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TANAFFOS

Validity of Questionnaire-Based Diagnosis of Chronic Obstructive Pulmonary Disease in Azar-Cohort Population

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Background: The clinical diagnosis of chronic obstructive pulmonary disease (COPD) should be considered in any patient who has dyspnea, chronic cough or sputum production, and diagnosis should be confirmed by performing spirometry in presence of airflow limitation. The aim of this study was to assess the validity of a questionnaire used to detect COPD based on spirometry findings.

Materials and Methods: The validity of a questionnaire for COPD diagnosis was examined using spirometry based on both Global Initiative for Chronic Obstructive Lung Disease (GOLD) and American Thoracic Society/European Respiratory Society (ATS/ERS) criteria for patients 35 years old and older. In total, 350 questionnaires were completed. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio and negative likelihood ratio were calculated to determine the accuracy of the questionnaire.

Results: The sensitivity of the questionnaire in detection of airflow limitation was 8.3% and 6.7% by the GOLD and the ATS/ERS criteria, respectively; whereas, specificity was 96% by both criteria.

Conclusion: The high specificity of the questionnaire indicates that the questionnaire is more capable to identify people who do not have airflow limitation; whereas, the low sensitivity of the questionnaire could underestimate the actual prevalence of COPD in the general population.

Key words: COPD, GOLD criteria, Spirometry, Validity

INTRODUCTION

Chronic obstructive pulmonary disease is an inflammatory disease of the airways that especially affects the small airways (1) and is associated with persistent airflow limitation, which is usually progressive (2).

Also, COPD is an important cause of morbidity and mortality worldwide and it is predicted that the global burden of COPD will increase in the next decades due to continued exposure to COPD risk factors and population aging (2-4). It moved from the fourth leading cause of death in 1990 to the third place in 2010 worldwide (5).

Dyspnea, chronic cough or sputum and exposure to risk factors for the disease must be considered for clinical diagnosis of COPD in patients (6); however, none of these symptoms alone are diagnostic. The chance of COPD diagnosis would increase if there were several symptoms and additional tests for definite diagnosis of the disease (2, 7).

Spirometry is routinely performed to detect airway obstruction and for diagnosis of COPD. Limitation in forced expiratory volume in one second (FEV1) is usually a key indicator of developing COPD (8).

The GOLD criteria is the most commonly used tool for diagnosis of COPD. A fixed ratio of FEV1/forced vital capacity (FVC) <0.7 after the administration of bronchodilator is used to diagnose COPD (9). Although the use of this constant ratio is easy, it results in over-estimation of COPD in the elderly (10) and its under-estimation in adults under 45 years, compared to when the lower limit of normal (LLN) is used instead of fixed ratio as the cut-off point. The LLN value is based on normal distribution and is defined as the lowest normal (5%) on the basis of age, gender and race in healthy non-smokers, and less than that is considered abnormal (2).

The ATS and ERS define airflow limitation by a reduced FEV1/FVC ratio below the fifth percentile in terms of age, sex and race, or in other words, LLN. Using this definition reduces the risk of over-diagnosis of COPD, especially in the elderly (11-13). In a study done in Sweden to examine the validity of a COPD diagnosis questionnaire using spirometry without the use of a bronchodilator, the sensitivity and specificity of 5.7% and 99.7% using the GOLD criteria and 9.85% and 99.5% using the ATS/ERS criteria were obtained for the question, "have you been diagnosed by a physician as having COPD or emphysema?". Sensitivity, specificity and PPV of the questions were higher in identification of airway obstruction compared to self-reported symptoms of chronic bronchitis (8). The prevalence of COPD varies in different countries based on the study methods and diagnostic criteria used in the studies (14). The lowest estimation of the prevalence is related to studies in which the self-reporting method is used (9).

This study aimed at both obtaining information about the COPD disease in Azar-cohort population (pilot study) and assessing the validity of COPD diagnosis questionnaire derived from the Framingham questionnaire (15) based on spirometry findings.

MATERIALS AND METHODS

The Azar-cohort study is at the state level of a nationwide cohort study (Persian cohort) that aimed to examine the risk factors of common non-communicable diseases in Iran. The Azar-cohort study has been conducted in Shabestar, a county located in East Azerbaijan Province by Tabriz University of Medical Sciences. All people 35 to 70 years of age are invited to take part in this study if they meet the inclusion criteria (permanent residents of this city, ability to respond to the questions, Iranian originality). The pilot phase of the Azar-cohort study was conducted in Khameneh, one of the cities of Shabestar county in October 2014.

