

Respiratory Symptoms and Undiagnosed Airflow Obstruction in Middle-Aged Adults*

The Korean Health and Genome Study

Chol Shin, MD, PhD, FCCP; Sungim Lee, PhD; Robert D. Abbott, PhD; Je Hyeong Kim, MD; Sang Yeub Lee, MD; Kwang Ho In, MD; and KuChan Kimm, MD, PhD

Background: The prevalence of undiagnosed airflow obstruction is difficult to measure since it requires screening in population-based samples to identify individuals free of clinical symptoms. The purpose of this report is to examine the prevalence of undiagnosed airflow obstruction and its relation with respiratory symptoms in middle-age adults in the Korean Health and Genome (KHG) Study.

Methods: The KHG study is an ongoing population-based study of Korean adults aged 40 to 69 years. The current report includes 8,140 men and women without a pulmonary disorder or obstructive lung disease. In this sample, undiagnosed airflow obstruction was defined on the basis of spirometric testing and in the absence of a medical history or a recognized pulmonary disorder. Respiratory symptoms included chronic cough, chronic phlegm, wheezing, and shortness of breath.

Results: Undiagnosed airflow obstruction was observed in 12.4% of the men (470 of 3,806 subjects) and in 3.5% of the women (152 of 4,334 subjects). In men, the age-adjusted prevalence of undiagnosed airflow obstruction increased consistently with increasing number of respiratory symptoms. In those who smoked, there was a 2.3-fold excess in its prevalence when three or more symptoms were present, as compared to when they were absent (27.4% vs 12.0%, $p < 0.001$). A 2.4-fold excess (20.6% vs 8.5%, $p = 0.004$) was observed in nonsmoking men, in whom respiratory symptoms were consistently less common than in those who smoked. Respiratory symptoms were unrelated to undiagnosed airflow obstruction in women smokers, although only 3.9% smoked cigarettes. In women who were nonsmokers, the prevalence of undiagnosed airflow obstruction increased from 2.3% in those without a respiratory symptom to 6.0% when three or more symptoms were present ($p = 0.003$).

Conclusions: Findings suggest that undiagnosed airflow obstruction is common in Korea with several respiratory symptoms. Whether respiratory symptoms with associations with undiagnosed airflow obstruction can be used to design early intervention strategies that prevent or delay the onset of COPD and its disabling consequences warrants further study. (CHEST 2004; 126:1234–1240)

Key words: airflow obstruction; epidemiology; Korea; respiratory symptoms

Abbreviation: KHG = Korean Health and Genome

Airflow obstruction is most often associated with diagnoses of asthma and COPD, with numerous consequences that often lead to disability, dependence on mechanical ventilation, and morbidity from cardiovascular disease.^{1–6} Although the prevalence

of airflow obstruction and its relation with respiratory symptoms have been well documented,^{7–11} studies of undiagnosed airflow obstruction in a large sample of adults are rare, particularly in developed regions of Asia. Studies of undiagnosed airflow obstruction are also difficult to undertake since they

*From the Department of Internal Medicine (Drs. Shin, Kim, S.Y. Lee, and In), School of Medicine, Korea University, Seoul, Korea; Division of Information and Computer Science (Dr. S. Lee), Dankook University, Seoul, Korea; Division of Biostatistics and Epidemiology (Dr. Abbott), University of Virginia, Charlottesville, VA; and Division of Epidemiology and Bioinformatics (Dr. Kimm), National Genome Research Institute, Seoul, Korea. Supported by a grant (348–6111-221) from the Korean National Institute of Health.

Manuscript received January 23, 2004; revision accepted May 17, 2004.

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Correspondence to: Sungim Lee, PhD, Division of Information and Computer Science, Dankook University, San 8, Hannam-Dong, Yongsan-Ku, Seoul, Korea, 140–714; e-mail: silee@dankook.ac.kr

require screening in population-based samples to identify individuals free of clinical symptoms. Such studies, however, are important since identification of respiratory symptoms with associations with undiagnosed airflow obstruction could lead to early intervention strategies that prevent or delay the onset of COPD and its disabling consequences. The purpose of the current report is to examine the prevalence of undiagnosed airflow obstruction and its relation with coexisting respiratory symptoms in middle-aged men and women in Korea.

