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Restrictive spirometric pattern in the general adult population: Methods of defining the condition and consequences on prevalence

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ABSTRACT

Background: Attempts have been made to use dynamic spirometry to define restrictive lung function, but the definition of a restrictive spirometric pattern (RSP) varies between studies such as BOLD and NHANES. The aim of this study was to estimate the prevalence and risk factors of RSP among adults in northern Sweden based on different definitions.

Methods: In 2008–2009 a general population sample aged 21–86y within the obstructive lung disease in northern Sweden (OLIN) studies was examined by structured interview and spirometry, and 726 subjects participated (71% of invited). The prevalence of RSP was calculated according to three different definitions based on pre-as well as post-bronchodilator spirometry:

1) FVC < 80% & FEV_1/FVC > 0.7
2) FVC < 80% & FEV_1/FVC > LLN
3) FVC < LLN & FEV_1/FVC > LLN

Results: The three definitions yielded RSP prevalence estimates of 10.5%, 11.2% and 9.4% respectively, when based on pre-bronchodilator values. The prevalence was lower when based on post-bronchodilator values, i.e. 7.3%, 7.9% and 6.6%. According to definition 1 and 2, the RSP prevalence increased by age, but not according to definition 3. The overlap between the definitions was substantial. When corrected for confounding factors, manual work in industry and diabetes with obesity were independently associated with an increased risk for RSP regardless of definition.

Conclusions: The prevalence of RSP was 7–11%. The prevalence estimates differed more depending on the choice of pre- compared to post-bronchodilator values than on the choice of RSP definition. RSP was, regardless of definition, independently associated with manual work in industry and diabetes with obesity.

1. Introduction

Restrictive lung function is defined as reduced lung expansion expressed as a decreased total lung capacity (TLC). It may reflect several underlying conditions and diseases, such as interstitial lung diseases, pleural effusions and disorders, thoracic deformities, neuromuscular diseases, diaphragmatic disorders, obesity, heart failure, pregnancy and pain [1]. Interstitial lung diseases comprise more than 200 diagnoses including idiopathic pulmonary fibrosis, several pneumoconiosis, sarcoidosis and several other conditions

Abbreviations: ATS, American Thoracic Society; BMI, Body Mass Index; BOLD, Burden of Obstructive Lung Disease; CI, Confidence Interval; ERS, European Respiratory Society; FEV1, Forced expiratory volume in one second; FVC, Forced expiratory volume; GA2LEN, Global Allergy and Asthma European Network; GLI, Global Lung Initiative; IHD, Ischemic Heart Disease; LLN, Lower Limit of Normal; NHANES, National Health and Nutrition Examination Survey; OLIN, Obstructive Lung Disease in Northern Sweden; OR, Odds Ratio; Post-BD, After bronchodilation; Pre-BD, Before bronchodilation; RSP, Restrictive Spirometric Pattern; TLC, Total Lung Capacity.

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[2,3]. The prevalence of most of these conditions is low, for instance the prevalence of idiopathic pulmonary fibrosis has been estimated at about 0.1% or even less [4].

Attempts have been made to use dynamic spirometry to identify restrictive lung function, using a low FVC and a normal FEV1/FVC ratio as a definition of a restrictive lung function [5]. Dynamic spirometry has limitations in identifying restrictive lung diseases [6,7], but it can effectively exclude a restrictive disease when FVC is normal and its specificity increases when the FEV1/FVC ratio is taken into account [7,8]. Further, a recent review stresses the many clinical, public health and eventually therapeutic implications of identifying subjects with a restrictive spirometry pattern (RSP) [9], since RSP is associated with high symptom burden, comorbidities and adverse outcomes including mortality.

The estimates of prevalence of restrictive conditions based on dynamic spirometry vary considerably, probably due to the various definitions used as described in the recent review [9]. Most commonly, fixed thresholds such as FVC < 80% of predicted and a FEV1/FVC ratio >0.7 have been utilized for the definition of RSP, but other types of thresholds are gaining ground. Further, most studies have used pre-bronchodilator (pre-BD) spirometry data for defining RSP, while in the Burden of Obstructive Lung Disease (BOLD) study post-bronchodilator (post-BD) data were used [8]. Data from the US National Health and Nutrition Examination surveys (NHANES) have presented consistent results with prevalence of RSP on general population level varying from 5.4% to 9.2% [10–14]. Prevalence estimates from other studies vary from 3% to 13% [15–19], while the prevalence among the BOLD centers vary from 4% to upward of 50% [8]. Co-existing diseases such as diabetes, obesity, cardiovascular and rheumatic diseases and other risk factors for RSP have been studied mainly in the US. To date, there are no studies comparing different definitions of RSP based on both pre- and post-BD spirometry in the general population.

