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ORIGINAL RESEARCH

Validity of physician-diagnosed COPD in relation to spirometric definitions of COPD in a general population aged 50–64 years – the SCAPIS pilot study

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Background: In epidemiological studies, items about physician-diagnosed COPD are often used. There is a lack of validation and standardization of these items.

Materials and methods: In a general population-based study, 1,050 subjects completed a questionnaire and performed spirometry, including forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) after inhalation of 400 µg of salbutamol. COPD was defined as the ratio of FEV_1/FVC <0.7 after bronchodilation. Physician-diagnosed COPD was defined as an affirmative answer to the single item: "Have you ever had COPD diagnosed by a physician?", physician-diagnosed COPD/emphysema as an affirmative answer to any of the two single items; "Have you ever had COPD diagnosed by a physician?" or "Have you ever been told by a physician that you have emphysema?", physician-diagnosed chronic bronchitis as an affirmative answer to; "Have you ever been told by a physician that you have chronic bronchitis?" and physician-diagnosed COPD, emphysema or chronic bronchitis was defined as an affirmative answer to either of the three items above.

Results: For the single item about physician-diagnosed COPD, the sensitivity was around 0.11 and the specificity was almost 0.99 in relation to COPD. The sensitivity of the combined items about COPD/emphysema in detecting COPD was 0.11 and the specificity was high, 0.985. When the items about physician-diagnosed COPD, emphysema or chronic bronchitis were merged as one entity, the sensitivity went up (0.13) and the specificity went down (0.95).

Conclusion: Items about physician-diagnosed COPD have low sensitivity but a very high specificity, indicating that these items will minimize the proportion of false positives. The low sensitivity will underestimate the total burden of COPD in the general population. Items about physician-diagnosed COPD may be used in studies of risk factors for COPD, but are not recommended in prevalence studies.

Keywords: validity, questionnaire, general-population, obstructive lung diseases, epidemiology

Introduction

COPD is an important cause of morbidity and mortality, and it has been estimated that COPD is the third leading cause of death worldwide.[1] Exposure to tobacco smoke is the most important cause of COPD with population attributable fractions around 70%–80%.[1] Other important potential risk factors are occupational exposure to vapor, gas and dust and fumes and exposure to indoor air pollutants including passive smoking.[2–4]

Spirometry after bronchodilatation is crucial for the diagnosis of COPD defined as the fixed ratio of forced expiratory volume in 1 second (FEV_1)/forced vital capacity

(FVC) <0.7.[5] However, the GOLD recommendations of the use of the fixed ratio of $FEV_1/FVC < 0.7$ have been challenged because a definition based on an $FEV_1/FVC < 0.7$ may cause overestimation of COPD in the older population in epidemiological studies.[6] An alternative approach is to use the lower limit of normal (LLN) of $FEV_1/FVC < 0.7$ as a cutoff.[7] The LLN is calculated using the distribution in a reference material adjusted for age, sex and height. Spirometric diagnosis of COPD, irrespectively if the GOLD approach or the LLN approach is applied, is sensitive, meaning that a high proportion of the diagnosed subjects has mild disease or are asymptomatic, which may result in a substantial proportion of false-positive diagnoses.[6,7]

In epidemiological studies investigating the risk of disease in relation to certain risk factors, there is preferential to have operational disease definitions with (very) high specificity.[8] Disease definitions with high specificity imply lower sensitivity, which altogether means that the fraction of false negatives increases and the fraction of false positives decreases. Outcome definitions using questionnaire items about self-reported physician diagnosed disease, such as asthma or diabetes, has been shown to have a high specificity.[9–11]

Items about physician-diagnosed COPD are used in epidemiological studies, but there is an obvious lack of studies validating items about physician-diagnosed COPD in relation to a spirometric gold standard. In a previous study performed in another population, we have validated the item "Have you been diagnosed by a physician as having COPD or emphysema?" against the ratio of $FEV_1/FVC < 0.7$.[12] The specificity was very high, 0.997, and the sensitivity was low, 0.057. However, the validation was in relation to spirometry before bronchodilation. To the best of our knowledge, we have not found any validation studies in general population settings validating questionnaire-based physician-diagnosed COPD in relation to spirometric diagnosis of COPD. We have now performed a validation study in the general population where we have access to spirometry before and after bronchodilation. We will have the possible to validate these items in relation to different definitions of airways obstruction and COPD.