MATERIALS AND METHODS

Background

The Korean Health and Genome (KHG) Study began in 2001 as an ongoing population-based study of Korean adults aged 40 to 69 years. Support for the study is from the National Genome Research Institute, as an effort to describe the frequency and determinants of chronic diseases in Korea. Participants include residents of an urban community 32 kilometers southwest of Seoul, South Korea (Ansan), and in a rural setting 100 kilometers south of Seoul (Ansung). Procedures were in accordance with institutional guidelines, and were approved by an institutional review committee. Informed consent was obtained from the study participants.

Study enrollment was based on knowledge about urban and rural differences in Korea, and on the most efficient method for recruiting representative samples of the Korean population. Since telephone use in Ansan is high, enrollment was based on random selection from directory listings that were made available from local telephone companies. In the Ansan sample, 2,523 men and 2,497 women agreed to participate in a baseline physical examination that included the routine assessment of anthropometry, BP, pulmonary function, ECG, lipid profiles, and other factors. In Ansong, sampling was based on both door-to-door and telephone solicitations within 5 randomly selected political regions from a total of 11 regions. Enrollment included 2,240 men and 2,780 women who underwent similar examinations as in Ansan. In both Ansan and Ansong, the age and sex distributions of those examined were comparable to those who were not examined. Although comparison of other characteristics is not possible, response rates are similar to other cohort studies.¹²⁻¹⁵

Spirometric Testing and Subjects

Spirometric testing was conducted by an experienced pulmonary technician through the use of a portable spirometer (Vmax-2130; SensorMedics; Yorba Linda, CA), according to criteria of the American Thoracic Society.¹⁶ Predicted FEV₁ and FVC were obtained from the methods of Morris.¹⁷

Subjects with a pulmonary disorder (including asthma, COPD, bronchiectasis, and pulmonary tuberculosis) based on responses from a self-administered questionnaire were excluded. Moreover, subjects with chest radiographs showing fibrotic lesions suggestive of old healed tuberculosis were evaluated for current symptoms of tuberculosis by a pulmonary specialist and radiologist, and they were also excluded in this report. In addition, subjects with reduced FEV₁ without apparent obstruction (FEV₁ < 80% predicted and FEV₁/FVC > 0.7) were also excluded because of a possibility of restrictive lung disease. Among the remaining sample, spirometric testing was completed in 8,140 subjects (3,806 men and 4,334 women).

Undiagnosed Airflow Obstruction and Respiratory Symptoms

In the absence of a medical history or a recognized pulmonary disorder, undiagnosed cases of airflow obstruction were identified as individuals with an FEV₁ < 70% of total FVC. Such cases were considered undiagnosed since pulmonary limitations would not have been identified without spirometric testing. Subjects also received thorough questioning about respiratory symptoms by trained interviewers using collection instruments from the European Community Respiratory Health Survey.¹⁸ Items included questions on cough, chronic phlegm, wheezing, and shortness of breath following guidelines from the British Medical Research Council.¹⁹ Shortness of breath was further characterized as occurring at rest, walking at a usual pace, and walking uphill.

Statistical Methods

Respiratory symptoms are described separately for men and women and according to age and smoking status. Prevalence of undiagnosed airflow obstruction was also estimated within gender and smoking strata, and in subjects with and without a respiratory symptom. In the latter comparisons, prevalence and tests of significance were based on standard analysis of covariance procedures and logistic regression models after age adjustment.²⁰ Prevalence of undiagnosed airflow obstruction was further assessed according to the increasing number of respiratory symptoms that characterized a study participant. All reported *p* values were based on two-sided levels of significance.

RESULTS

Undiagnosed airflow obstruction was observed in 12.4% of the men (470 of 3,806 subjects) and in 3.5% of the women (152 of 4,334 subjects). Tables 1, 2 present the overall prevalence of each respiratory symptom within 10-year age groups, and according to smoking status in men and women, respectively. Among the respiratory symptoms, those that were the most common included chronic phlegm, wheezing, shortness of breath, and shortness of breath at rest and when walking uphill.

In men who smoked cigarettes (Table 1), all but chronic cough and nocturnal shortness of breath increased significantly with age. In those who were nonsmokers, chronic cough and wheezing, and shortness of breath at rest were not significantly related with age. In contrast to men, women (Table 2) rarely smoked cigarettes (49.8% of the men vs 3.9% of the women). Perhaps due to the smaller sample of smoking women, associations between respiratory symptoms and age were harder to detect. Here, only chronic phlegm and nocturnal shortness of breath increased with age. In nonsmoking women, the frequency of all respiratory symptoms significantly increased with age (*p* < 0.01).

