

Development of a self-scored persistent airflow obstruction screening questionnaire in a general Japanese population: the Hisayama study

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Background: The use of a simple screening questionnaire to detect persistent airflow obstruction (AO) in COPD may facilitate the early, accurate diagnosis of COPD in general practice settings.

Objective: This study developed an original persistent AO questionnaire for screening individuals with COPD in a general Japanese population.

Methods: A working group was established to generate initial draft questionnaire items about COPD. Eligible subjects aged 40 and older living in Japan were solicited to participate in a health checkup from 2014 to 2015. In study I, 2,338 subjects who fully completed the initial draft questionnaire and who had valid spirometry measurements were statistically analyzed to determine the final questionnaire items as a COPD screening questionnaire (COPD-Q). Persistent AO was defined as a post-bronchodilator $FEV_1/FVC < 0.70$. In study II, the working group analyzed the weighted scores for individual items and established a cutoff point for the COPD-Q based on the data of 2,066 subjects in the Hisayama study. Receiver operating characteristic (ROC) curves were used to examine the ability of the COPD-Q to discriminate between subjects with and without AO.

Results: The five-item COPD-Q was established based on 19 initial draft items in study I and the weighted scores of individual items. The overall area under the ROC curve for the COPD-Q was 0.796 (95% confidence interval, 0.707–0.788). A cutoff of 4 points resulted in a sensitivity of 71.0% and a specificity of 70.1%. The positive predictive value was 10.8%, and the negative predictive value was 97.9%. The crude odds ratio of the COPD-Q for AO was 5.8.

Conclusion: The five-item COPD-Q is a useful questionnaire for diagnosing persistent AO in a general Japanese population and is expected to be an effective first-stage screening tool for detecting COPD.

Keywords: COPD screening, questionnaires, Japanese population, bronchodilator, pulmonary function tests, airflow obstruction

Introduction

COPD is a common condition that progresses into a life-threatening disease, and it has become the third leading cause of death in the world in 2012.¹ Population-based studies have demonstrated overall COPD prevalence rates of between 5% and 15%.^{2–6}

A large epidemiological study (the Nippon COPD Epidemiological [NICE] study) in Japan showed that the prevalence of airflow limitation was 10.9%, and at least 8.6% of subjects were estimated to have COPD.⁷ COPD is commonly underdiagnosed and untreated,^{7,8} and many patients with early COPD are unaware of related symptoms.^{9,10} The importance of early COPD detection has been emphasized,¹¹ since

it is a preventable and treatable disease. However, in its advanced stages, there is a greater risk of developing other comorbidities, and mortality is increased.

The diagnosis of COPD is based on physiological pulmonary function tests using spirometry. Specifically, there must be persistent airflow obstruction (AO), defined by a post-bronchodilator forced expiratory volume in 1 second (FEV_1)/forced vital capacity (FVC) ratio <0.7 ,¹² or by age-dependent values below the lower fifth percentile of this ratio (the lower limit of normal [LLN]).^{13,14} However, it is difficult to screen the general population for COPD using spirometry, since it is not available in many settings. There is no proven benefit of using spirometry to screen adults who have no smoking history and no respiratory symptoms.¹⁵

The use of simple COPD screening tools, such as the COPD Population Screener (COPD-PS)¹⁶ and the International Primary Care Airways Guidelines (IPAG) questionnaires,¹⁷ has been shown to be helpful for people at risk of developing COPD. These questionnaires reliably detect AO in the general population, and may facilitate the early, accurate diagnosis of COPD in general practice settings.^{18,19}

However, the COPD-PS and IPAG questionnaires were originally developed and primarily validated in Western countries. We recently validated the COPD-PS and IPAG questionnaires in a general Japanese population and determined that the diagnostic cutoff point was different from the originally established cutoff points.^{20,21} One study found that the body mass index (BMI) item in the IPAG questionnaire was not statistically relevant in Japanese subjects who had early COPD identified by questionnaires.²² Thus, these questionnaires may inadequately assess COPD in the general Japanese population. Therefore, for the early detection of COPD in general Japanese populations, we sought to develop an original persistent AO questionnaire as a COPD screening questionnaire (COPD-Q).

Methods

Overview

To develop a self-scored persistent AO screening questionnaire, we performed the following two studies (Figure 1). In study I, a working group was assembled to generate initial draft items for the development of the COPD-Q. These items were administered to subjects at a comprehensive health examination²³ in Kagoshima Kouseiren Medical Health Care Center in Japan, and the final questionnaire items comprising the COPD-Q were determined statistically by comparing their responses to FEV_1 /FVC scores to identify individuals likely to have COPD.

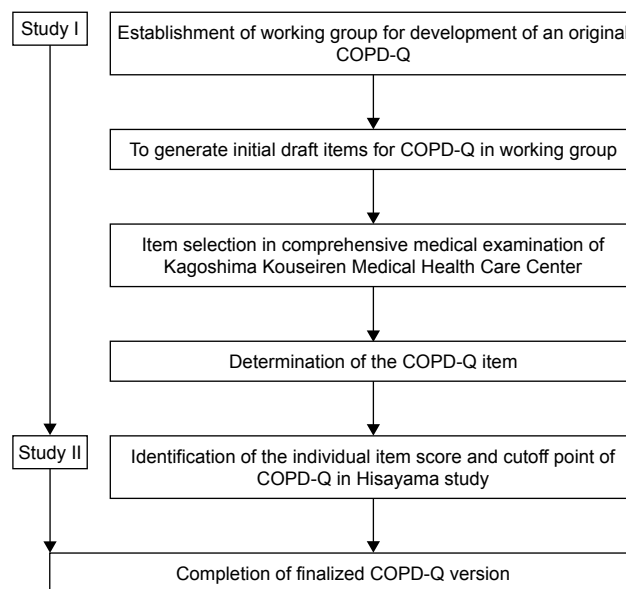


Figure 1 Study protocol.