Materials and methods

The study data were derived from the pilot part of the Swedish CArdioPulmonary bioImage Study (SCAPIS Pilot), a Swedish general population-based study.[13–15] Briefly, a randomly selected population sample including 2,243 adults aged 50–64 years were invited to the investigation and 1,111 subjects agreed to participate. All of these subjects answered an extensive respiratory questionnaire comprising items about physician-diagnosed COPD, emphysema, asthma and chronic bronchitis, respiratory symptoms and smoking habits.

Dynamic spirometry, including FEV_1 and FVC, was performed. All spirometric maneuvers were performed before and 15 minutes after inhalation of 400 μg of salbutamol using a nose clamp with the subject in the sitting position. A Jaeger Master Screen PFT (Hoechberg, Germany) was used for all measurements. Predicted values of FEV_1, FVC and FEV_1/FVC were calculated based on a recent Swedish population and FEV_1 and FVC are expressed as percent predicted.[16,17]

Definitions

Airways obstruction was defined as the ratio of $FEV_1/FVC < 0.7$ before bronchodilation. $COPD_{GOLD}$ was defined as the ratio of $FEV_1/FVC < 0.7$ after bronchodilation.[5] $COPD_{LLN}$ was defined as the ratio of FEV_1/FVC below the LLN after bronchodilation.[7]

Physician-diagnosed COPD was defined as an affirmative answer to the single item: "Have you ever had COPD diagnosed by a physician?"

Physician-diagnosed COPD/emphysema was defined as an affirmative answer to any of the two single items: "Have you ever had COPD diagnosed by a physician?" or "Have you ever been told by a physician that you have emphysema?"

Physician-diagnosed chronic bronchitis was defined as an affirmative answer to: "Have you ever been told by a physician that you have chronic bronchitis?"

Physician-diagnosed COPD, emphysema or chronic bronchitis was defined as an affirmative answer to either of the three items above.

Physician-diagnosed asthma was defined as an affirmative answer to "Have you ever had asthma diagnosed by a physician?"

Smoking was categorized as current smokers, former smokers or never-smokers. Former smokers were defined as those who have smoked for at least 1 year but not during the last year. In this analysis, current smokers and former smokers were categorized as ever-smokers. The study was approved by the Regional Committee of Ethics in Umeå, 2010/228-31, and all included subjects gave their written informed consent to participate in the study.

Statistics

All calculations were performed using SAS version 9.2 (SAS Institute, Cary, NC, USA). The 95% CIs for specificity,

sensitivity, positive predictive value (PPV) and negative predictive value (NPV) were calculated using exact methods. 95% CIs were also calculated applying exact methods.

Results

Of the 1,111 subjects, 61 were excluded because of incomplete data resulting in a final study population of 1,050 subjects. Descriptive data on age, sex, smoking, lung function and prevalence of airways obstruction and COPD according to different definitions are shown in Table 1.

Twenty-one subjects (2.0%) responded affirmatively to the single item about physician-diagnosed COPD, seven subjects (0.7%) responded affirmatively to the item about physician-diagnosed emphysema and three subjects affirmed both items. Hence, 25 subjects (2.4%) were defined as having physician-diagnosed COPD/emphysema, that is, responding affirmatively to either of the two items about physician-diagnosed COPD or physician-diagnosed emphysema. The prevalence of physician-diagnosed chronic bronchitis was 4.4% (n=46), and 5.7% (n=60) responded affirmatively to the merged items of physician-diagnosed COPD, emphysema or chronic bronchitis.

Specificity, sensitivity, PPV and NPV of physician-diagnosed COPD, physician-diagnosed COPD/emphysema and the merged item about COPD, emphysema and chronic bronchitis in relation to a different definitions of COPD and airways obstruction are shown in Table 2.

For the single item about physician-diagnosed COPD, the sensitivity was around 0.11 and the specificity was almost 0.99 in relation to both definitions of COPD

(Table 2). The sensitivity of the combined items about COPD/emphysema in detecting $COPD_{GOLD}$ was 0.105 (95% CI 0.054–0.180), and for $GOLD_{LLN}$, it was 0.110 (95% CI 0.056–0.188). The specificity was high, 0.985 (95% CI 0.975–0.992), for both definitions of COPD. When the COPD items were validated in relation to airways obstruction, the sensitivity was lower, 0.057 (95% CI 0.030–0.098), but the specificity was similar, 0.985–0.989. When the items about physician-diagnosed COPD, emphysema or chronic bronchitis were merged as one entity, the sensitivity went up (0.11–0.15) and the specificity went down (0.95) (Table 2).