Figure 1 describes the prevalence of undiagnosed airflow obstruction for men and women across 10-year age groups by smoking status. In all instances, the prevalence of undiagnosed airflow obstruction

Table 1—Prevalence of Respiratory Symptoms by Age and Smoking Status in the Sample of Korean Men*

Respiratory Symptoms	Age Range, yr			Overall
	40–49	50–59	60–69	
Smokers				
Sample size	1,072	454	371	1,897
Chronic cough	3.8	4.9	4.7	4.2
Chronic phlegm†	24.7	27.2	31.5	26.6
Wheeze†	9.4	10.7	13.0	10.4
Nocturnal shortness of breath	3.6	4.9	3.9	4.0
Shortness of breath‡	28.1	34.5	41.4	32.2
At rest‡	10.1	15.9	19.5	13.3
Walking at usual pace‡	1.5	1.3	5.8	2.3
Walking uphill‡	22.9	28.0	33.7	26.2
Nonsmokers				
Sample size	942	494	473	1,909
Chronic cough	2.4	1.4	2.6	2.2
Chronic phlegm‡	12.8	15.2	21.4	15.5
Wheeze	3.4	4.5	5.5	4.2
Nocturnal shortness of breath‡	1.3	4.7	4.1	2.9
Shortness of breath‡	18.6	27.4	30.4	23.8
At rest	8.7	12.4	11.1	10.2
Walking at usual pace‡	0.2	1.6	2.6	1.2
Walking uphill‡	14.2	21.3	26.3	19.0

*Data are presented as %.

†Significant increase with advancing age ($p < 0.05$).

‡Significant increase with advancing age ($p < 0.01$).

increased significantly with age. In smoking men, the association between undiagnosed airflow obstruction and age was particularly strong, with prevalence increasing from 4.6% in those aged 40 to 49 years to

> 40% in those aged 60 to 69 years. Although smoking appeared unrelated to undiagnosed airflow obstruction in the youngest men, smoking was associated with a twofold excess in undiagnosed airflow

Table 2—Prevalence of Respiratory Symptoms by Age and Smoking Status in the Sample of Korean Women*

Respiratory Symptoms	Age Range, yr			Overall
	40–49	50–59	60–69	
Smokers				
Sample size	77	34	58	169
Chronic cough	6.6	8.8	3.5	6.0
Chronic phlegm†	23.7	35.3	38.6	30.5
Wheeze	18.4	29.4	24.6	23.4
Nocturnal shortness of breath†	2.6	9.1	8.6	6.6
Shortness of breath	58.4	55.9	60.3	58.6
At rest	29.0	14.7	26.8	25.9
Walking at usual pace	9.1	11.8	12.1	11.2
Walking uphill	52.0	55.9	55.2	53.9
Nonsmokers				
Sample size	1,874	1,081	1,210	4,165
Chronic cough‡	3.1	3.6	5.8	4.0
Chronic phlegm‡	12.4	16.1	19.9	15.5
Wheeze‡	4.5	6.1	11.3	6.9
Nocturnal shortness of breath‡	2.8	4.0	6.3	4.1
Shortness of breath‡	45.9	47.5	59.3	50.2
At rest‡	17.5	17.5	27.2	20.3
Walking at usual pace‡	3.5	7.3	14.6	7.7
Walking uphill‡	41.5	43.6	53.2	45.5

*Data are presented as %.

†Significant increase with advancing age ($p < 0.05$).

‡Significant increase with advancing age ($p < 0.01$).

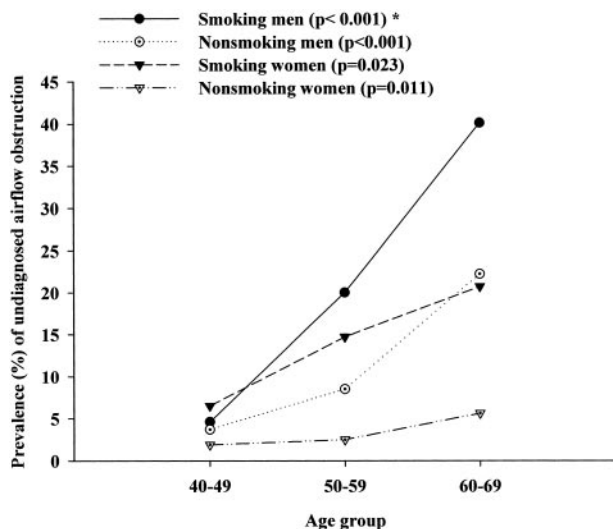


FIGURE 1. The prevalence of undiagnosed airflow obstruction according to age in the sample of Korean men and women who were smokers and nonsmokers.

obstruction in men aged 60 to 69 years. Women who smoked cigarettes experienced similar rates of undiagnosed airflow obstruction with increasing age as nonsmoking men. For nonsmoking women, the prevalence of undiagnosed airflow obstruction increased modestly with age, while being consistently < 6% across all age strata.