Abbreviation: COPD-Q, COPD screening questionnaire.

In study II, the working group determined weighted scores for individual items and the cutoff point for the COPD-Q based on data derived from June 2015 to August 2015 from the Hisayama study, an ongoing, population-based epidemiologic study designed to investigate the morbidity, mortality, and risk factors of cardiovascular and smoking-related diseases in the community of Hisayama, Japan.

Working group and item generation

The working group comprised three pulmonologists, one general physician, and one statistician, and met from August 2013 to April 2014 to generate initial draft items for the development of the COPD-Q. First, initial items were identified based on the following seven conceptual domains that were relevant to the detection of COPD and that could be easily evaluated by subjects: dyspnea, cough, phlegm, colds/bronchitis, wheezing, functional impact, and personal characteristics. The initial draft questionnaire consisted of 19 items (53 total questions) assessing the conceptual domains in terms of presence, frequency, duration, and/or quality.

Study population

In study I, Japanese participants aged 40–79 years who received comprehensive health examinations at Kagoshima Kouseiren Medical Health Care Center were enrolled in this study.

Study II was based on data from the Hisayama study, a town located in a suburban area adjacent to Fukuoka City, a large urban center on Kyushu Island in the southern part of Japan.

The population of Hisayama is approximately 8,000 and has been stable for over 50 years. National census data show that the distributions of age and occupation in Hisayama have been almost identical to those across Japan since the 1960s.

Study design

The initial draft questionnaire was administered to the participants of study I. Of the 2,367 subjects who were enrolled from April 2014 to February 2015, three were excluded due to having asthma and 26 were excluded because data were missing in their records. The final analysis included data for 2,338 subjects with fully completed initial draft questionnaires and valid spirometry measurements. A random subsample of subjects (22.9%) completed the survey again 2–4 weeks later to generate an estimate of test–retest reliability.

In study II, registered subjects aged 40 years and older were solicited to participate in a town-wide health checkup that included spirometry. Of the 2,598 subjects who were enrolled from June 2015 to August 2015, 532 were excluded for the following reasons: 342 were not between the ages of 40 and 79 years, 67 had physician-diagnosed asthma, 12 had a previous lung resection, two had poor study data, and 64 had records with missing data. Furthermore, 45 subjects who had pre-bronchodilator $FEV_1/FVC < 0.70$ were not eligible for post-bronchodilator testing because of underlying heart disease or other reasons. The final analysis included data for 2,066 subjects who had fully completed the COPD-Q and had valid spirometry measurements.

All subjects underwent spirometry using a CHEST-GRAPH HI-105 spirometer (Chest MI, Tokyo, Japan). The subjects performed at least three FVC maneuvers according to the recommended methods. The data were examined by two pulmonary physicians who visually inspected the flow–volume curves and excluded subjects with poor study data. The highest FEV_1 and FVC values were used in the present study. The reference values for percent predicted FEV_1 were based on Japanese criteria. Subjects with a pre-bronchodilator $FEV_1/FVC < 0.70$ were required to undergo post-bronchodilator spirometry after 15-minute inhalation of salbutamol (GlaxoSmithKline, Tokyo, Japan) via a metered-dose inhaler with a spacer, according to the recommended procedure. Persistent AO was defined as a post-bronchodilator $FEV_1/FVC < 0.70$. The severity of subjects with persistent AO was categorized in accordance with the Global Initiative for Chronic Obstructive Lung Disease criteria (mild, $FEV_1 \geq 80\%$ predicted; moderate, FEV_1 50%–80% predicted; severe, FEV_1 30%–50% predicted; very severe, $FEV_1 < 30\%$ predicted).

The study protocol was approved by the Institutional Review Board for Clinical Research of Kyushu University, by Kagoshima University, and by the Kagoshima Prefectural Federation of Agricultural Cooperatives for Health and Welfare. All subjects provided written informed consent prior to study participation.

Statistical analysis

The demographic characteristics of each study population and the questionnaire results were summarized with descriptive statistics. For subjects who used a bronchodilator, the post-bronchodilator FEV_1/FVC values were utilized as the FEV_1/FVC data. Each demographic characteristic was compared between groups using the Kruskal–Wallis test.

For study I, univariate/multivariate logistic regression models were used to compare questionnaire responses in the No-AO and AO groups, and to investigate initial draft items for the development of the COPD-Q. Test–retest reliability of the initial draft questionnaire was assessed with Pearson's correlations between scores at study entry and after 2–4 weeks of follow-up.

For study II, multivariate logistic regression analysis was performed to determine the weighted scores of each response to questions in the COPD-Q and to identify the COPD-Q cutoff point that would discriminate between subjects with and without persistent AO.

Sensitivity, specificity, and positive (PPV) and negative predictive value (NPV) were calculated. Receiver operating characteristic (ROC) curves were generated and area under the ROC curves (AUC) were determined to reflect the ability of the COPD-Q to discriminate between subjects with and without persistent AO graphically and quantitatively. Distribution of the number of subjects and COPD-Q scores, and their estimated probabilities of AO were evaluated.

