Active case finding strategy for chronic obstructive pulmonary disease with handheld spirometry

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Abstract

The early detection and diagnosis of chronic obstructive pulmonary disease (COPD) is critical to providing appropriate and timely treatment. We explored a new active case-finding strategy for COPD using handheld spirometry.

We recruited subjects over 40 years of age with a smoking history of more than 10 pack-years who visited a primary clinic complaining of respiratory symptoms. A total of 190 of subjects were enrolled. Medical information was obtained from historical records and physical examination by general practitioners. All subjects had their pulmonary function evaluated using handheld spirometry with a COPD-6 device. Because forced expiratory volume in 6 seconds (FEV_6) has been suggested as an alternative to FVC, we measured forced expiratory volume in 1 second (FEV_1)/FEV_6 for diagnosis of airflow limitation. All subjects were then referred to tertiary referral hospitals to complete a "Could it be COPD?" questionnaire, handheld spiromtery, and conventional spirometry. The results of each instrument were compared to evaluate the efficacy of both handheld spirometry and the questionnaire.

COPD was newly diagnosed in 45 (23.7%) patients. According to our receiver-operating characteristic (ROC) curve analysis, sensitivity and specificity were maximal when the FEV_1/FEV_6 ratio was less than 77%. The area under the ROC curve was 0.759. The sensitivity, specificity, positive predictive value, and negative predictive value were 72.7%, 77.1%, 50%, and 90%, respectively. The area under the ROC curve of respiratory symptoms listed on the questionnaire ranged from 0.5 to 0.65, which indicates that there is almost no difference compared with the results of handheld spirometry.

The present study demonstrated the efficacy of handheld spirometry as an active case-finding tool for COPD in a primary clinical setting. This study suggested that physicians should recommend handheld spirometry for people over the age of 40, who have a smoking history of more than 10 pack-years, regardless of respiratory symptoms. Furthermore, people who have abnormal results, determined using the FEV_1/FEV_6 ≤ 0.77 cut-off, should be referred for further conventional spirometry to confirm the diagnosis of COPD. However, further studies within the general population are necessary to establish efficacy in the public.

Abbreviations: AUC = area under curve, COPD = Chronic obstructive pulmonary disease, FEV_1 = forced expiratory volume in 1 second, FEV_6 = forced expiratory volume in 6 seconds, FVC = forced vital capacity, GERD = gastroesophageal reflux disease, GOLD = Global Initiative for Obstructive Lung Disease, mMRC = modified Medical Research Council, NPV = negative predictive value, PPV = positive predictive value, ROC = receiver-operator characteristic.

Keywords: active case finding, COPD-6, efficacy, handheld spirometry

1. Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by persistent and progressive airflow limitation.[1] COPD has emerged as a serious public health concern in recent years, and is predicted to become the fourth leading cause of death worldwide by 2030.[1,2] However, public awareness of COPD is limited.[3–5] Moreover, some studies have demonstrated that a significant number of individuals have undiagnosed airflow limitation.[6,7] COPD is not usually diagnosed until lung function has deteriorated by at least 50%.[8] Thus, there have been recent efforts to improve the detection and diagnosis of COPD. Early diagnosis and treatment of COPD can prevent the progressive deterioration of lung function and improve outcomes. This can be done through pharmacological intervention, or targeted interventions to help patients quit smoking, which is a major cause of COPD.[9,10] However, the routine screening of COPD is not recommended for the general population.[11,12] Therefore, the Global Initiative for Obstructive Lung Disease (GOLD) advocates active case finding.[1]

Spirometry is required for the diagnosis of COPD. A ratio of postbronchodilator forced expiratory volume in 1 second (FEV_1) to forced vital capacity (FVC) less than 0.7 is the standard diagnostic measure for the presence of airflow limitation.[1] Recently, measuring the forced expiratory volume in 6 seconds (FEV_6) has been suggested as an alternative to measuring FVC, because FVC is difficult to measure, can cause patients discomfort, and has poor reproducibility.[13] Handheld spirometry, which is small, inexpensive, and portable, measures both FEV_1 and FEV_6, instead of FVC. For active case finding, recent studies suggested the application of combined handheld spirometry and a COPD questionnaire.[14,15] Studies identifying the cut-off value for FEV_1/FEV_6 to diagnose airflow limitation have produced variable results, with values between 0.7 and 0.8.[16,17] Therefore, the purpose of this study was to determine the applicability of handheld spirometry as an active case-finding tool for the patients with risk factors for development of COPD in a primary clinical setting. We also explored the efficacy of the "Could it be COPD?" questionnaire developed by GOLD, in conjunction with measurement of FEV_1/FEV_6.