For the purpose of the pilot study, all residents of Khameneh city who were 35 years old and older were invited by phone to participate in this cohort study. The respiratory disease and symptoms questionnaires were completed by two general practitioners for all of the participants in the healthcare center of Khameneh. The questions related to respiratory disease and symptoms were based on a questionnaire derived from the Framingham questionnaire (original cohort-exam 29- form, and generation 3 exam 1 & 2-form) (15).

Spirometry without bronchodilator was performed by a trained technician for all participants in the same center and confirmed and interpreted by a pulmonologist. Spirometry results of 350 people were used for analysis in this study. The questionnaire consisted of two parts: there were questions about COPD symptoms including cough, sputum and dyspnea in the first part, and the second part was about lung examination. If a person had cough and sputum production for at least 3 months during the past year and continued for two consecutive years, he/she was diagnosed with bronchitis (2). Some questions such as, "have you ever had any of the following conditions diagnosed by a physician or other health care professional? COPD, chronic bronchitis, emphysema, pulmonary fibrosis and sleep apnea" as well as questions related to asthma were asked.

Age was classified into three categories: <45, 45-65, and >65 years. Smoking status was classified as never or occasional smoker (someone who never smoked or smoked less than 100 cigarettes in their lifetime), current smoker (someone who currently smokes one or more cigarettes per day) and ex-smoker (someone who does not smoke currently but used to smoke regularly in the past). Current passive smoking was considered positive if someone was exposed to cigarette smoke by smoking of other household members or co-workers. Exposure to passive smoke during childhood was also considered positive if someone had exposure to cigarette smoke due to parental smoking. Spirometry (alpha 6000 vitalograph, Ireland) was performed for all those who completed the questionnaires. The participants' weight and height were measured before spirometry. The FEV1 and FVC were also measured.

The FEV1/FVC ratio of <0.7 indicates COPD after using a short-acting bronchodilator based on the GOLD criteria; but the researchers did not use a bronchodilator in this study. The LLN was used instead of a fixed ratio of 0.7 in the ATS/ERS criteria and COPD was considered if the FEV/FVC ratio was less than the LLN based on age and sex.

Spirometry was not performed for those who had a contraindication for spirometry (including myocardial infarction, pulmonary embolism, dissecting aneurysm, uncontrolled blood pressure> 200/120 and recent surgery of the eye, ear, brain, abdomen or thorax) (16).

The study was approved by ethical committee of Tabriz University of Medical Sciences.

Statistical analysis

The mean and standard deviation (SD) were reported for quantitative variables, and frequency and percentage were reported for qualitative variables. T-test was used to compare quantitative data between males and females and chi-square test was used to compare qualitative data between males and females. Sensitivity, specificity, PPV, NPV, positive likelihood (LR+) and negative likelihood (LR-) were calculated to determine the validity of the 95% confidence interval (CI). Statistical analysis was performed using SPSS software version 21.

RESULTS

In this study, the validity of 350 completed questionnaires was examined using spirometry. Of 350 participants in the study, 195 were females and 155 were males with a mean age of 54±12 years, and 55% of participants were in the age range of 45-65 years. The age difference between men and women was not statistically significant (P=0.20). The characteristics of the participants are shown in Table 1.

The mean FEV1 in women and men was 2.2 and 1.3L, respectively, and the mean FEV1/FVC ratio in women and men was 0.78 and 0.76, respectively, which had a statistically significant difference (P<0.001). Based on the GOLD criteria, 36 patients (10.3%) were diagnosed with COPD, 15 patients (4.3%) were diagnosed with COPD according to the ATS/ERS criteria, and on the basis of the questionnaire, 13 patients (3.7%) were diagnosed with COPD.

Non-smokers comprised 75% of the participants in our study, and 14.6% of participants were current smokers. Almost 50% of the study population was exposed to cigarette smoke during their childhood and most women had a history of passive smoking at home; this difference was statistically significant (P<0.001). The average number of packs of cigarettes smoked by current smokers and former smokers was 24 per year and there was a difference between women and men in the number of cigarettes smoked and duration of smoking (P = 0.028, Table 1).