These statistical analyses were performed using STATA Release 13 (StataCorp, College Station, TX, USA) and SAS Release 9.4 (SAS Institute Inc., Cary, NC, USA). Results were considered statistically significant when $P < 0.05$.

Results

Study I: subject characteristics

Table 1 shows the baseline characteristics of the 2,338 subjects in study I, stratified by AO category following post-bronchodilator spirometry. The majority of subjects (95.8%) showed an initial $FEV_1/FVC \geq 0.70$. Following post-bronchodilator spirometry, 2.8% were found to have AO. Many AO subjects (89.2%) were estimated as having mild or moderate COPD, while only 10.8% of AO subjects had

Table 1 Baseline characteristics in study I

Characteristics	No AO		AO	P-value
	Pre-BD			
	FEV ₁ /FVC ≥0.70	FEV ₁ /FVC <0.70		
Subjects, n (2,338)	2,240	33	65	
Age (years), mean (SD)	56.7 (9.5)	59.1 (8.7)	63.1 (9.3)	<0.001
Male (%)	73.1	90.9	96.9	
Female (%)	26.9	9.1	3.1	
BMI (kg/m ²), mean (SD)	23.6 (3.4)	23.2 (2.8)	23.5 (3.1)	0.977
Brinkman index (%)				
Never smoker	46.0	24.2	10.8	
1–199	10.6	9.1	4.6	
200–399	12.3	12.1	12.3	
400–999	26.4	45.5	47.7	
>1,000	4.7	9.1	24.6	
Mean (SD)	266.2 (364.1)	419.6 (393.4)	654.3 (425.0)	<0.001
Median (IQR)	60 (0–460)	400 (32–615)	600 (360–940)	
% FVC, mean (SD)	104.4 (14.5)	106.6 (13.2)	91.3 (20.8)	<0.001
Pre-BD FEV ₁ (% predicted), mean (SD)	105.6 (15.4)	91.9 (14.2)	75.8 (20.3)	<0.001
Post-BD FEV ₁ (% predicted), mean (SD)	NA	103.1 (13.0)	82.0 (19.2)	
Pre-BD FEV ₁ /FVC (%), mean (SD)	81.6 (5.0)	67.7 (2.1)	62.7 (6.4)	<0.001
Post-BD FEV ₁ /FVC (%), mean (SD)	NA	73.5 (2.2)	64.1 (6.1)	
Reversibility (%)	NA	45.5	24.6	
COPD stage (%)				
I (mild)	NA	NA	44.6	
II (moderate)	NA	NA	44.6	
III (severe)	NA	NA	9.2	
IV (very severe)	NA	NA	1.5	

Notes: No AO: post-bronchodilator FEV₁/FVC ≥0.70; AO: post-bronchodilator FEV₁/FVC <0.7.

Abbreviations: AO, airflow obstruction; BD, bronchodilator; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; SD, standard deviation; BMI, body mass index; IQR, interquartile range; NA, not applicable.

severe or very severe COPD. AO subjects were older, predominantly male, had a higher number of pack-years smoked, and were more likely to be former or current smokers (Table 1).

Questionnaire item selection

The 19 initial draft items were administered to all 2,338 subjects. Less than 4.0% of total item-level data were missing. Scale reliability was confirmed with the test–retest reliability method, with analysis of 535 subjects (22.9%) who completed the study survey at entry and at 2–4 weeks of follow-up. In this population, the test–retest Pearson's correlation coefficient was 0.946 ($P < 0.001$).

Initial univariate logistic regression analysis was performed on the initial draft items (Tables S1 and 2). As stated above, items were grouped into the following conceptual domains: dyspnea, cough, phlegm, wheezing, functional impact, and personal characteristics. A combination of one item based on two conceptual domains, namely cough and phlegm, and one based on dyspnea on exertion, showed a significant ability to discriminate between subjects with and

without AO. The final version of the COPD-Q consisted of the five questions (Q) that demonstrated the greatest discriminatory capacity: How old are you? (Q1); How often do you cough up phlegm when you are not sick? (Q2); Are you prone to being out of breath when running or carrying a heavy load, compared to people of your own age group? (Q3); In the past year, have you ever had wheezing or whistling when breathing while running or carrying a heavy load? (Q4); How many cigarettes do you smoke? (Brinkman index: the number of cigarettes × the number of years) (Q5). Table 2 presents the results of univariate logistic regression analysis of these five questions (COPD-Q) as a screening questionnaire for persistent AO estimated to have COPD. Table 3 presents the results of odds ratios, and the corresponding 95% confidence intervals [CIs] were obtained by multivariable logistic regression analysis using age and cigarette consumption as covariates.

