor in males, and a history of pulmonary disease was a risk factor in females (Table 4). Multiple logistic regression analysis identified male sex, age 60 years or greater, and a positive smoking history as risk factors for COPD (Table 5). When risk analysis was conducted by sex in patients 60 years of age or older, the same risk factors as previously identified

(a pack-year smoking index greater than 30 in males and a history of pulmonary disease in females) were confirmed to be independent risk factors for COPD (Table 6).

Discussion

The purpose of this project was to identify which individuals should be examined by PFT for the purpose of detecting COPD. Almost a quarter of study participants were considered to be COPD candidates and were recommended to undergo on-site PFT, and 11.4% of these were diagnosed with COPD. We therefore conclude that approximately 2.4% of Japanese individuals aged 40 years or older who undergo routine lung cancer screening may have COPD. Almost three-quarters of those with COPD were staged as moderate or worse and required medical treatment. Those with a positive personal smoking history were significantly more likely to have COPD than those with a passive smoking history. Although COPD patients frequently have comorbid lifestyle-related disease, these diseases did not prove to be risk factors for COPD in our study. The diagnosis rate of COPD rapidly increased in patients 60 years of age or older. From these results, we can suggest that individuals in this age-group with a positive smoking history should undergo PFT to detect COPD. By multivariate analysis, positive smoking history was not a risk factor for COPD. A smoking index more than 30 pack-years was only a
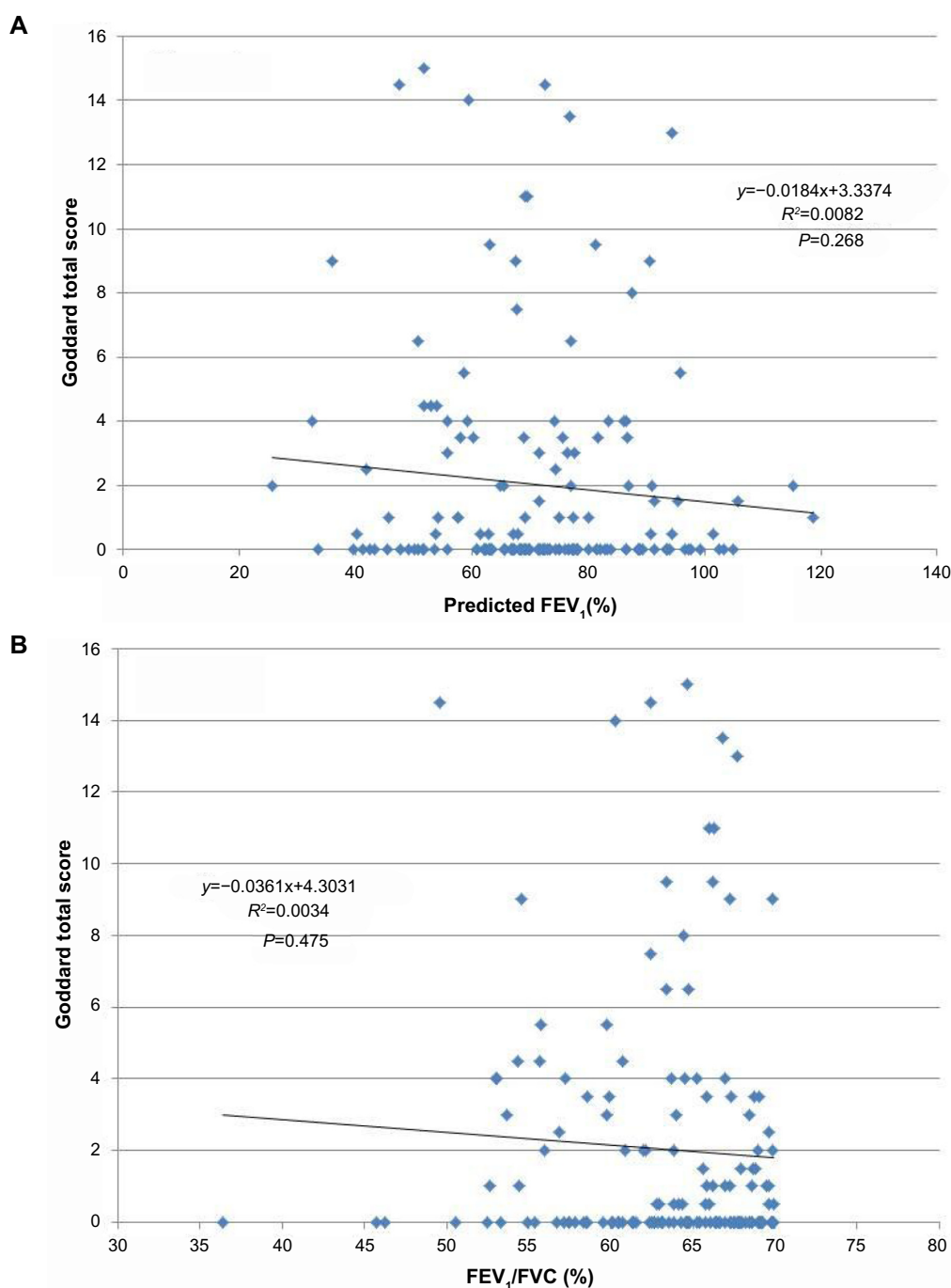
A