The aim of this study was to estimate the prevalence of RSP in an adult general population using different definitions of restrictive spirometry, and to study associated risk factors and co-existing diseases.

2. Materials and methods

2.1. Study population

In 2006 a random sample in ages 20–69 years in Norrbotten county in Northern Sweden, n = 7997, was invited to participate in a postal questionnaire survey [20]. Another randomly selected population sample in ages 30–84 years, which had participated in a similar questionnaire survey in 1996 [21], was also invited, n = 7004. Overall 12,055 subjects (80% of the invited) participated [22].

Of the questionnaire responders, a randomly selected sample, n = 1016, after stratification for the sex and age distribution of the county population, was invited to clinical examinations including pre- and post-bronchodilator (BD) spirometry and a structured interview in 2008–2009. Of the invited, 726 (71.5%) subjects performed spirometry with adequate technique and completed the interview [22], with mean age 53 years (range 21–86 years) and 50% women. The participants at the clinical examinations were representative for the entire cohort with respect to age, gender and prevalence of respiratory symptoms and diseases and their comorbidities [23]. The Study was approved by the Regional Ethical Review Board at Umeå University.

2.2. Questionnaire

The questionnaire consists of a self-administrated short version for postal surveys [24] and a version for interviews [25]. It has been used in several epidemiological studies [26–29] and is validated against the GA2LEN questionnaire [30]. The questions are focused on respiratory symptoms and diseases, their comorbidities, allergy, medication, family history of asthma and allergic diseases, smoking habits, occupation, area of domicile and other potential risk factors for respiratory diseases.

2.3. Spirometry

A Masterscope (Jaeger, Germany) flow-volume spirometer was used. The procedure followed the ATS/ERS recommendations [31] but with a reproducibility criterion of ≤5% deviation from the second highest value [32]. At least three and maximum six forced vital capacity (FVC) maneuvers were performed. A reversibility test was performed using 0.4 mg salbutamol powder via discus. Reference values for spirometry derived from the population living in the study area were used [33]. The Global Lung Initiative (GLI) reference values [34] were used in sensitivity analyses presented in the Results section and Table A.1.

2.4. Definitions

RSP was defined as a decreased FVC in combination with a normal or increased FEV1/FVC ratio. The definitions thereof are based both on fixed thresholds, i.e. FVC < 80% of predicted and ratio of FEV1/FVC > 0.7, and also on the lower limit of normal (LLN), i.e. the fifth percentile (approximately corresponding to a Z-score < −1.645). Both pre- and post-BD spirometry was used, where post-BD values were defined as the highest of pre- and post-BD results. The use of LLN is strongly recommended by the ERS/ATS task force on standardization of lung function testing [31]. Three different definitions based on pre- and post-BD values respectively were analyzed (Table 1). Severity grading was based both on the level of FEV_1 as recommended by the ERS/ATS task force [31] and on the level of FVC, and the limit for severity was defined as <70% of predicted for both. Subjects with obstructive spirometry were excluded from analyses comparing RSP with normal spirometry.

Information about *heart diseases*, *hypertension*, *diabetes* and *rheumatic disease* was collected through interviews. *Ischemic heart disease* (IHD) was defined as a history of myocardial infarction, coronary artery bypass surgery, percutaneous coronary intervention or angina pectoris. *Any heart disease* was defined as a report of IHD, heart failure, arrhythmia or other heart disease. Height and weight was measured and Body Mass Index (BMI, kg/m^2) calculated. Underweight was classified as BMI < 20, normal weight as 20 ≤ BMI < 25, overweight as 25 ≤ BMI < 30 and obesity as BMI ≥ 30. The classification of *socio-economic status* was based on occupation. Smoking habits were classified as *ever-smokers* (current or ex-smokers) and *never-smokers*, and by number of pack-years. Ex-smokers were defined as those who had smoked for at least one year but not during the last 12 months.

2.5. Analyses

The Fisher's exact test (two-sided) was used for bivariate comparisons of proportions. For comparisons of proportions across more than two groups, Mantel-Haenszel test for trend was used. A p-value <0.05 was considered statistically significant. Multiple logistic regression was used to test independent risk factors for RSP with results presented as adjusted odds ratios (OR) with 95% confidence intervals (CI). Variables significantly associated with RSP in unadjusted analyses (Table A.2) were included in the regression analyses. An interaction term between diabetes and obesity was also analyzed. Age was dichotomized in the regression analyses