Tables 3, 4 present the age-adjusted prevalence of

undiagnosed airflow obstruction in the presence and absence of each respiratory symptom in men and women, respectively, and according to cigarette smoking status. The estimated relative odds of undiagnosed airflow obstruction are also given for those with a respiratory symptom vs those without the symptom. In smoking men (Table 3), compared to when a symptom was absent, wheezing was associated with a near threefold excess in the odds of undiagnosed airflow obstruction followed by a 1.9-fold excess in the presence of chronic cough. Shortness of breath and shortness of breath at rest were associated with a 1.5-fold and 1.6-fold excesses in the odds of undiagnosed airflow obstruction, respectively. Chronic phlegm was also associated with a 1.4-fold excess in the odds of undiagnosed airflow obstruction. In nonsmoking men, each association of wheezing and shortness of breath at rest related to undiagnosed airflow obstruction was similar to each association that was observed in those who smoked.

In women who smoked cigarettes (Table 4), there were no associations between respiratory symptoms and undiagnosed airflow obstruction, a possible consequence of the limited number of women who smoked. In nonsmoking women, however, wheezing and shortness of breath while walking at a usual pace were each associated with a similar twofold excess in the odds of undiagnosed airflow obstruction. Shortness of breath and shortness of breath while walking

Table 3—Age-Adjusted Prevalence of Undiagnosed Airflow Obstruction According to the Presence and Absence of a Respiratory Symptom in the Sample of Korean Men*

Respiratory Symptoms	Present	Absent	Relative Odds (95% Confidence Interval)
Smokers			
Chronic cough†	22.7 (20/79)	14.8 (262/1,786)	1.9 (1.1–3.4)
Chronic phlegm†	17.6 (96/499)	14.2 (189/1,376)	1.4 (1.0–1.8)
Wheeze‡	27.6 (59/194)	13.5 (226/1,677)	2.9 (2.0–4.3)
Nocturnal shortness of breath	19.8 (15/74)	14.9 (266/1,788)	1.5 (0.8–2.9)
Shortness of breath§	18.2 (124/605)	13.5 (161/1,275)	1.5 (1.1–2.0)
At rest†	19.7 (60/248)	14.5 (225/1,616)	1.6 (1.1–2.2)
Walking at usual pace	18.3 (13/43)	15.1 (272/1,831)	1.3 (0.6–2.8)
Walking uphill	17.5 (97/490)	14.2 (186/1,379)	1.3 (1.0–1.8)
Nonsmokers			
Chronic cough	10.8 (5/41)	9.5 (176/1,852)	1.2 (0.4–3.2)
Chronic phlegm	11.8 (41/295)	9.0 (140/1,604)	1.4 (0.9–2.0)
Wheeze‡	22.1 (20/80)	8.8 (159/1,813)	3.3 (1.9–5.8)
Nocturnal shortness of breath	5.7 (4/54)	9.7 (176/1,836)	0.5 (0.2–1.5)
Shortness of breath	11.5 (61/454)	8.8 (121/1,451)	1.4 (1.0–1.9)
At rest†	13.2 (28/193)	9.1 (152/1,695)	1.6 (1.0–2.5)
Walking at usual pace	19.8 (7/22)	9.4 (175/1,870)	2.6 (1.0–6.7)
Walking uphill	11.3 (49/360)	9.1 (132/1,534)	1.3 (0.9–1.9)

*Data are presented as % (cases of undiagnosed airflow obstruction/sample at risk) unless otherwise indicated.

†Significant excess in the odds of undiagnosed airflow obstruction ($p < 0.05$).

‡Significant excess in the odds of undiagnosed airflow obstruction ($p < 0.001$).

§Significant excess in the odds of undiagnosed airflow obstruction ($p < 0.01$).