The characteristics of COPD diagnosed with the questionnaire, the GOLD and the ATS/ERS guideline are shown comparatively in Table 2.

Table 3 shows sensitivity, specificity, PPV, NPV, LR + and LR- of the study population.

Sensitivity of the questionnaire for the diagnosis of airflow obstruction was 8.3% by the GOLD criteria, and 6.7% by the ATS/ERS criteria; however, the specificity of the questionnaire was 96% by both criteria. The sensitivity of the question, "have you ever been diagnosed by a physician as having chronic bronchitis, emphysema, or COPD?" was low (1.4% with GOLD criteria and 3.2% with ATS/ERS criteria), but its specificity was 99% for both

criteria. Likelihood ratios summarize the same kind of information as sensitivity and specificity and can be used to calculate the probability of disease after a positive or negative test. In general, tests with LRs farther away from 1.0 are associated with few false positives and few false negatives; whereas, those with LRs close to 1.0 give less accurate results. The positive LR of the aforementioned question was higher using the ATS/ERS criteria than the GOLD criteria (Table 3).

Diagnostic accuracy of COPD in smokers and non-smokers by the questionnaire, the GOLD and the ATS/ERS criteria is demonstrated in Table 4. The sensitivity and PPV of the questionnaire were higher in current smokers and ex-smokers than non-smokers using both criteria, but the NPV was high in non-smokers. PPV and LR^+ of the questionnaire were higher in the former group than non-smokers and current smokers.

Table 1. Characteristics of the study population

	Total	Women	Men	P value
Number,%	350	195(55.7%)	155(44.3%)	0.47
Age (mean± SD ‖)	54.6%±12.4	53.7±12.3	55.7±12.5	0.20
Age				
<45 years	23.7%	20%	26.7%	
45-65 years	55.4%	57.4%	53.8%	0.34
> 65 years	20.9%	22.6%	19.5%	
COPD† with Questionnaire,%	3.7%	3.1%	4.5%	0.48
COPD with GOLD* criteria	10.3%	7.7%	13.5%	0.073
COPD with ATS/ERS criteria**	4.3%	3.6%	5.2%	0.47
FEV1§(L) (mean± SD)	2.6±0.76	2.2±0.51	3.1±0.75	< 0.001
FEV1/FVC¶ ratio (mean± SD)	0.77±0.06	0.78±0.057	0.76±0.068	0.002
FEV1/FVC < 0.7,%	10.3%	7.7%	13.5%	0.07
bronchodilator	1.7%	1%	2.6%	0.26
Never – smoker,%	74.9%	96.4%	47.5%	<0.001
Former – smoker,%	10.3%	0.5%	22.6%	<0.001
Current-smoker,%	14.6%	2.5%	29.7%	<0.001
Passive smoker at home	18.3%	28.7%	5.2%	<0.001
Passive smoker in childhood	46.9%	43.6%	51%	0.22
Pack/years in current and former smoker (mean ± SD)	24.2±2.2	5.3±10.6	25.7±22	0.028
Asthma,%	3.1%	3.1%	3.2%	0.93

*GOLD: Global Initiative for Chronic Obstructive Lung Disease ; **ATS/ERS : American Thoracic Society /European Respiratory Society ;§FEV1:Forced Expiratory Volume in 1 second ;¶FVC: Forced Vital Capacity; ‖ SD: Standard Deviation; †COPD: Chronic Obstructive Pulmonary Disease

Table 2. Characteristics of COPD diagnosed with questionnaire, GOLD and ATS/ERS

	COPD with questionnaire	COPD with GOLD	COPD with ATS/ERS
Number	13	36	15
Sex			
Women	46.2%	41.7%	46.7%
Men	53.8%	58.3%	53.3%
Age			
<45	23.1%	5.6%	20%
45-65	53.8%	33.3%	33.3%
>65	23.1%	61.1%	46.7%
FEV1(mean ±SD)	2.85 ± 0.58	2.05 ± 0.62	1.93 ±0.46
FEV1/FVC (mean ±SD)	0.76 ±0.09	0.64 ± 0.04	0.63 ±0.05
FEV1/FVC <0.7	23.1%	100%	86.7 %
Smoking history			
Non- smoker	61.5%	61.1%	66.7%
Current smoker	23.1%	22.2%	26.7%
Ex- smoker	7.7%	16.7%	6.7%
Passive smoker at home	53.8%	13.9%	6.7%
Passive smoker in childhood	53.8%	38.9%	46.7%
Pack/years(mean± SD)	32.8±15	33.6±18.9	27.5±7.3