2. Methods

2.1. Study participants

This study was a prospective cohort study, which aimed to identify undiagnosed COPD patients using handheld spirometry. We enrolled subjects who visited a primary clinic complaining of respiratory symptoms from April to August of 2015. All participants were aged 40 years or older, had a history of smoking of more than 10 pack-years irrespective of their current smoking state, and had no previous diagnosis of COPD. We excluded patients with a history of disease that might have influenced spirometry results, such as tuberculosis-destroyed lungs, bronchiectasis, asthma, or lung cancer. All subjects provided informed written consent before inclusion in this study.

2.2. Procedure

Information such as symptoms, age, and smoking history was gathered from history taking and physical examination by primary care physicians. Subjects were then asked to perform handheld spirometry without a bronchodilator under supervision by their primary care physicians. The handheld spirometry used in this study was a COPD-6 device (Vitalograph, UK).

Upon completion of initial evaluation at the primary care clinics, subjects were referred to tertiary referral hospitals to conduct handheld spirometry for a second time, in addition to conventional spirometry with and without a bronchodilator according to standard procedure.[18] We selected tertiary referral hospitals that had more than 3 pulmonary specialists on staff. In addition, subjects were also asked to complete the "Could it be COPD?" questionnaire, which was developed by GOLD to assess the possibility of a COPD diagnosis (Table S1, http://links.lww.com/MD/B471),[19] as well as questionnaires on the severity of their dyspnea and comorbidities (Table S2, http://links.lww.com/MD/B471). Conventional spirometry was conducted by well-trained technicians, and interpreted by pulmonologists. Airflow limitation was defined by a postbronchodilator FEV_1/FVC ratio lower than 0.7.[1] The results of conventional spirometry were compared with those of the handheld spirometry performed both at the primary clinics and tertiary referral hospitals. We also explored the predictive value of the "Could it be COPD?" questionnaire in conjunction with FEV_1/FEV_6 measurement.

2.3. Statistical analysis

In determining the number of subjects required, we referred to previously the reported sensitivity (89%), specificity (98%) of the COPD-6, and the known prevalence of COPD in Korea (13.4%).[20] We attempted to obtain more than 90% specificity using handheld spirometry and a desired confidence level of 0.05, and determined that at least 161 patients were required for this study. All data are presented as mean ± standard deviation (SD) where appropriate, and were analyzed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY) and MedCalc Statistical Software version 16.4.3 (MedCalc Software bvba, Ostend, Belgium; https://www.medcalc.org; 2016). Descriptive analyses were performed to assess baseline patient characteristics. The relationship between FEV_1/FEV_6 and FEV_1/FVC was evaluated using a Pearson correlation analysis. Receiver-operator characteristic (ROC) curves were used to determine a cut-off value for handheld spirometry that corresponded to the optimal combination of sensitivity and specificity for a diagnosis of airflow limitation, defined by a postbronchodilator $FEV_1/FVC < 0.7$.[1] The area under the ROC curve for each respiratory symptom was used to evaluate its efficacy as active case-finding tool. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for the questionnaire using 2×2 tables. To compare the efficacy of the combination of handheld spirometry and the questionnaire with that of its components, we determined a regression equation through a binomial logistic regression test. After creating a new variable, we evaluated whether the combination could be better than its components alone by determining the area under the ROC curve. A P value of <0.05 was considered statistically significant.

2.4. Ethical statement

This study was approved by the board of each participating institution. IRB number of Hallym Sacred Heart Hospital was 2015-I027. All subjects provided written informed consent before conducting handheld spirometry at primary clinic.