When the analyses were separated according to sex (Table 3), the results were also similar, with no obvious differences according to gender. Among ever-smokers, the combined COPD/emphysema items reached a similar specificity, 0.981 (95% CI 0.965–0.991), in relation to $COPD_{GOLD}$ and $COPD_{LLN}$ compared to the whole population.

Discussion

The main results extracted from the present study are that items about physician-diagnosed COPD have a very high specificity (and low sensitivity) in relation to a golden standard of COPD based on spirometry after bronchodilation. Especially, the single item comprising only COPD had, in our national context, a very high specificity. Furthermore, the common approach to merge items about COPD and emphysema also has high specificity (and low sensitivity). However, combining items with COPD and chronic bronchitis resulted in lower specificity, and hence a larger degree of false positives. In this population aged 50–64 years, there

Table 1 Age, gender, smoking habits, symptoms and lung function values in 1,050 subjects according to different definitions of airways obstruction and COPD

Variables	Airways obstruction (N=212)	COPD$_{GOLD}$ (N=105)	COPD$_{LLN}$ (N=100)
All (n=1,050)	20.2% (N=212)	10.0% (N=105)	9.5% (N=100)
Males (n=525)	18.3% (N=96)	11.4% (N=60)	10.9% (N=57)
Females (n=525)	22.1% (N=116)	8.6% (N=45)	8.2% (N=43)
Age (years)	58.1	58.7	58.1
Never-smokers (n=448)	13.2% (N=59)	4.7% (N=21)	7.1% (N=32)
Ever-smokers (n=602)	25.4% (N=153)	14.0% (N=84)	11.3% (N=68)
Physician-diagnosed asthma (n=97)	38.1% (N=37)	23.7% (N=23)	21.7% (N=21)
FEV$_1$ (% pred)	90.2	83.1	86.3
FVC (% pred)	101.7	100.6	104.7
Current wheeze (n=87)	17.5% (N=37)	26.7% (N=28)	27.0% (N=27)
Physician-diagnosed COPD/emphysema (n=25)	48.0% (N=12)	44.0% (N=11)	48.0% (N=12)
Physician-diagnosed chronic bronchitis (n=46)	41.3% (N=19)	19.6% (N=9)	21.7% (N=10)
Physician-diagnosed COPD/emphysema or chronic bronchitis (n=60)	40.0% (N=24)	23.3% (N=14)	25.0% (N=15)

Abbreviations: FEV$_1$, forced expiratory volume in 1 second; FVC, forced vital capacity; $_{LLN}$, lower limit of normal.

Table 2 Validity of items about physician-diagnosed COPD and chronic bronchitis

	Airways obstruction (n=212)		COPD$_{GOLD}$ (n=105)		COPD$_{LLN}$ (n=100)	
	Value	95% CI	Value	95% CI	Value	95% CI
Physician-diagnosed COPD (n=21)						
Sensitivity	0.057	0.030–0.098	0.106	0.054–0.181	0.111	0.056–0.188
Specificity	0.989	0.980–0.995	0.989	0.981–0.995	0.989	0.981–0.995
PPV	0.571	0.340–0.782	0.524	0.298–0.743	0.524	0.299–0.743
NPV	0.806	0.780–0.830	0.909	0.890–0.926	0.914	0.895–0.930
Physician-diagnosed COPD/emphysema (n=25)						
Sensitivity	0.057	0.030–0.097	0.105	0.054–0.180	0.110	0.056–0.188
Specificity	0.985	0.974–0.992	0.985	0.975–0.992	0.985	0.975–0.992
PPV	0.480	0.278–0.687	0.440	0.244–0.651	0.440	0.244–0.651
NPV	0.805	0.779–0.829	0.908	0.889–0.925	0.913	0.894–0.930
Physician-diagnosed chronic bronchitis (n=46)						
Sensitivity	0.090	0.055–0.136	0.086	0.040–0.157	0.100	0.049–0.176
Specificity	0.968	0.954–0.979	0.961	0.946–0.972	0.962	0.948–0.973
PPV	0.413	0.270–0.568	0.196	0.094–0.339	0.217	0.110–0.364
NPV	0.808	0.782–0.832	0.904	0.885–0.922	0.910	0.891–0.927
Physician-diagnosed COPD, emphysema and chronic bronchitis (n=60)						
Sensitivity	0.113	0.074–0.164	0.133	0.075–0.214	0.15	0.087–0.235
Specificity	0.957	0.941–0.970	0.951	0.936–0.964	0.953	0.937–0.965
PPV	0.400	0.276–0.535	0.233	0.134–0.360	0.250	0.147–0.379
NPV	0.810	0.784–0.834	0.908	0.888–0.926	0.914	0.895–0.931

Abbreviations: NPV, negative predictive value; PPV, positive predictive value; $_{LLN}$, lower limit of normal.

was no difference whether the golden standard was based on the GOLD concept or on the LLN concept. There was neither any significant difference with regard to gender.