Study II: subject characteristics

Table 4 shows the baseline characteristics of the 2,069 subjects, based on data from the Hisayama study, stratified

Table 2 Results of univariate logistic regression analyses

Item	Analytic subjects (N=2,338)		
	OR	95% CI	P-value for trend
Q1 How old are you? (years)			
40–49	1.0	Reference	<0.001
50–59	1.4	0.6–3.4	
60–69	3.7	1.6–8.6	
≥70	5.1	2.1–13	
Q2 How often do you cough up phlegm when you are not sick?			
Almost never	1.0	Reference	<0.001
Rarely	1.6	0.8–4.4	
Sometimes	2.3	1.2–4.4	
Frequently	4.6	1.7–13	
Very frequently	3.1	0.4–24	
Q3 Are you prone to being out of breath when running or carrying a heavy load, compared to people of your own age group?			
No	1.0	Reference	
Yes	2.2	1.3–3.6	
Q4 In the past year, have you ever had wheezing or whistling when breathing while running or carrying a heavy load?			
Almost never	1.0	Reference	<0.001
Rarely	3.7	2.0–6.8	
Sometimes	3.7	1.8–7.4	
Frequently	4.9	1.8–13	
Very frequently	2.9	0.4–23	
Q5 How many cigarettes do you smoke? (Brinkman index)			
Never smoked	1.0	Reference	<0.001
1–299	1.7	0.6–5.3	
300–499	3.3	1.2–8.7	
500–999	8.4	3.8–19	
≥1,000	19	8.0–46	

Notes: Brinkman index: number of cigarettes smoked per day × number of years of the habit. P-value for trend was obtained by logistic regression models using each variable as a continuous variable.

Abbreviations: OR, odds ratio; CI, confidence interval.

by airflow limitation category following post-bronchodilator spirometry. The majority of subjects (95.2%) showed an initial $FEV_1/FVC \geq 0.70$. Following post-bronchodilator spirometry, 4.8% were found to have AO. Almost all AO subjects (93.0%) were classified as having mild or moderate COPD, while only 7.0% had severe or very severe COPD. As in study I, AO subjects were older, predominantly male, had a higher number of pack-years smoked, and were more likely to be former or current smokers (Table 4).

Item-weighted scoring and cutoff point

The COPD-Q was administered to all 2,069 subjects in Hisayama, and several versions of weighted scores were assessed to produce the best results for discriminating between patients with and without AO. We ultimately derived weighted scores for the five COPD-Q questions according to individual coefficients of the multivariate logistic regression analysis (Table 5). Responses to each question were assigned weighted

Table 3 Results of multivariable logistic regression analyses

Item	Analytic subjects (N=2,338)		
	OR	95% CI	P-value for trend
Q1 How old are you? (years)			
40–49	1.0	Reference	<0.001
50–59	1.1	0.4–2.8	
60–69	2.5	1.0–5.8	
≥70	4.3	1.7–11	
Q2 How often do you cough up phlegm when you are not sick?			
Almost never	1.0	Reference	<0.001
Rarely	1.5	0.8–2.9	
Sometimes	2.1	1.1–4.0	
Frequently	2.7	0.9–7.7	
Very frequently	2.6	0.3–21	
Q3 Are you prone to being out of breath when running or carrying a heavy load, compared to people of your own age group?			
No	1.0	Reference	
Yes	1.9	1.1–3.2	
Q4 In the past year, have you ever had wheezing or whistling when breathing while running or carrying a heavy load?			
Almost never	1.0	Reference	<0.001
Rarely	3.5	1.9–6.6	
Sometimes	3.1	1.5–6.4	
Frequently	4.3	1.5–12	
Very frequently	2.9	0.4–24	
Q5 How many cigarettes do you smoke? (Brinkman index)			
Never smoked	1.0	Reference	<0.001
1–299	2.1	0.7–6.6	
300–499	3.9	1.5–11	
500–999	9.3	4.2–21	
≥1,000	17	7.1–41	

Notes: Brinkman index: number of cigarettes smoked per day × number of years of the habit. ORs and corresponding 95% CIs were obtained by multivariable logistic regression analysis using age and cigarette consumption as covariates.

Abbreviations: OR, odds ratio; CI, confidence interval.

scores (specifically, depending on the question, 0 or 1; 0, 1, or 2; or 0, 1, 2, or 3) based on the relative contribution of the response to identifying AO, and response values were summed across the items to produce a scale score ranging from 0 to 10. Three of the five COPD-Q assessed COPD-related symptoms, namely coughing up phlegm (Q2; 5-point scale), breathlessness on exertion (Q3; 2-point scale), and wheezing on exertion (Q4; 5-point scale). One evaluated subject age (Q1; four categories), and the last assessed smoking history (Q5; 4-point scale) (Figures 2 and S1). An ROC curve was generated to evaluate the ability of the final version of the COPD-Q to discriminate subjects without AO from those with AO in study II (Hisayama study) (Figure 3). The overall AUC for the continuous COPD-Q score for discriminating AO from No AO was 0.796 (95% CI, 0.750–0.841). The appropriateness of various cutoff points of the COPD-Q was then evaluated (Table 6). A cutoff of 4 points showed a sensitivity of 71.0% and a specificity of 70.1%. The PPV was 10.8%,