3. Results

3.1. Study population

A total of 190 subjects from 9 primary clinics were enrolled in the present study (Figure S1, http://links.lww.com/MD/B471). The

mean age was 60.3 ± 10.6 years and the mean smoking history was 28.5 ± 14.6 pack-years. In the primary clinic setting, the proportion of subjects who complained of cough, phlegm, and dyspnea were 66.8%, 85.3%, and 36.5%, respectively. Conversely, the proportion of subjects who complained of cough, phlegm, and dyspnea on the "Could it be COPD?" questionnaire administered at tertiary referral hospitals were 33.2%, 43.7%, and 38.4%, respectively. The mean values for FEV_1/FEV_6 obtained using handheld spirometry at primary clinics was $79.6\pm10.9\%$ of the predicted value, whereas that obtained at tertiary referral hospitals was $77.3\pm7.6\%$ of the predicted value. For conventional spirometry, the mean FEV_1 and FEV_1/FVC with a bronchodilator were $92.8\pm14.7\%$ of the predicted value and $74.5\pm8.8\%$, respectively (Table 1). The FEV_1/FEV_6 for handheld spirometry and postbronchodilator FEV_1/FVC for conventional spirometry were well correlated ($r=0.504$, $P<0.001$) (Fig. 1).

3.2. Prevalence and distribution of severity of airflow limitation

A total of 45 (23.7%) subjects had airflow limitation confirmed by conventional spirometry, indicative of COPD. Among these newly diagnosed COPD patients, 95.6% had mild-to-moderate airflow limitation according to the GOLD guideline.[1] About 57.8% were classified as having GOLD 1, 37.8% as GOLD 2, and 4.4% as GOLD 3. No patient was classified as having GOLD 4 airflow limitation (Fig. 2).

3.3. Receiver-operating characteristic (ROC) curve for handheld spirometry

Using $FEV_1/FVC <0.7$ as a definition of airflow limitation by conventional spirometry, $FEV_1/FEV_6 \leq77\%$ by handheld spirometry had the best sum of sensitivity (72.7%), specificity (77.1%), PPV (50%), and NPV (90%), according to the ROC curve analysis. The area under the curve (AUC) was 0.759 (Fig. 3).
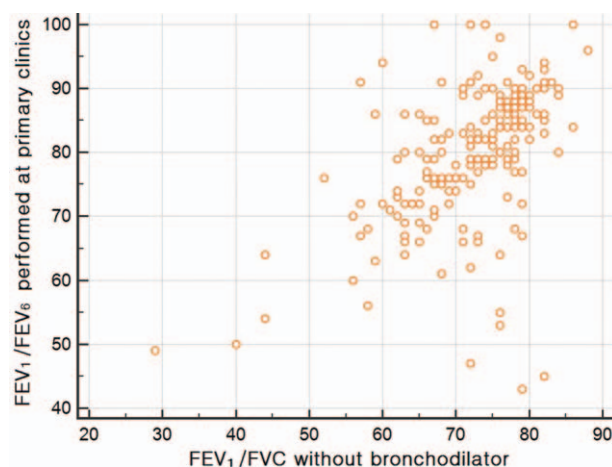
Figure 1. Relationship between handheld spirometric FEV_1/FEV_6 and postbronchodilator conventional spirometric FEV_1/FVC values. $FEV_1=$ forced expiratory volume in 1 second, $FEV_6=$ forced expiratory volume in 6 seconds, $FVC=$ forced vital capacity.