B

Figure 2 (**A** and **B**) Correlation between PFT and emphysema score (Goddard classification) in 152 participants who underwent both PFT and CT. The emphysema score was not correlated with either the percentage predicted FEV_1 ($P=0.268$) or the FEV_1/FVC ($P=0.475$) values. (**A**) Percentage predicted FEV_1; (**B**) FEV_1/FVC.
Abbreviations: PFT, pulmonary function testing; CT, computed tomography; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity.

risk factor for males. This may be because 1,067 participants (groups B and D) did not have any respiratory symptoms. Therefore, we cannot say that females with smoking history do not need PFT for COPD screening.

We previously reviewed the association between COPD and lung cancer, and proposed that early detection of COPD is important for lung cancer surveillance.[15] The present study is the second to describe the utilization of regional mass

screening for lung cancer to detect COPD.[16] Of course, screening programs are clearly targeted at specific disease entities. For example, lung cancer screening is designed to detect early stage lung cancer, and the questionnaires and radiological examinations are focused on detecting that disease. However, patient age, smoking history, and the presence of chronic respiratory symptoms are important history items for both lung cancer and COPD. In fact, a positive smoking history

Table 4 Univariate analysis of risk factors for COPD according to sex and age

	Male			Female		
	Non-COPD (%)	COPD (%)	*P*-value	Non-COPD (%)	COPD (%)	*P*-value
Younger than 60 years	n=133	n=4		n=165	n=4	
Smoking index (>30 pack-years)	45.1	50.0	0.847	11.5	0	0.471
Positive respiratory symptoms*	57.9	50.0	0.753	43.6	75.0	0.212
Smoking status			0.382			0.343
Current smoker	54.9	25.0		29.1	0	
Past smoker	40.6	75.0		28.5	25.0	
Passive smoker	4.5	0		42.4	75.0	
Lifestyle-related disease	54.9	50.0	0.847	61.8	50.0	0.631
Hypertension	33.8	25.0	0.712	41.2	50.0	0.724
AP/MI	4.5	0	0.664	0.6	0.0	0.876
Diabetes mellitus	11.3	0	0.477	5.5	0	0.631
Dyslipidemia	17.3	25.0	0.690	15.8	0	0.388
Osteoporosis	0	0		7.3	0	0.576
History of pulmonary disease	12.0	50.0	0.027	13.9	50.0	0.045
Lung cancer	0	0		0	0	
Tuberculosis	0	0		0	25.0	0.000
Emphysema	0	0		0	0	
Pneumonia	5.3	0.0	0.638	2.4	50.0	0.000
Asthma	4.5	50.0	0.000	9.1	50.0	0.007
Pleurisy	0	0		0	0	
Chronic bronchitis	3.0	0	0.725	2.4	0	0.753
60 years of age or older	n=659	n=130		n=372	n=33	
Smoking index (>30 pack-years)	56.2	70.8	0.002	13.2	6.1	0.238
Positive respiratory symptoms*	24.9	33.1	0.052	18.3	12.1	0.375
Smoking status			0.003			0.800
Current smoker	24.7	39.2		15.1	18.2	
Past smoker	71.2	58.5		19.1	15.2	
Passive smoker	4.1	2.3		65.9	66.7	
Lifestyle-related disease	85.0	80.8	0.228	88.7	90.9	0.700
Hypertension	66.6	67.7	0.812	65.3	54.5	0.215
AP/MI	9.3	6.2	0.252	2.2	3.0	0.742
Diabetes mellitus	17.8	13.8	0.280	8.6	6.1	0.614
Dyslipidemia	14.0	6.9	0.028	31.7	36.4	0.584
Osteoporosis	0.9	0.0	0.275	10.2	12.1	0.731
History of pulmonary disease	12.8	14.6	0.572	12.9	30.3	0.006
Lung cancer	0.2	0	0.657	0	0	
Tuberculosis	3.3	3.8	0.771	1.3	0	0.503
Emphysema	0.6	2.3	0.059	0	0	
Pneumonia	4.2	0.8	0.054	3.2	3.0	0.951
Asthma	1.1	4.6	0.004	3.8	12.1	0.026
Pleurisy	1.7	0.0	0.138	0.8	3.0	0.216
Chronic bronchitis	1.5	0.8	0.506	2.7	9.1	0.046