Table 4—Age-Adjusted Prevalence of Undiagnosed Airflow Obstruction According to the Presence and Absence of a Respiratory Symptom in the Sample of Korean Women*

Respiratory Symptoms	Present	Absent	Relative Odds (95% Confidence Interval)
Smokers			
Chronic cough	10.6 (1/10)	13.3 (21/157)	0.8 (0.1–6.5)
Chronic phlegm	18.1 (10/51)	10.8 (12/116)	1.9 (0.7–4.7)
Wheeze	14.7 (6/39)	12.7 (16/128)	1.2 (0.4–3.3)
Nocturnal shortness of breath	21.2 (3/11)	12.5 (19/156)	1.9 (0.4–8.3)
Shortness of breath	11.9 (12/99)	14.7 (10/70)	0.8 (0.3–2.0)
At rest	13.8 (6/43)	13.1 (16/123)	1.1 (0.4–3.0)
Walking at usual pace	13.6 (3/19)	12.9 (19/150)	1.1 (0.3–4.2)
Walking uphill	12.9 (12/91)	13.2 (10/78)	1.0 (0.4–2.4)
Nonsmokers			
Chronic cough	3.6 (7/165)	3.0 (119/3,962)	1.2 (0.6–2.7)
Chronic phlegm	3.7 (26/643)	2.9 (99/3,495)	1.3 (0.8–2.0)
Wheeze†	5.4 (19/283)	2.8 (107/3,849)	2.0 (1.2–3.3)
Nocturnal shortness of breath	3.9 (8/170)	3.0 (119/3,950)	1.3 (0.6–2.7)
Shortness of breath†	3.8 (85/2,085)	2.3 (45/2,068)	1.7 (1.2–2.4)
At rest	3.5 (33/836)	3.0 (94/3,282)	1.2 (0.8–1.8)
Walking at usual pace‡	5.1 (22/319)	2.9 (106/3,818)	1.9 (1.1–3.0)
Walking uphill§	4.0 (79/1,878)	2.4 (51/2,254)	1.7 (1.2–2.4)

*Data are presented as % (cases of undiagnosed airflow obstruction/sample at risk) unless otherwise indicated.

†Significant excess in the odds of undiagnosed airflow obstruction ($p < 0.01$).

‡Significant excess in the odds of undiagnosed airflow obstruction ($p < 0.05$).

uphill were associated with a 1.7-fold excess in the odds of undiagnosed airflow obstruction.

Figure 2 further describes the age-adjusted relationship between the frequencies of undiagnosed airflow obstruction according to the increasing number of respiratory symptoms that characterized a study participant. Here, respiratory symptoms include chronic cough, chronic phlegm, wheezing,

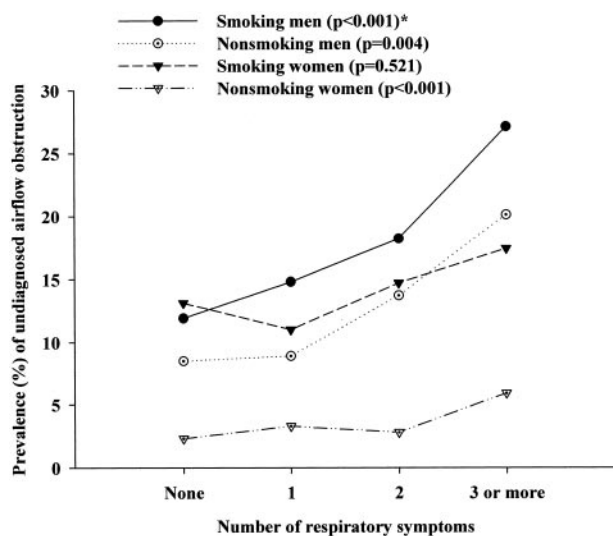


FIGURE 2. Age-adjusted prevalence of undiagnosed airflow obstruction according to the number of respiratory symptoms in the sample of Korean men and women who were smokers and nonsmokers.

nocturnal shortness of breath, and shortness of breath. Subjects with three symptoms were pooled with those with four or more symptoms, since the latter group comprised a small fraction of the study sample. As seen in Figure 2, men who smoked cigarettes experienced a 2.3-fold excess in the prevalence of undiagnosed airflow obstruction when three or more symptoms were present, as compared to when they were absent (27.4% vs 12.0%). In the same comparison for nonsmoking men, there was a 2.4-fold excess in undiagnosed airflow obstruction (20.6% vs 8.5%). In smoking and nonsmoking women, while the prevalence of undiagnosed airflow obstruction seemed to increase with the number respiratory symptoms, the increases were modest compared to men. For smoking women, the association was not statistically significant.

