



COPD in chronic heart failure: Less common than previously thought?

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ABSTRACT

Background: Using a fixed ratio of forced expiratory volume in 1 s to forced vital capacity (FEV_1/FVC) < 0.70 instead of the lower limit of normal (LLN) to define chronic obstructive pulmonary disease (COPD) may lead to overdiagnosis of COPD in elderly patients with heart failure (HF) and consequently unnecessary treatment with possible adverse health effects.

Objective: The aim of this study was to determine COPD prevalence in patients with chronic HF according to two definitions of airflow obstruction.

Methods: Spirometry was performed in 187 outpatients with stable chronic HF without pulmonary congestion who had a left ventricular ejection fraction < 40% (mean age 69 ± 10 years, 78% men). COPD diagnosis was confirmed 3 months after standard treatment with tiotropium in newly diagnosed COPD patients.

Results: COPD prevalence varied substantially between 19.8% (LLN-COPD) and 32.1% (GOLD-COPD). Twenty-three of 60 patients (38.3%) with GOLD-COPD were potentially misclassified as having COPD (FEV_1/FVC < 0.7 but > LLN). In contrast to patients with LLN-COPD, potentially misclassified patients did not differ significantly from those without COPD regarding respiratory symptoms and risk factors for COPD.

Conclusions: One fifth, rather than one third, of the patients with chronic HF had concomitant COPD using the LLN instead of the fixed ratio. LLN may identify clinically more important COPD than a fixed ratio of 0.7.

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Introduction

Chronic obstructive pulmonary disease (COPD) frequently co-exists with heart failure (HF), leading to poor prognosis as well as diagnostic and therapeutic challenges.¹ However, estimates of COPD prevalence in patients with HF with reduced or preserved left

ventricular ejection fraction (LVEF) vary substantially between 9% and 52%, depending on study design, population (age, gender, smoking habits, inpatients versus outpatients, acute versus chronic HF, primary, secondary, or tertiary care), and diagnostic criteria.¹ Although spirometry is considered to be the gold standard for the diagnosis of COPD,² data on the prevalence of COPD based on

Abbreviations: ABHR, aspecific bronchial hyperreactivity; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ATS/ERS, American Thoracic Society/European Respiratory Society; BMI, body mass index; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CRT, cardiac resynchronization therapy; CS, current smokers; FEV_1/FVC , ratio of forced expiratory volume in 1 s to forced vital capacity; FS, former smokers; GOLD, Global Initiative for Chronic Obstructive Lung Disease; HF, heart failure; ICD, implantable cardioverter defibrillator; LLN, lower limit of normal; LVEF, left ventricular ejection fraction; LVSD, left ventricular systolic dysfunction; MLHFQ, Minnesota Living with Heart Failure Questionnaire; MRC, modified Medical Research Council dyspnea scale; NS, non-smokers; NT-pro-BNP, N-terminal pro-B natriuretic peptide; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; PFT, pulmonary function tests; PY, pack-years.

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spirometry in patients with HF are scarce.^{3–7} Moreover, even when spirometry is used, in general there is still no consensus on how to define COPD.^{8–11} The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines recommend the use of a fixed ratio of forced expiratory volume in 1 s to forced vital capacity (FEV_1/FVC) < 0.70 for the sake of simplicity.² However, a growing body of literature indicates that considering the physiological decline of the FEV_1/FVC ratio with age the use of a fixed ratio may lead to overdiagnosis of COPD in elderly subjects^{12–19} and underdiagnosis of COPD in young adults.^{15–17,20} Therefore, to avoid misclassification, the American Thoracic Society/European Respiratory Society (ATS/ERS) recommends the use of statistically derived lower limit of normal (LLN) values for FEV_1/VC that are based on the normal distribution and that classify the bottom 5% of the healthy population as abnormal.²¹ This is particularly important in patients with HF, given that HF is most prevalent among elderly individuals.²² Thus, a COPD prevalence of 30–44% may have been overestimated in prior studies that used a fixed ratio of 0.7 to define COPD in patients with HF.^{3–7} Subsequently, an incorrect diagnosis of COPD may result in unnecessary treatment for COPD and undertreatment with beta-blockers, with possible adverse health effects.^{8,23,24}

Although population-based studies have shown that the application of different criteria to define airflow obstruction dramatically changes the prevalence of COPD,^{18,25–30} it is less well understood to what extent this occurs in patients with chronic HF.^{6,7} Therefore, the primary aim of this study was to determine COPD prevalence according to two definitions of airflow obstruction (FEV_1/FVC < 0.70 versus FEV_1/FVC < LLN) in outpatients with stable chronic HF with left ventricular systolic dysfunction (LVSD). The secondary aim of this study was to determine whether patients potentially misclassified as having COPD (FEV_1/FVC < 0.7 but > LLN) had clinical features of COPD or those of the healthy population.