Note: *Positive respiratory symptoms include cough, cough producing sputum, and dyspnea on effort.
Abbreviations: COPD, chronic obstructive pulmonary disease; AP, angina pectoris; MI, myocardial infarction.

and chronic respiratory symptoms are reportedly crucial factors that should trigger clinicians to suspect COPD.[17,18] Therefore, we expected that COPD could be detected using the lung cancer mass-screening program, with a small additional expense for PFT at the primary evaluation.

The prevalence of COPD in the general population is thought to be about 1%, and the prevalence increases to 8%–10% of the population over 40 years of age.[19] In this study, approximately 2.4% of all participants aged 40 years or older who underwent routine lung cancer screening may have COPD. This seems to be a lower detection rate than other cohorts.[4,19] However, 11.4% of the COPD candidates in this study were diagnosed with COPD. Furthermore, by focusing on smokers (groups A and B), 12.7% of participants (143 of 1,124) were

Table 5 Multivariate analysis of risk factors for COPD

Variables	β	Wald	Hazard ratio	95% CI	P-value
Sex (male)	0.656	6.014	1.928	1.141–3.257	0.014
Age (>60 years)	1.652	19.248	5.215	2.494–10.907	0.000
Smoking index (>30 pack-years)	0.452	5.396	1.571	1.073–2.300	0.020
History of pulmonary disease*	0.489	5.016	1.630	1.063–2.500	0.025
Group	1.306				
Group C			1	Reference	
Group A	−0.109	0.040	0.897	0.309–2.603	0.841
Group B	−0.305	0.331	0.737	0.261–2.084	0.565
Group D	−0.095	0.033	0.910	0.327–2.530	0.856

Note: *History of pulmonary disease includes lung cancer, tuberculosis, emphysema, pneumonia, asthma, pleurisy, and chronic bronchitis.
Abbreviations: COPD, chronic obstructive pulmonary disease; CI, confidence interval.

diagnosed with COPD. This means that our screening system can obtain the same detection rate as other trials.

In our study, the PFT participation rate was very high, allowing the diagnosis of COPD to be made at the time of initial screening. Lyngsø et al reported the use of a simple postal questionnaire containing questions about risk factors to screen for COPD.[18] Although the rates of COPD risk and actual, spirometry-confirmed COPD were 58.5% (3,376 of 5,767) and 10.3% (596 of 5,767), respectively, the rate of participation in PFT was only 40.0% (1,352 of 3,376), perhaps because of the time-consuming nature of the spirometry appointment. In our study, 89% of the subjects at risk for COPD were able to undergo PFT at the time of initial screening, as testing was immediately available on site. Since a high participation rate is crucial for the effect of screening to be felt in a population, and is a requirement for the implementation of organized screening, our on-site program seems ideal.

In this study, we considered individuals with a passive smoking history and lifestyle-related disease to be at risk for COPD. Jordan et al reported that increasing passive smoke exposure is independently associated with an increased risk for COPD.[20] Certain comorbidities, including lifestyle-related diseases, are also more likely to be present in COPD patients.[9] Therefore, we hypothesized that individuals with these factors present would have a relatively high prevalence of COPD. In actuality, we found that increasing age (60 years or older), a smoking index of 30 pack-years or more, and a history of pulmonary disease, but not lifestyle-related disease or passive smoking history, were significant risk factors for COPD. Therefore, nonactive smokers or individuals with lifestyle-related disease should not be a target for COPD screening. Of course, since COPD may be hidden in patients with lifestyle-related disease, general practitioners should pay attention to subtle symptoms and have a high index of suspicion for COPD.