3.4. Comparison of characteristics according to the result of handheld spirometry in patients with airflow limitation
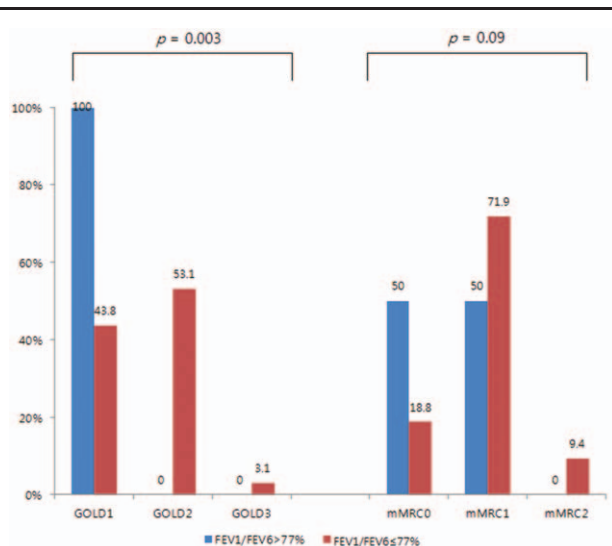
Among the newly diagnosed COPD patients, 12 patients demonstrated $FEV_1/FEV_6 \leq77\%$. Patients with abnormal handheld spirometry results also had lower pre and postbronchodilator FEV_1 values determined by conventional spirometry. According to the GOLD spirometric classification, the number of GOLD 1 patients was 12 (100.0%) and 14 (43.8%) for patients with normal and abnormal handheld spirometry results, respectively. All GOLD2 and GOLD3 patients had abnormal handheld spirometry results ($P=0.003$). Conversely, there were no significant differences in mean age, smoking history, respiratory symptoms, modified Medical Research Council

Table 1

Baseline characteristics of participants.

Characteristics	Total (N = 190)
Age (y, mean ± SD)	60.3 ± 10.6
Smoking amount (pack-years, mean ± SD)	28.5 ± 14.6
Symptoms assessed at primary clinic	
Cough (N, %)	127 (66.8)
Phlegm (N, %)	162 (85.3)
Dyspnea (N, %)	69 (36.5)
Symptoms from the "Could it be COPD?" questionnaire	
Cough (N, %)	63 (33.2)
Phlegm (N, %)	83 (43.7)
Dyspnea (N, %)	73 (38.4)
Mean mMRC	0.7 ± 0.6
Results of handheld spiromtery (%, mean ± SD)	
FEV_1/FEV_6 (primary clinics)	79.6 ± 10.9
FEV_1/FEV_6 (tertiary referral hospital)	77.3 ± 7.6
Results of spirometry (%, mean ± SD)	
Prebronchodilator FEV_1 of predicted value	90.3 ± 15.5
Prebronchodilator FEV_1/FVC	71.9 ± 8.6
Postbronchodilator FEV_1 of predicted value	92.8 ± 14.7
Postbronchodilator FEV_1/FVC	74.5 ± 8.8

$FEV_1=$ forced expiratory volume in 1 second, $FEV_6=$ forced expiratory volume in 6 seconds, $FVC=$ forced vital capacity, mMRC = modified Medical Research Council.

Figure 2. The distribution of patients according to GOLD spirometric classification and mMRC in newly diagnosed COPD patients. COPD = chronic obstructive pulmonary disease, GOLD = Global Initiative for Obstructive Lung Disease, mMRC = modified Medical Research Council.
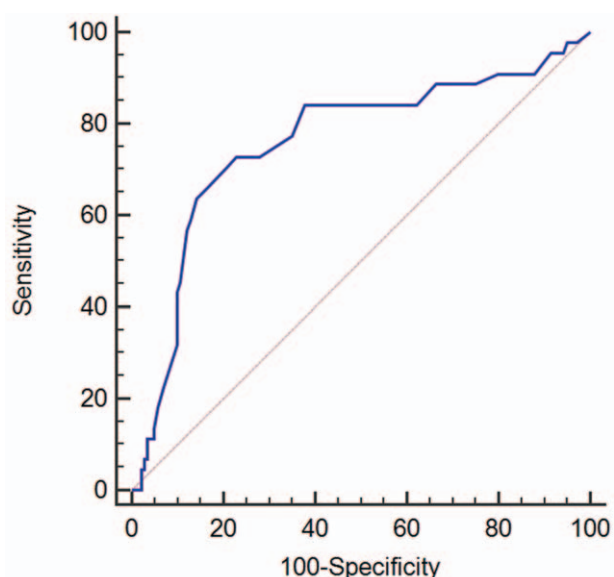
Figure 3. Determination of a cut-off FEV_1/FEV_6 value to predict COPD using handheld spirometry in a primary clinical setting. COPD = chronic obstructive pulmonary disease, FEV_1 = forced expiratory volume in 1 second, FEV_6 = forced expiratory volume in 6 seconds.

dyspnea scale, and comorbidities between patients with normal and abnormal handheld spirometry results (Table 2, Fig. 2).