DISCUSSION

Findings from the present study suggest that respiratory symptoms are common in middle-aged men and women in Korea. Increases in the prevalence of undiagnosed airflow obstruction with advancing age are also substantial. Among the respiratory symptoms associated with undiagnosed airflow obstruction, wheezing seemed to be the most important, followed by shortness of breath under various conditions and chronic cough. The prevalence of undiagnosed airflow obstruction also increased as the number of respiratory symptoms increased.

An important feature of the current report is that emphasis is on undiagnosed airflow obstruction in the absence of a recognized pulmonary disorder or obstructive lung disease. As a result, findings may be especially relevant for the typical man or woman in a general clinical setting where pulmonary testing is rare. Whether the presence of the respiratory symptoms considered in this report can be used as a guideline for further follow-up or as a referral for pulmonary testing warrants consideration.

Since standard medical practice tends to include spirometric testing based on referral by a primary care physician or in the presence of overt pulmonary indications, the prevalence of undiagnosed airflow obstruction in a general population-based setting cannot be easily determined. For the current report, however, screening of unselected individuals without a medical history or the presence of a pulmonary disorder makes it possible to approximate the true prevalence of undiagnosed airflow obstruction in Korea. Screening was also based on a rigid protocol of spirometric testing. Others²¹ have observed that the detection of undiagnosed airflow obstruction can have an important role as an indicator of pulmonary function and general health.

Unfortunately, due to the use of different criteria for the diagnosis of airflow obstruction, it is difficult to make direct comparisons with other studies. Nevertheless, our findings are not unexpected based on observations that have been made elsewhere. For example, in a report²² from Spain, 14.3% of men and 3.9% of women aged 40 to 79 years had some form of obstructed airflow. In a general population-based sample in Britain, 9.9% were observed to have airflow obstruction, with 52% of the cases being undiagnosed.²³ Airflow obstruction is also higher in men vs women.^{1,22-28} In white men and women aged ≥ 45 years in the National Health and Nutrition Examination Survey, 14.2% and 9.9% had obstructive airflow, respectively.²¹

Others^{1,22-28} describe an excess of respiratory symptoms in smokers vs nonsmokers. The excessive prevalence of undiagnosed airflow obstruction that was observed in our sample of Korean men vs women (12.2% vs 3.5%, respectively) could in large part be due to differences in the use of cigarettes. Women rarely smoked cigarettes (3.9%), while nearly half of the men smoked. More than 25% of US women smoke cigarettes.

Among the specific respiratory symptoms, difference in frequencies also occurs across ethnicities. In cohort studies from the Netherlands²⁹ and Australia,¹⁰ the prevalence of wheezing (24% and 20%, respectively) and nocturnal shortness of breath (13% and 9%, respectively) were notably higher than in the KHG study. In contrast, shortness of breath

while walking uphill was less prevalent in Australia (27%) than in the KHG cohort. Although wide variation in study methods could contribute to the diversity of findings between Korea and those described in westernized societies, ethnic differences could also be real. It is well established that differences in rates of cardiovascular disease exist between developed regions of Asia and the United States and Europe. As with cardiovascular disease, differences in pulmonary function between Asia and the West are equally important to identify, since it could lead to the discovery of factors (both genetic and environmental) that make some groups more resistant to the development of respiratory symptoms, including undiagnosed and more severe types of airflow obstruction.

Although smoking and age are generally associated with an increased prevalence of undiagnosed airflow obstruction, the presence of respiratory symptoms in cigarette smokers may be interpreted as the consequence of smoking cigarettes and not as a sign of airflow obstruction. Even in smokers, however, respiratory symptoms remain a meaningful and significant correlate of undiagnosed airflow obstruction. In contrast, respiratory symptoms in nonsmokers may be more meaningful in the absence of smoking as an explanatory factor, particularly in the vast majority of nonsmoking Korean women. Here, other factors that may be associated with undiagnosed airflow obstruction need to be identified. Even in nonsmoking men with three or more respiratory symptoms, 20% had undiagnosed airflow obstruction in the Korean sample. Whether combinations of respiratory symptoms can be used to identify individuals for further follow-up and possible pulmonary testing warrants consideration. Such individuals, who could be at an elevated risk for severe forms of COPD, may be the most suitable candidates for early intervention for the prevention of future disabilities.

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