This is, to the best of our knowledge, the first study in the general population validating questionnaire items about physician-diagnosed COPD in relation to a spirometric diagnosis of COPD. The results indicate a very high specificity, which minimizes the proportion of false positives. The PPVs are around 0.50, with the highest values, 0.524, for the single-item about physician-diagnosed COPD. This means that almost half of the subjects responding affirmatively to the item about physician-diagnosed COPD do not have spirometric COPD. Due to the low prevalence of physician-diagnosed COPD, this misclassification only marginally

Table 3 Validity of items about physician-diagnosed COPD and emphysema among men, women and ever-smokers in relation with different spirometry definitions of airway obstruction and COPD

	Airways obstruction (n=212)		COPD$_{GOLD}$ (n=105)		COPD$_{LLN}$ (n=100)	
	Value	95% CI	Value	95% CI	Value	95% CI
Physician-diagnosed COPD/emphysema (n=25)						
Males (n=14)						
Sensitivity	0.063	0.023–0.131	0.100	0.038–0.205	0.105	0.040–0.215
Specificity	0.981	0.964–0.992	0.983	0.967–0.993	0.983	0.967–0.993
PPV	0.429	0.177–0.711	0.429	0.177–0.711	0.455	0.168–0.767
NPV	0.824	0.789–0.856	0.894	0.864–0.920	0.900	0.871–0.925
Females (n=11)						
Sensitivity	0.052	0.019–0.109	0.111	0.037–0.241	0.116	0.039–0.251
Specificity	0.988	0.972–0.996	0.988	0.973–0.995	0.988	0.973–0.995
PPV	0.546	0.234–0.833	0.455	0.168–0.766	0.429	0.177–0.711
NPV	0.786	0.748–0.821	0.922	0.900–0.944	0.926	0.900–0.947
Ever-smokers (n=20)						
Sensitivity	0.072	0.036–0.125	0.119	0.059–0.208	0.125	0.062–0.218
Specificity	0.980	0.962–0.991	0.981	0.965–0.991	0.981	0.965–0.991
PPV	0.550	0.315–0.770	0.500	0.272–0.728	0.500	0.272–0.728
NPV	0.756	0.719–0.790	0.873	0.843–0.899	0.880	0.851–0.905

Abbreviations: NPV, negative predictive value; PPV, positive predictive value; $_{LLN}$, lower limit of normal.

affects the specificity. In the US Nurses' Health Study, the PPV for physician-diagnosed COPD, emphysema and chronic bronchitis was higher, around 0.70.[18]

We found in our previous study where the golden standard was spirometric airways obstruction (before bronchodilation), a sensitivity of 0.057 and specificity of 0.997, for an item comprising both COPD and emphysema (but not chronic bronchitis).[12] Those results resemble our present estimates. A very high specificity is of uttermost importance when designing epidemiological studies investigating the risk of COPD in relation to different exposures (tobacco, occupation and air pollution). When studying outcomes with low prevalence, high number of false positives will increase the misclassification, which will lead to decreased risk estimates.[8]

There is, however, of importance to underscore that these results and conclusions are only valid in national contexts similar to ours, that is, where there are similar traditions of diagnosing COPD. Undiagnosed COPD (false negatives) will not be detected with items about physician-diagnosed COPD. If the aim is to detect (screening) undiagnosed COPD, the most valid way is to measure lung function, which we also have performed and used as our golden standard.[19] However, in some situations spirometric investigations may be difficult to perform, and in such situations questionnaire-based

identification of COPD may be an option. There are studies where many subjects can be dispersed of a large area, such as Nurses' Health Study.[18] When estimating the relative risk of COPD, the false negatives is a minor problem for a correct estimation of relative risk in relation to certain exposures, as long as the misclassification is nondifferential.[18,20]

Items about physician-diagnosed COPD are used in epidemiological studies, but there is an obvious lack of validation and standardization of these items. One of the first groups to apply items about physician-diagnosed COPD was the Tucson Group, and they were followed by the studies from National Health and Nutrition Examination Surveys.[21,22] However, the items are worded in different ways. Table 4 presents the wordings of the most common items obtained from different studies including the present study.[12,21–25] The initial items comprised wordings about emphysema and chronic bronchitis, and during the last years, the term COPD have been included in some of the items. That reflects the increased acceptance of the term COPD.[26]

In the present study, when physician diagnosed chronic bronchitis was analyzed as one entity together with COPD and emphysema, the diagnostic accuracy decreased. This reflects that the number of false positives increased, as in current practice chronic bronchitis is not diagnosed as COPD.