3.5. Analysis from the "Could it be COPD?" questionnaire and its combination with handheld spirometry

We analyzed the sensitivity, specificity, PPV, and NPV of the "Could it be COPD?" questionnaire completed by subjects at tertiary referral hospitals. Complaint of cough had a sensitivity of 35.6%, specificity of 67.6%, PPV of 25.4%, and NPV of 77.2%, respectively. Complaint of the 3 respiratory symptoms of cough, phlegm, and dyspnea had a sensitivity of 20.0%, specificity of 91.0%, PPV of 40.9%, and NPV of 78.6%, respectively. The area under the ROC curve for each of these 3 respiratory symptoms and their combination ranged from 0.5 to 0.65 (Table 3).

We created a new variable combining and held spirometry performed at primary clinics and respiratory symptoms from the "Could it be COPD?" questionnaire using a binomial logistic regression. Cough and phlegm were excluded variables from the estimation of the regression equation, because they were not statistically significant. When dyspnea was combined with the results from handheld spirometry, the regression equation was $1.003 \times Dyspnea - 0.073 \times FEV_1/FEV_6 + 4.077$. The area under the ROC curve for this combination was 0.77 and did not differ significantly from the AUC of the ROC curve for handheld spirometry alone ($P = 0.71$) (Figure S2, http://links.lww.com/MD/B471).

Characteristics of patients with newly diagnosed COPD according to the results of handheld spirometry using cut-off value of FEV_1/FEV_6 ≤77% after ROC curve analysis.

	Total (N = 45)	FEV_1/FEV_6 >77% by handheld spirometry conducted at primary clinics (N = 12)	FEV_1/FEV_6 ≤77% by handheld spirometry conducted at primary clinics (N = 32)	P[*]
Age (y, mean ± SD)	68.3 ± 8.4	72.0 ± 8.3	66.6 ± 8.1	0.09
Smoking amount (pack-years, mean ± SD)	31.0 ± 12.9	28.6 ± 15.6	31.6 ± 12.1	0.57
prebronchodilator FEV_1 (% of predicted value, mean ± SD)	78.9 ± 19.2	96.5 ± 13.1	73.4 ± 16.4	< 0.001
postbronchodilator FEV_1 (% of predicted value, mean ± SD)	82.6 ± 17.7	99.3 ± 11.0	77.5 ± 15.1	<0.001
Respiratory symptoms				
Cough (N, %)	15 (35.6)	5 (41.7)	10 (31.3)	0.52
Phlegm (N, %)	21 (48.9)	7 (58.3)	14 (43.8)	0.39
Dyspnea (N, %)	26 (60.0)	8 (66.7)	18 (56.3)	0.53
mMRC dyspnea scale	0.8 ± 0.6	0.5 ± 0.5	0.9 ± 0.5	0.03
Comorbidities (N, %)				
Myocardial infarction	4 (8.9)	1 (8.3)	3 (9.4)	0.92
Congestive heart failure	1 (2.2)	0	1 (3.1)	0.22
Diabetes mellitus	8 (17.8)	3 (25.0)	5 (15.6)	0.47
Hypertension	18 (40.0)	4 (33.3)	13 (40.6)	0.66
Osteoporosis	1 (2.2)	0 (0)	1 (3.1)	0.54
GERD	3 (6.7)	0 (0)	2 (6.3)	0.38
Hyperlipidemia	7 (15.6)	1 (8.3)	6 (18.8)	0.69

COPD = chronic obstructive pulmonary disease, FEV_1 = forced expiratory volume in 1 second, FEV_6 = forced expiratory volume in 6 seconds, GERD = gastroesophageal reflux disease, ROC = receiver-operating characteristic.
[*] Comparison between normal and abnormal handheld spirometry result.

Table 3

Sensitivity, specificity, positive predictive value, negative predictive value, and area under the ROC curve for each symptom listed on the "Could it be COPD?" questionnaire.