Table 4 Baseline characteristics in study II

Characteristics	No AO		AO	P-value
	Pre-BD			
	FEV ₁ /FVC ≥0.70	FEV ₁ /FVC <0.70		
Subjects, n (2,066)	1,903	63	100	
Age (years), mean (SD)	61.1 (10.7)	67.9 (8.7)	68.0 (8.1)	<0.001
Male (%)	41.9	39.7	71.0	
Female (%)	58.1	60.3	29.0	
BMI (kg/m ²), mean (SD)	23.2 (10.7)	22.8 (3.3)	22.6 (3.0)	0.256
Brinkman index (%), mean (SD)				
Never smoker	57.8	65.1	26.0	
1–199	8.4	6.3	6.0	
200–399	8.9	3.2	7.0	
400–999	19.6	22.2	30.0	
>1,000	5.3	3.2	31.0	
Mean (SD)	227.5 (374.0)	206.0 (338.6)	630.5 (546.9)	<0.001
Median (IQR)	0 (0–390)	0 (0–360)	600 (0–1,000)	
% FVC, mean (SD)	100.4 (13.3)	102.6 (14.3)	92.6 (15.9)	<0.001
Pre-BD FEV ₁ (% predicted), mean (SD)	95.8 (13.7)	87.1 (13.2)	73.5 (15.3)	<0.001
Post-BD FEV ₁ (% predicted), mean (SD)	NA	93.3 (13.3)	77.1 (16.4)	
Pre-BD FEV ₁ /FVC (%), mean (SD)	78.1 (4.8)	67.9 (1.8)	63.6 (4.8)	<0.001
Post-BD FEV ₁ /FVC (%), mean (SD)	NA	72.3 (2.4)	64.7 (5.1)	
Reversibility (%)	NA	12.7	14.0	
COPD stage (%)				
I (mild)	NA	NA	34.0	
II (moderate)	NA	NA	59.0	
III (severe)	NA	NA	7.0	
IV (very severe)	NA	NA	0.0	

Notes: No AO: post-bronchodilator FEV₁/FVC ≥0.70; AO: post-bronchodilator FEV₁/FVC <0.7.

Abbreviations: AO, airflow obstruction; BD, bronchodilator; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; SD, standard deviation; BMI, body mass index; IQR, interquartile range; NA, not applicable.

Table 5 Weighted scores based on coefficients in multivariate logistic regression analyses of COPD-Q

Question	Point scale	Coefficient	Standard error	P-value	Weighted score
Q1	40–49 years old	–	–	–	0
	50–59 years old	0.589	0.619	0.342	1
	60–69 years old	1.613	0.541	0.003	2
	Over 70 years old	2.068	0.539	<0.001	3
Q2	Almost never	–	–	–	0
	Rarely	–0.210	0.341	0.537	0
	Sometimes	0.672	0.276	0.015	1
	Frequently	0.594	0.582	0.307	1
	Very frequently	0.373	0.838	0.656	1
Q3	No	–	–	–	0
	Yes	0.506	0.262	0.053	1
Q4	Almost never	–	–	–	0
	Rarely	0.383	0.324	0.238	0
	Sometimes	0.333	0.356	0.351	0
	Frequently	0.937	0.597	0.117	1
	Very frequently	1.743	0.746	0.019	2
Q5	No smoking	–	–	–	0
	1–199	0.627	0.471	0.183	1
	200–399	0.754	0.457	0.099	1
	400–999	1.116	0.288	<0.001	2
	Over 1,000	2.089	0.306	<0.001	3

Notes: Q1, How old are you?; Q2, How often do you cough up phlegm when you are not sick?; Q3, Are you prone to being out of breath when running or carrying a heavy load, compared to people of your own age group?; Q4, In the past year, have you ever had wheezing or whistling when breathing while running or carrying a heavy load?; Q5, How many cigarettes do you smoke? (Brinkman index: number of cigarettes smoked per day × years smoked).

Abbreviation: COPD-Q, COPD screening questionnaire.

COPD screening questionnaire (COPD-Q)				
Q1. How old are you?				
40–49 years old	50–59 years old	60–69 years old	Over 70 years old	
<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	
Q2. How often do you cough up phlegm when you are not sick?				
Almost never	Rarely	Sometimes	Frequently	Very frequently
<input type="checkbox"/> 0	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 1	<input type="checkbox"/> 1
Q3. Are you prone to being out of breath when running or carrying a heavy load, compared to people of your own age group?				
No		Yes		
<input type="checkbox"/> 0		<input type="checkbox"/> 1		
Q4. In the past year, have you ever had wheezing or whistling when breathing while running or carrying a heavy load, compared to people of your own age group?				
Almost never	Rarely	Sometimes	Frequently	Very frequently
<input type="checkbox"/> 0	<input type="checkbox"/> 0	<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2
Q5. How many cigarettes do you smoke? Please input a number in the brackets. If you do not have a regular habit of smoking, check off "No smoking".				
Average number of cigarettes per day () × Number of years smoking () = Total ()				
What was the total number?				
No smoking	1–399	400–999	Over 1,000	
<input type="checkbox"/> 0	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	

Figure 2 A self-scored COPD screening questionnaire.

the NPV was 97.9%, and the crude odds ratio (OR) of the COPD-Q for AO was 5.8. The relationship between COPD-Q score of AO subjects ranging from 0 to 10 and estimated probability is shown in Figure 4. The estimated probabilities for AO tended to increase with COPD-Q scores.

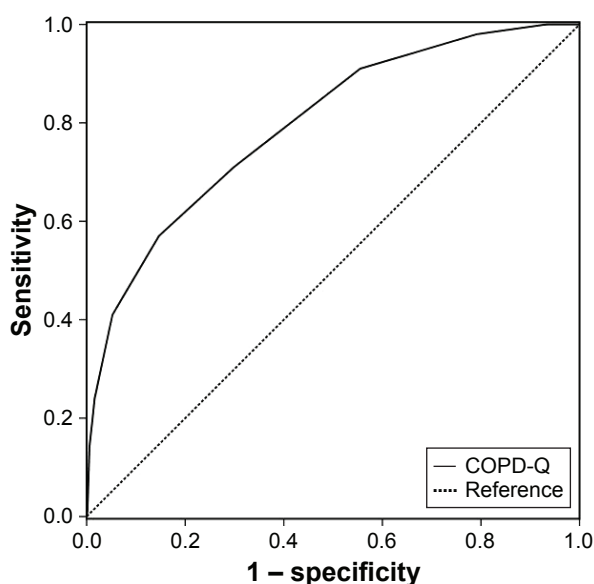


Figure 3 Receiver operating characteristic curve of the COPD-Q for discriminating between subjects with and without AO.