In females, a history of pulmonary disease was a risk factor for COPD. A history of pulmonary disease includes lung cancer, tuberculosis, emphysema, pneumonia, asthma, pleurisy, and chronic bronchitis. Many pulmonary diseases interact with each other, and airway obstruction can be induced. Therefore, this result may suggest that patients who

Table 6 Multivariate analysis of risk factors for COPD in patients aged >60 years, according to sex

Variables	β	Wald	Hazard ratio	95% CI	P-value
Male (n=786)					
Smoking index (>30 pack-years)	0.594	7.605	1.811	1.187–2.761	0.006
Positive smoking history	0.165	0.067	1.179	0.339–4.099	0.795
Lifestyle-related disease*	−0.333	2.507	0.716	0.474–1.083	0.113
History of pulmonary disease#	0.087	0.097	1.091	0.631–1.884	0.756
Female (n=405)					
Smoking index (>30 pack-years)	−1.058	1.697	0.347	0.071–1.705	0.193
Positive smoking history	0.266	0.392	1.304	0.568–2.996	0.531
Lifestyle-related disease*	0.705	1.510	2.023	0.658–6.224	0.219
History of pulmonary disease#	1.216	8.277	3.374	1.473–7.725	0.004

Notes: *Lifestyle-related disease includes hypertension, angina pectoris/myocardial infarction, diabetes mellitus, dyslipidemia, and osteoporosis; #history of pulmonary disease includes lung cancer, tuberculosis, emphysema, pneumonia, asthma, pleurisy, and chronic bronchitis.
Abbreviations: COPD, chronic obstructive pulmonary disease; CI, confidence interval.

had any pulmonary disease should confirm the possibility of airway obstruction.

There are several limitations to our study. We adopted the criterion of FEV_1/FVC less than 70%, without the use of bronchodilators, to define COPD. A simple fixed FEV_1/FVC ratio (the GOLD definition) used to define lung-function impairment has been shown to overestimate COPD with increasing age, particularly among men, compared with such statistical approaches as the lower limit of normal.[21] Therefore, our COPD definition might have been inaccurate in patients of advanced age. However, the GOLD criterion is a clear, easy-to-understand recommendation. Spirometry without the use of bronchodilators may also have resulted in overestimation of airflow limitation. However, the more complicated and difficult technique involved with bronchodilator testing is not appropriate for a screening examination. Therefore, subjects who are diagnosed with COPD on screening should be examined more precisely by a pulmonologist at the secondary evaluation for a definitive diagnosis and treatment plan.

In our study, we did not calculate the actual cost at the screening. However, we were able to limit COPD candidates by questionnaires without any expense. Salameh et al reported that they created a diagnosis score for COPD, and clarified the usefulness of this score without spirometry for detection of COPD.[22] We also performed PFT only for the participants who were suspected to be at high risk for COPD. Furthermore, data from Haroon et al are instructive, as they compared the yield and cost-effectiveness of two COPD case-finding approaches for ever-smokers aged 35–79 years with no history of COPD or asthma in primary care.[23] They reported that respiratory questionnaires were posted to patients in the "targeted" arm and provided to patients in the "opportunistic" arm at routine general practitioner appointments. Patients allocated to the targeted arm were sent an invitation letter, respiratory questionnaire, consent form, and a prepaid return envelope in the post by the research team. In the opportunistic arm, electronic prompts were added to medical records to provide the same questionnaire pack when patients next presented to their general practitioner or practice nurse. They concluded that opportunistic case finding may be more effective and cost-effective than targeting patients with a postal questionnaire alone. These results suggest that PFT should be done only for high-risk individuals in community-based mass screening.

In conclusion, COPD can be effectively detected using an established community-based lung cancer-screening program. Individuals 60 years of age or older with a positive smoking history should undergo PFT to detect COPD. After COPD is identified on screening, further precise diagnostic assessment is required for correct staging and treatment decisions. We should note that because both COPD and lung cancer have high mortality rates and incur severe economic burdens, encouragement of smoking cessation and early detection and intervention for both diseases should be initiated through these screenings.

Acknowledgments

Disclosure

The authors report no conflicts of interest in this work.

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