Methods

Study design and participants

All patients visiting two outpatient cardiology departments of a large general hospital in The Netherlands were screened for inclusion in this prospective observational study between October 2009 and December 2010. In addition, existing patient lists were used to ensure that the majority of the HF population had been examined for eligibility. Inclusion criteria were stable chronic HF with LVSD, i.e., LVEF < 40%, without pulmonary congestion, New York Heart Association (NYHA) class I–IV, and age \geq 18 years. Chronic HF was defined according to the European Society of Cardiology guidelines.²² Echocardiography was performed in patients without a recent (\leq 6 months) echocardiography to confirm persisting LVSD. Patients were classified as having stable HF in the absence of hospitalization due to progression of HF within 3 months, change in diuretics within 1 month, 3% or more weight gain within 3 days, and more than 50% increase of N-terminal pro-B natriuretic peptide (NT-pro-BNP) within 1 month when the baseline NT-pro-BNP was 100 pmol/L or higher or more than 100 pmol/L increase of NT-pro-BNP within 1 month when the baseline NT-pro-BNP was below 100 pmol/L.³¹ Pulmonary congestion was evaluated on standard posterior–anterior and lateral chest radiographs for the presence or absence of alveolar edema, pleural effusion, Kerley-B lines, and/or the redistribution of pulmonary blood flow by independent radiologists who qualitatively assessed the chest radiographs with an overall clinical impression. Patients who were not able to cooperate or undergo spirometry or who had asthma according to their medical chart were excluded. Other exclusion

criteria were malignancy with a poor prognosis (survival < 6 months) and participation in another study. Patients who had been hospitalized in the pulmonary department in the past 6 weeks were included 6 weeks after discharge to ensure that their pulmonary function was stable at the time of spirometry testing.

In conformity with the ethical guidelines of the 1975 Declaration of Helsinki, this study was conducted with the approval of the regional Research Ethics Committee Arnhem-Nijmegen in The Netherlands (2009/101, NL27798.091.09, ClinicalTrials.gov Identifier NCT01429376). All patients gave written informed consent.

Measurements and data collection

At baseline, a first blood sample was taken for the measurement of NT-pro-BNP according to standard methods used in the hospital laboratory. One month later, the participants visited the hospital for an interview with the investigator and several examinations, including height and weight measurement, spirometry, and a chest radiograph. In addition, a second blood sample (NT-pro-BNP) was taken to determine the stability of HF. A 10-point Borg score³² was used to evaluate dyspnea at rest. Additional data were collected from medical records and personal interviews. Arterial blood gas analysis was performed on patients with severe airflow obstruction to determine whether they had chronic respiratory failure.²

Patients with newly diagnosed COPD according to either definition were followed up 3 months after standard treatment for COPD with once-daily 18 μ g tiotropium. A third blood sample (NT-pro-BNP) was taken, and spirometry was repeated to confirm persistent airflow obstruction characteristic of COPD in an attempt to exclude asthma as much as possible. Thus only patients with persistent airflow obstruction on 3 months of follow-up were classified as having COPD.

Spirometry testing

Spirometry (MasterLab Pro; Jaeger; Würzburg, Germany) was performed by trained and certified operators using standard techniques and according to ERS standards for acceptability and reproducibility.³³ The reference values of the European Community for Coal and Steel were used.³³ Subjects with airflow obstruction according to either definition underwent post-bronchodilator spirometry 30 min after inhalation of four doses of 100 μ g aerosolized salbutamol and four doses of 20 μ g aerosolized ipratropium via Volumatic spacer. Participants were instructed not to take bronchodilators 6–24 h before the tests, depending on the type of bronchodilator used. At follow-up, salbutamol and ipratropium were used, as previously described, when patients discontinued the use of tiotropium >24 h prior to spirometry. Care was taken to match the timing of the second spirometry testing to the first to reduce variations that may occur over a 24-h period.

Definitions

COPD was defined according to two criteria: post-bronchodilator FEV_1/FVC < 0.7 (GOLD-COPD)² and post-bronchodilator FEV_1/FVC < LLN (LLN-COPD).²¹ LLN was regarded as the lower fifth percentile of the frequency distribution of a healthy reference population and was calculated by subtracting 1.64 times the residual standard deviation from the predicted value. The investigator who identified the GOLD or LLN criteria was not blinded to the other rating.

Smoking status was defined as never (<100 cigarettes in a lifetime), former (\geq 3 months ago), or current smoker (<3 months). Smoking pack-years (PY) were based only on the tobacco cigarette

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