Abbreviations: COPD-Q, COPD screening questionnaire; AO, airflow obstruction.

Discussion

The five-item, self-scored COPD-Q is a simple and reliable Japanese-language questionnaire that was developed to screen for persistent AO estimated to have COPD in a general Japanese population.

In study I, the working group generated initial draft items derived from 19 items comprising 53 total questions based on seven conceptual domains. Ten items demonstrated a particularly strong relationship to COPD. Although BMI was assessed by an item in the IPAG questionnaire, it was not a significant predictive factor for AO in this study (Tables 1 and 4), a result that is consistent with a previous report.²² An obvious problem concerning BMI is that the cutoff values of BMI of 25.4 and 29.7 kg/m² in the IPAG questionnaire are well above the average BMI of Japanese subjects, and even above the Japanese criteria for obesity of 25.0 kg/m². Thus, there are reports stating that modified cutoff values for BMI should be used for determining the discriminatory power of the IPAG questionnaire for the Japanese population.^{22,24} However, regarding BMI in the present study, there were no significant differences between subjects with AO and those without AO in study I (Table 1) or study II (Table 4), and as a result, we excluded BMI as an item in the COPD-Q. In addition, some reports have shown that the association between BMI and

Table 6 Various cutoff points for the COPD-Q

Cutoff point	OR	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Percent correctly classified	AUC (%)
2	13.0	98.0	20.9	5.9	99.5	24.6	59.5
3	8.1	91.0	44.5	7.7	99.0	46.8	67.8
4	5.8	71.0	70.1	10.8	97.9	70.2	70.6
5	7.2	57.0	85.4	16.5	97.5	84.0	71.2
6	12.6	41.0	94.8	28.5	96.9	92.2	67.6
7	19.1	24.0	98.4	42.9	96.2	94.8	61.2

Abbreviations: COPD-Q, COPD screening questionnaire; OR, odds ratio; AUC, area under the receiver operating characteristic curve.

mortality was especially significant in severe COPD and differed according to the severity of AO;^{25,26} however, subjects of AO in the present study (89.2% in study I and 93.0% in study II) were in Global Initiative for Chronic Obstructive Lung Disease stage I and II. The BMI in subjects with early-detected COPD may not be a significant item in Japanese population.

Univariate logistic regression analyses were used to identify five items that predicted COPD (Table 2). Coughing, as identified by a general clinician in relation to COPD, did not by itself distinguish between subjects with AO and those without AO. The combination of coughing and phlegm production (addressed by Q2) showed significant discriminatory ability, similar to that of dyspnea on exertion (addressed by Q3), and the ORs of both Q2 and Q3 were significant in a multivariate logistic regression analysis (Table 3).

Study I has several limitations regarding data interpretation. The prevalence of persistent AO estimated to have COPD was 2.8%, which is very low compared with a previous report.⁷ The study population comprised individuals who voluntarily agreed to participate in an annual comprehensive health examination program that is conducted in Japan to detect potential health risks at an early stage.²³ This survey population may be healthier or more health conscious than the general Japanese population, which

would affect the prevalence of persistent AO estimated to have COPD in study I. Therefore, we analyzed the weighted scores for individual items and established a cutoff point for the COPD-Q based on the data from the Hisayama study (study II). It is necessary in the future to confirm the performance of the COPD-Q in other validation cohorts.

In study II, the five items on the COPD-Q were scored as 0, 1, 2, or 3 based on coefficients of multivariate logistic regression analysis for identifying AO, with a summed total score ranging from 0 to 10 (Figure 2). To evaluate the contribution of smoking status, we used the Brinkman index and derived weighted scores based on coefficients of multivariate logistic regression analysis for predicting COPD. The COPD-PS¹⁶ used the question “Have you smoked at least 100 cigarettes in your ENTIRE LIFE”, and a “Yes” response was assigned a value of 2. Conversely, in the present study, the responses to the smoking status item were assigned values of 0, 1, 2, or 3, because a total Brinkman index value over 1,000 was most useful for distinguishing COPD (Table 5).

The overall AUC for the continuous COPD-Q score was 0.796 (95% CI, 0.750–0.841) (Figure 3). In a previous study, we administered the COPD-PS and IPAG questionnaires to a general Japanese population (Hisayama study),²¹ and found that the overall AUC for the COPD-PS was 0.747 (95% CI, 0.707–0.788) and 0.775 (95% CI, 0.735–0.816) for the IPAG questionnaire. In the present study with almost the same population, the COPD-Q showed a large AUC for distinguishing subjects with AO from those without AO compared to the COPD-PS and IPAG questionnaire.