	Sensitivity	Specificity	PPV	NPV	AUC
Cough	35.6%	67.6%	25.4%	77.2%	0.516
Phlegm	48.9%	57.9%	26.5%	78.5%	0.534
Dyspnea	60.0%	68.3%	37.0%	84.6%	0.641
Cough and phlegm	26.7%	78.6%	27.9%	77.6%	0.526
Cough and dyspnea	22.4%	88.3%	39.3%	79.0%	0.564
Phlegm and dyspnea	26.7%	84.8%	35.3%	78.8%	0.557
Cough and phlegm and dyspnea	20.0%	91.0%	40.9%	78.6%	0.555

AUC = area under the curve, COPD = chronic obstructive pulmonary disease, NPV = negative predictive value, PPV = positive predictive value, ROC = receiver-operating characteristic.

4. Discussion

At present, few studies have addressed the application of handheld spirometry and a questionnaire for COPD active case finding in a primary clinical setting. The aim of this study was to evaluate the efficacy of handheld spirometry as an active case-finding tool in people at risk of developing of COPD. We found that 23.7% of the participants were newly diagnosed with COPD using conventional spirometry at tertiary referral hospitals. Of note, this prevalence was higher than that reported in previous studies evaluating the prevalence of COPD.[20,21] Because we recruited subjects aged over 40 years with at least 10 pack-years smoking history, the prevalence of COPD for these individuals would be expected to be higher than for the general population. This finding is consistent with reports indicating a higher prevalence of COPD among people with known risk factors.[3] Furthermore, we observed that most newly diagnosed COPD patients had mild-to-moderate airflow limitation according to the GOLD guideline. This distribution is consistent with previous prevalence studies, which demonstrated that mild-to-moderate COPD is more prevalent than severe or very severe COPD.[20,21]

According to ROC curve analysis, we identified that a cut-off FEV_1/FEV_6 value of $\leq 77\%$ is an effective indicator of airflow limitation using handheld spirometry. This value could be used when referring patients to tertiary hospitals for confirmation of COPD diagnoses using conventional spirometry with a bronchodilator. The area under the ROC curve was 0.759, and therefore, this handheld spirometry method is classified as a moderately accurate test.[22] It is acceptable for use as an active case-finding test in primary clinics. We also tested the validity of a suggested $FEV_1/FEV_6 < 0.72$ cut-off for airway limitation reported in studies conducted in Japan and China.[23,24] We chose this value among others because of the similar ethnicity between these and our study population, which is an important consideration for evaluating pulmonary function.[25] Using this cut-off for our study population, sensitivity was 45.5%, specificity was 89.3%, PPV was 57.1%, and NPV was 83.9%. This difference probably arose from difference in methodology. The previously mentioned studies used conventional spirometry to assess airway function, whereas we used handheld spirometry. Furthermore, the differences in study populations could also contribute to the differences in results. They enrolled community-dwelling adults, regardless of smoking status, and respiratory symptoms, whereas we recruited individuals with known risk factors for COPD.

Although we enrolled subjects on the basis of subjective complaints of respiratory symptoms, the "Could it be COPD?" questionnaire in tertiary referral hospitals served as an objective measure of COPD-related respiratory symptoms. The results of the ROC curve analysis for the "Could it be COPD?" questionnaire suggest that respiratory symptom reporting is not appropriate as an active case-finding tool in subjects aged over 40 years with a smoking history of at least 10 pack-years.

When estimating a regression equation via a binominal logistic regression test, cough and phlegm were excluded because there was no statistical significance. Although dyspnea was the only respiratory symptom with which we could estimate a regression equation combined with the handheld spirometry results, the area under the ROC curve was not significantly different from the AUC of the ROC curve for handheld spirometry alone. Therefore, we propose that physicians should recommend handheld spirometry to individuals aged more than 40 years with a smoking history of at least 10 pack-years, regardless of respiratory symptoms.