Table 3. Diagnostic accuracy of the question "Have you been diagnosed by a physician as having COPD, chronic bronchitis or emphysema?" and of self-reported, questionnaire-based chronic bronchitis symptoms to detect COPD

		FEV1/FVC<0.7(GOLD)		FEV1/FVC<LLN (ATS/ERS)	
		Value	**95% CI**	**Value**	**95% CI**
COPD diagnosed with questionnaire	sensitivity	0.083	0.02-0.21	0.067	0.012-0.298
	specificity	0.96	0.94-0.98	0.964	0.938-0.979
	PPV*	0.23	0.08-0.53	0.077	0.014-0.333
	NPV**	0.90	0.86-0.92	0.958	0.931-0.975
	LR+ ¶	2.6	0.75-9.07	1.861	0.259-13.39
	LR-†	0.94	0.85-1.04	0.968	0.844-1.11
Question of "Physician-Diagnosed COPD"	sensitivity	0.014	0.001-0.119	0.032	0.003-0.247
	specificity	0.998	0.985-1	0.999	0.986-1
	PPV	0.5	0.055-0.945	0.5	0.055-0.945
	NPV	0.897	0.861-0.925	0.957	0.931-0. 974
	LR+	8.616	0.174-427	21.645	0.444-1055.2
	LR-	0.988	0.951-1.027	0.969	0.885-1.062
Question of " Physician- Diagnosed Chronic Bronchitis or Emphysema"	sensitivity	0.014	0.001-0.119	0.032	0.003-0.247
	specificity	0.998	0.985-1	0.999	0.986-1
	PPV	0.5	0.055-0.945	0.5	0.055-0.945
	NPV	0.897	0.861-0.925	0.957	0.931-0.974
	LR+	8.616	0.174-427	21.645	0.444-1055.2
	LR-	0.988	0.951-1.027	0.969	0.885-1.062

* PPV: positive predictive value ;**NPV: negative predictive value; ¶LR+: positive likelihood ratio; †LR-: negative likelihood ratio

Table 4. Diagnostic accuracy of self-reported, questionnaire-based chronic bronchitis symptoms to detect chronic obstructive pulmonary disease (COPD), in current smoker, Former smoker and non-smoker

		FEV1/FVC<0.7(GOLD)		FEV1/FVC<LLN(ATS/ERS)	
		Value	**95% CI**	**Value**	**95% CI**
Sensitivity	current smoker	0.125	0.022-0.471	0.111	0.012-0.569
	Former smoker	0.214	0.051-0.58	0.333	0.036-0.871
	non-smoker	0.045	0.008-0.218	0.1	0.018-0.405
specificity	current smoker	0.953	0.845-0.987	0.935	0.825-0.978
	Former smoker	0.984	0.863-0.998	0.971	0.851-0.995
	non-smoker	0.971	0.941-0.986	0.972	0.944-0.986
PPV	current smoker	0.333	0.061-0.792	0.143	0.015-0.644
	Former smoker	0.75	0.198-0.973	0.333	0.369-0.871
	non-smoker	0.125	0.022-0.471	0.125	0.022-0.471
NPV	current smoker	0.854	0.728-0.928	0.915	0.801-0.966
	Former smoker	0.847	0.697-0.93	0.917	0.851-0.995
	non-smoker	0.917	0.876-0.945	0.965	0.934-0.981
LR+	current smoker	2.688	0.275-26.242	1.704	0.1-28.959
	Former smoker	13.286	0.602-293.0	11.33	0.579-222.0
	non-smoker	1.552	0.2-12.047	3.6	0.488-26.54
LR-	current smoker	0.918	0.7-1.202	0.951	0.68-1.33
	Former smoker	0.799	0.541-1.179	0.687	0.221-2.133
	non-smoker	0.983	0.895-1.08	0.926	0.952-1.139