The PPV of 10.8% with a COPD-Q cutoff point of 4 is lower than the PPVs obtained using the COPD-PS and IPAG questionnaires in our previous study.²¹ However, PPV and NPV vary with disease prevalence, with PPV decreasing with lower disease prevalence. The NICE study estimated that the COPD prevalence in Japan ranged from 8.6% to 10.9%.⁷ In residents aged 40 years or older from Hisayama, Matsumoto et al estimated that the combined prevalence of COPD and a COPD phenotype with variable airflow limitation was 9.3%.²⁷

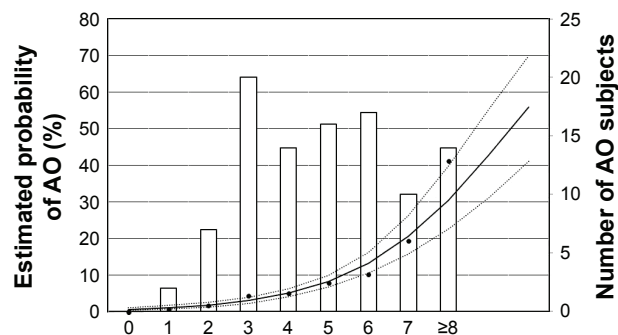


Figure 4 The relationship between COPD-Q score and estimated probability of AO (%). Bars represent the number of AO subjects. Black circles: observed AO (%), curve: estimated AO (%), dotted curves: 95% CI, and horizontal axis: COPD-Q scores. **Abbreviations:** COPD-Q, COPD screening questionnaire; AO, airflow obstruction; CI, confidence interval.

However, the prevalence of confirmed persistent AO in the present study was 4.8% (Table 3) in residents from Hisayama aged 40–79 years. The following reasons may account for the underestimated persistent AO prevalence in study II. First, 342 subjects were excluded from the present study because they were not between 40 and 79 years old, and since the prevalence of COPD increases with older age, this age restriction may have affected the prevalence of AO. The prevalence of AO was previously found to be 19% in individuals in Hisayama between the ages of 80 and 89 years.²⁷ The second potential reason for the underestimated persistent AO prevalence is that 67 subjects with physician-diagnosed asthma were excluded; however, these subjects may have had a COPD phenotype with variable AO, which exhibits features of both asthma and COPD.^{28–30} The third possible explanation is that the 45 subjects with pre-bronchodilator $FEV_1/FVC < 0.7$ were ineligible for post-bronchodilator testing and were excluded from the present study, and this group may have included subjects with persistent AO.

Another limitation of this study was that persistent AO estimated to have COPD was defined as a post-bronchodilator $FEV_1/FVC < 0.7$ without using an LLN, though previous studies demonstrated the successful use of an LLN for defining AO in Japanese populations.^{31,32} Application of an LLN value for determining the existence of COPD may prevent overdiagnosis in elderly subjects and underdiagnosis in young subjects.³³

Despite these limitations, the COPD-Q developed in the present study was found to be a simple and useful screening questionnaire for persistent AO in a general Japanese population.

Conclusion

The COPD-Q is a five-item screening questionnaire for persistent AO. Although validation studies are necessary to confirm the performance of the COPD-Q in other cohorts, the COD-Q can be evaluated for its utility as a first-stage screening tool for detecting COPD in the general Japanese population.

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Author contributions

All authors contributed toward data acquisition, data analysis, and drafting and critically revising the paper and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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Supplementary materials

Table S1 The initial draft questionnaire

Items	Odds ratio*	95% CI*
Q1 During the past year, how often did you cough?		
Almost every day	1.2	0.4–3.3
2–3 times per week	1.4	0.6–3.5
Several days per month	1.7	0.8–3.6
Only when you had a cold or pneumonia	1.0	0.5–1.9
Almost never	1.0	Reference
	P-value for trend =0.315	
Q2 Under which of the following conditions does the coughing worsen?***		
Change of seasons	1.3	0.7–2.4
During cold winters	1.3	0.8–2.4
When walking in the morning	1.4	0.7–2.9
When entering an air-conditioned room	1.4	0.7–2.9
When a typhoon is nearby	NA	
In dusty environments	1.1	0.6–2.0
When there is volcanic ash in the air	1.4	0.4–4.7
On rainy days	NA	
Q3 Does the coughing last longer than 3 weeks when you have a cold?		
Yes	0.7	0.6–1.8
No	1.0	Reference
Q4 During the past year, how often did you produce phlegm?		
Almost every day	1.7	0.8–3.7
2–3 times per week	1.7	0.7–4.2
Several days per month	1.0	0.4–2.5
Only when you had a cold or pneumonia	0.9	0.4–1.8
Almost never	1.0	Reference
	P-value for trend =0.136	
Q5 Are you more likely to produce phlegm under the following conditions?***		
When walking in the morning	1.3	0.7–2.3
When you have a runny nose	1.0	0.5–1.8
Q6 During the past year, did you have any of the following symptoms for more than 3 months?***		
Cough only	1.9	0.8–4.3
Phlegm only	1.4	0.7–2.9
Cough and phlegm	2.9	1.4–5.9
Q7 On average, during the day, how much phlegm do you produce?		
None	1.0	Reference
Less than 15 mL (1 tbsp)	1.6	0.9–2.8
More than 15 mL (1 tbsp)	3.1	1.2–8.0
	P-value for trend =0.011	
Q8 How often do you cough up phlegm when you do not have a cold?		
Always	2.6	0.3–2.1
Almost always	2.7	0.9–7.7
Sometimes	2.1	1.1–4.0
Rarely	1.5	0.8–2.9
Almost never	1.0	Reference
	P-value for trend =0.009	
Q9 During the past year, under which of the following conditions have you had difficulty breathing or felt out of breath?***		
At rest	0.2	0.03–1.6
When washing yourself or changing clothes	0.8	0.3–2.1
When walking indoors	2.0	1.0–4.1
When walking on a flat surface outdoors	2.2	1.2–4.1
During light exercise (climbing a hill or stairs)	1.6	0.9–2.6
During strenuous exercise (lifting heavy objects or running)	1.4	0.8–2.5