Table 4 Different wordings in questionnaire items about chronic obstructive pulmonary disease

References	Wording	Additional comments
Lebowitz and Burrows[21]	During the past year, have you seen a doctor for: a. Emphysema? b. Chronic bronchitis?	
Whittemore et al[22]	Has a doctor ever told you that you had chronic bronchitis? Has a doctor ever told you that you had emphysema?	Positive response to either item and negative response to current asthma was defined as physician-diagnosed COPD
Schnell et al[23]	Has a doctor or other health professional ever told you that you had chronic bronchitis? Has a doctor or other health professional ever told you that you had emphysema?	Positive response to any was defined as physician-diagnosed COPD
Ford et al[24]	Have you ever been told by a doctor or other health professional that you have COPD, emphysema or bronchitis?	From the Behavioral Risk factor Surveillance System
Ford et al[24]	Have you been told by a doctor or other health professional that you had emphysema? During the past 12 months, have you been told by a doctor or other health professional that you have chronic bronchitis?	From the National Health Interview Survey An affirmative response to one or both questions was defined as physician-diagnosed COPD
Murgia et al[12]	Have you been diagnosed by a physician as having COPD or emphysema	One item
Mirabelli et al[25]	Have you ever been told by a doctor or other health professional that you have COPD? Have you been told by a doctor or other health professional that you have emphysema? Have you been told by a doctor or other health professional that you have chronic bronchitis?	Positive response to any of the three items was defined as physician-diagnosed COPD
Present study	Have you ever been diagnosed by a physician as having COPD? Have you been diagnosed by a physician as having emphysema?	Positive response to any of two items was defined as physician-diagnosed COPD
Present study	Have you ever been diagnosed by a physician as having COPD?	Single item

Our recommendation is, hence, not to include items about chronic bronchitis in items about physician-diagnosed COPD. This is an important message, as it is quite common to include chronic bronchitis in the set of COPD items.

Previous studies have shown that women with an identical medical history are less likely to be diagnosed with COPD compared to men.[27,28] However, in our study, there were marginal differences regarding specificity, sensitivity and the PPVs between men and women.

We did not exclude subjects with asthma in our analyses. In older subjects, as in our study, the items about physician-diagnosed asthma are misclassified in relation to COPD.[9,27] We could have excluded subjects with wheezing, but that would also affect subjects with COPD, why we in our main analyses kept all subjects, also those with wheezing and physician-diagnosed asthma. However, in sensitivity analyses, we excluded subjects with current wheezing and reversibility of FEV_1 over 9% predicted.[15] That resulted in similar results with small deviations from the main results. The sensitivity of physician-diagnosed COPD in relation to airways obstruction was 0.054 (95% CI 0.017–0.022), in relation to $GOLD_{GOLD}$ was 0.106 (95% CI 0.041–0.171) and in relation to $GOLD_{LLN}$ was 0.111 (95% CI 0.043–0.180). The specificity was 0.990 in all three analyses.

The main weakness with the present study is the small study sample. We have outlined 95% CI around our estimates to be able to judge the reliability of our results. Another limitation is the narrow age interval 50–64 years, making the conclusions only valid for that age group. Another limitation in the present study is that we have used definitions of COPD based solely on chronic airflow limitation. In the recent GOLD document, it has been proposed to define COPD as a combination of chronic airflow limitation and certain key symptoms, such as dyspnea, wheezing or cough with phlegm.[5]

Conclusion

In conclusion, our results indicate that questionnaire items about physician-diagnosed COPD have a very high specificity which will minimize the number of false positives, indicating that such self-reported COPD may be used in estimation of relative risks. The low sensitivity will underestimate the total burden of COPD in the general population. Items about physician-diagnosed COPD may be used in studies of risk factors for COPD, but are not recommended in prevalence studies.

Acknowledgments

Disclosure

The authors report no conflicts of interest in this work.

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