We evaluated the correlation between FEV_1/FEV_6 determined by handheld spirometry at primary clinics and FEV1/FVC determined by conventional spirometry. The Pearson correlation coefficient was 0.504, which is considered a moderate correlation.[26] This correlation was the basis of our study, and suggests that further evaluations of the methods described here would be of value. To evaluate the accuracy of handheld spirometry, we compared the results of handheld and conventional spirometry. The mean FEV_1 of conventional spirometry was $8.0 \pm 12.4\%$ higher than that of handheld spirometry performed at primary clinics ($P < 0.001$). Interestingly, there was also a difference in the results of handheld spirometry performed at primary clinics and tertiary referral hospitals; the mean FEV_1 obtained with the handheld spirometry from tertiary referral hospitals was $7.7 \pm 11.1\%$ higher than that of primary clinics ($P < 0.001$). There was no difference between FEV_1 from conventional and handheld spirometry performed at tertiary referral hospitals ($P = 0.903$). These trends may be due to the order in which tests were conducted; subjects always performed handheld spirometry at tertiary referral hospitals after first attempting it at primary clinics. There could be a bias caused by the order of examination, a so-called learning effect.[27] If handheld spirometry from tertiary referral hospitals had been performed better than from primary clinics, the correlation coefficient would be higher between the FEV_1/FEV_6 from handheld spirometry performed at tertiary referral hospitals and FEV1/FVC by conventional spirometry; in fact, the Pearson correlation coefficient increased to 0.845.

Among patients with newly diagnosed COPD following conventional spirometry, the patients with abnormal handheld spirometry results in primary clinics had lower FEV_1 values determined by conventional spirometry, than those with normal

handheld spirometry results. Applying the GOLD spirometric classification, GOLD 1 was more significantly prevalent in patients with abnormal handheld spirometry results. Furthermore, GOLD 2 and GOLD 3 were only present in patients with abnormal handheld spirometry results. We interpreted this as an indication that handheld spirometry has a higher potential for misdiagnosis in patients with better pulmonary function. In previous studies, subjects classified as false negatives had either mild or moderate COPD, rather than severe or very severe COPD in screening using handheld spirometry devices.[28,29] Although the reason for this observation is unclear, it is acceptable that handheld devices are unable to clearly discriminate mild cases of disease. In a practical setting, if individuals with risk factors for COPD were misjudged as normal determined by handheld spirometry, they would expected to have a lower probability of COPD or if this were not identified, they would mild COPD.

For diagnosis of COPD, spirometry with a bronchodilator is required. However, handheld spirometry was not performed in conjunction with the administration of a bronchodilator. Due to safety concerns, it is not appropriate to administer a bronchodilator in a primary clinic in which monitoring and emergency procedures are insufficient. Alternatively, we suggest a novel strategy in which conventional spirometry with bronchodilator is recommended only for patients with abnormal findings using handheld spirometry, which can be performed in a primary clinical setting. This strategy could therefore decrease the unnecessary use of bronchodilator for COPD diagnosis.

This study had some limitations. We recruited the participants in summer, so a concern might arise that we could not recruit participants appropriate for the purpose of the study. Nevertheless, although COPD symptoms may be aggravated by cold weather, the airflow limitation required to diagnose COPD is persistent.[1] Not only that, the participants were asked again to make sure about their symptoms using "Could it be COPD" questionnaire released by GOLD, which does not include the questions about the symptoms affected by the weather. We thought that the participants were able to provide us with appropriate results. Furthermore, the exact number of subjects screened in the primary care clinic was not assessed. We only used the data of the participants who were referred to the tertiary referral hospitals, which might cause some skewness in the collected data. To overcome these limitations, a larger study to validate our suggested strategy with carefully handing the excluded subjects is needed.

5. Conclusion

We evaluated a new case finding strategy using handheld spirometry in a primary clinical setting. Implementation of handheld spirometry has the potential to improve early detection and diagnosis of COPD. This study suggested that physicians should recommend handheld spirometry for people over the age of forty, who have a smoking history of more than 10 pack-years, regardless of respiratory symptoms. Furthermore, people who have abnormal results, determined using the $FEV_1/FEV_6 \leq 0.77$ cut-off, should be referred for conventional spirometry to confirm the diagnosis of COPD. However, further studies within the general population are necessary to establish efficacy in public.

Acknowledgment

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