DISCUSSION

This study aimed to examine the diagnostic accuracy of a COPD questionnaire in the Azar-cohort population during the pilot phase. The GOLD and the ATS/ERS criteria were used to assess the validity of the questionnaire. The results showed that the questionnaire had low sensitivity (8% using the GOLD criteria and 6.7% using the ATS/ERS criteria), but high specificity (96% using both criteria) for the diagnosis of airflow obstruction. Its PPV was low (23% based on the GOLD and 7.7% based on the ATS/ERS criteria), but its NPV was high (90% to 95% based on the GOLD and the ATS/ERS guidelines) to identify airflow obstruction. While the nature of COPD is progressive, it is also preventable and treatable and its prevention (such as smoking cessation and nicotine replacement in smokers) and treatment are non-invasive. Thus, a method with high sensitivity and low false negative results seems to be appropriate. A test with high

specificity can be used when false-positive results can be physically, emotionally or financially harmful for patients (17). The high specificity of this questionnaire helps healthy people not to undergo spirometry, which is expensive. The reasons for low sensitivity of the questionnaire are: first, when a test is used for screening rather than diagnostic purposes, it is influenced by the disease spectrum (asymptomatic to severe cases) and disease prevalence (17). The fact that this study was conducted on the general population and COPD is diagnosed in the final stages (18) led to lower sensitivity of the questionnaire. Second, since a completed questionnaire containing several questions about cardiovascular, pulmonary, neurological, psychological and rheumatologic diseases and cancer was used in the Azar-cohort study and a chronic lung disease questionnaire was a part of this larger questionnaire, it can be a justification for low sensitivity of the questionnaire due to the high volume of questions. Third, using spirometry without the use of a bronchodilator in this study, which can increase the number of cases with diagnosis of airflow obstruction using spirometry, could have reduced the sensitivity of the questionnaire. In a study conducted in Sweden on general population, spirometry without bronchodilator was performed, and the sensitivity of the questionnaire was low (4.6% based on GOLD criteria, and 7.4% based on ATS/ERS criteria) (8).

Studies have shown that the prevalence of COPD after using a bronchodilator in spirometry could be 5-50% less compared to when a bronchodilator is not used. Although the study of lung function after use of bronchodilator using the GOLD criteria is the standard method, it is not used in most studies (19). The method by which the prevalence of COPD is estimated (e.g. specialists' opinions, diagnosis based on patient reports, diagnosis based on symptoms or spirometry) will affect the estimation (20). The sensitivity of the question, "have you ever been diagnosed by a physician as having COPD or chronic bronchitis?" was low using spirometry (1.4% by the GOLD criteria, and 3.2% by the ATS/ERS criteria), indicating that people may have been experiencing early symptoms of the disease for years (cough and sputum), but ignoring them and seeking treatment after they develop dyspnea and have irreversibly lost more than half of their ventilation supply (18). The specificity of this question was high (99% with both criteria), meaning that the possibility of positive test result in healthy people is rare (false positive). However, in a study conducted on female nurses diagnosed by a physician as having COPD, their medical documents were requested to verify their reports and the results showed that the accuracy of the report was high, which shows that health workers are more likely to have an accurate report of their disease history than other groups due to their medical education (21). In our study, the sensitivity of the questionnaire to identify individuals with COPD was higher among smokers than non-smokers, which is consistent with the results of other studies (8, 18). In general, questionnaire sensitivity in diagnosis of COPD among smokers is low (12%). When a screening test is done on a population with less exposure to disease risk factors, its sensitivity will be low; whereas, its specificity will be high compared to the test done on the people with high exposure to risk factors (17). In this study, non-smoking participants accounting for 75% of the study population can partly justify the low sensitivity of the test. In a study that was done on smokers only, airflow obstruction was reported in 24.3% of the participants using spirometry (17). It is estimated that about 20% of smokers will eventually develop COPD (22).

Study limitations

The researchers only used spirometry data without a bronchodilator in this study. Because the GOLD guidelines give a FEV1/FVC ratio of < 0.7 after the use of a bronchodilator as cutoff point to diagnose COPD, it seems that the main limitation of this study was conduction of spirometry without a bronchodilator.

It is recommended to use a short questionnaire to assess the validity of the questionnaire and spirometry

should be done before and after the use of a bronchodilator.

CONCLUSION

Specificity and NPV of the questionnaire indicate that the questionnaire is likely able to identify people with airflow obstruction, but the low sensitivity of the questionnaire can underestimate COPD in the general population.

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Conflict of interest

There are no conflicts of interest.

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