(Continued)

Table S1 (Continued)

Items	Odds ratio*	95% CI*
Q10 Under which of the following conditions are you more likely to be out of breath compared to people of the same age?***		
When walking on a flat surface outdoors	1.8	0.8–4.3
During light exercise (climbing a hill or stairs)	1.9	1.1–3.3
During strenuous exercise (lifting heavy objects or running)	1.9	1.1–3.2
Q11 How active are you in your daily life (at work and home)?		
Very active	NA	
Active	1.0	Reference
Somewhat active	0.9	0.5–1.6
Not active	0.6	0.2–2.2
	P-value for trend =0.505	
Q12 During the past year, have you ever noticed wheezing while breathing?		
Almost every day	9.4	2.7–32
2–3 times per week	NA	
Several days per month	7.1	3.2–16
Only when you had a cold or pneumonia	2.4	1.2–4.6
Almost never	1.0	Reference
	P-value for trend <0.001	
Q13 During the past year, under which of the following conditions have you noticed wheezing while breathing?***		
When you awoken during the night	6.2	3.2–12
When you awoken in the morning	5.5	2.7–11
When walking indoors	6.6	2.4–18
When walking on a flat surface outdoors	5.1	2.4–11
During light exercise (climbing a hill or stairs)	3.3	1.9–5.7
During strenuous exercise (lifting heavy objects or running)	3.2	1.9–5.4
Q14 During the past year, which of the following problems with activities of daily living have you had due to respiratory symptoms (such as cough, phlegm, or shortness of breath)?***		
You are unable to sleep	1.0	0.4–2.5
You are walking slower than people of your age	1.8	0.8–4.0
You need to rest even when walking on flat surfaces	4.2	1.6–11
Light exercise is difficult (climbing a hill or stairs)	2.6	1.2–5.6
Strenuous exercise is difficult (lifting heavy objects or running)	2.3	1.3–3.9
Q15 Are your activities of daily living restricted by respiratory (lung) symptoms?		
Yes	2.5	0.5–13
No	1.0	Reference
Q16 During the past year, were you ever worried or panicked because you had difficulty breathing?		
Yes	0.8	0.1–6.9
No	1.0	Reference
Q17 During the past year, were you ever depressed (down) because you had respiratory symptoms (such as cough, phlegm, or shortness of breath)?		
Yes	2.0	0.8–5.2
No	1.0	Reference
Q18 Has there ever been a person who smoked in the same room as you, either in your house or at your workplace, for more than 1 year?		
Yes	1.8	1.1–3.1
No	1.0	Reference
If yes, for how long? (vs “nonpassive smoker” group)		
< 10 years	1.4	0.5–4.2
10–19 years	1.6	0.6–4.3
20–29 years	2.7	1.3–5.7
30–39 years	1.1	0.4–2.9
>40 years	1.6	0.6–4.5
	P-value for trend =0.110	
Q19 How much of the time have you lived in an environment where you were breathing exhaust gas or polluted air?		
Always	NA	
Sometimes	1.7	0.9–3.2
Almost never	1.0	Reference

Notes: NA: not available because of no subjects in both/either cases and controls. *Odds ratios and corresponding 95% CIs were estimated models by logistic regression using age and cigarette consumption as covariates. **Odds ratios were estimated using “No” group as reference for all conditions. ***“Almost none” group was used as reference, and the risk estimates for the remaining groups are shown for all conditions.

Abbreviations: CI, confidence interval; NA, not available.

COPDスクリーニングのための質問(COPD-Q)				
1. 現在、おいくつですか？				
40～49歳	50～59歳	60～69歳	70歳以上	
<input type="checkbox"/> ₀	<input type="checkbox"/> ₁	<input type="checkbox"/> ₂	<input type="checkbox"/> ₃	
2. かぜをひいていないのに、たんがからんでせきをすることがありますか？				
いつも	ほとんどいつも	ときどき	まれに	ほとんどない
<input type="checkbox"/> ₁	<input type="checkbox"/> ₁	<input type="checkbox"/> ₁	<input type="checkbox"/> ₀	<input type="checkbox"/> ₀
3. 走ったり、重い荷物を運んだりしたとき、 <u>同年代の人と比べて</u> 、息切れしやすいほうですか？				
はい		いいえ		
<input type="checkbox"/> ₁		<input type="checkbox"/> ₀		
4. この一年間で、走ったり、重い荷物を運んだりしたとき、ゼイゼイやヒューヒューを感じることはありましたか？				
いつも	ほとんどいつも	ときどき	まれに	ほとんどない
<input type="checkbox"/> ₂	<input type="checkbox"/> ₁	<input type="checkbox"/> ₀	<input type="checkbox"/> ₀	<input type="checkbox"/> ₀
5. これまで、たばこをどれくらい吸いましたか？ ()に数字を記入し、次の計算をしてください。				
1日の平均本数() × 喫煙年数() = 合計()				
合計はどれですか？				
吸わない	1～399	400～999	1000以上	
<input type="checkbox"/> ₀	<input type="checkbox"/> ₁	<input type="checkbox"/> ₂	<input type="checkbox"/> ₃	

Figure S1 Japanese version of the COPD-Q.

Abbreviation: COPD-Q, COPD screening questionnaire.