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COPD in patients with stable heart failure in the primary care setting

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Background: Presence of chronic obstructive pulmonary disease (COPD) in heart failure (HF) has prognostic and therapeutic implications. Exact prevalence estimates are lacking because most previous studies estimated the prevalence of COPD among HF patients while unstable and in the presence of pulmonary congestion.

Methods: Community-dwelling patients with an established diagnosis of HF and in a stable phase of their disease were invited for spirometry. COPD was defined according to the Global initiative for chronic Obstructive Lung Disease (GOLD) classification and considered present if the ratio of the post-bronchodilator forced expiratory volume in 1 second and forced vital capacity was below 0.7.

Results: Thirty of the 106 patients with HF (mean age 76 [standard deviation] 11.9 years, 57% male) had COPD (prevalence 28.3% [95% confidence interval (CI) 19.7%–36.9%]), with similar rates among those with HF and a reduced ejection fraction (18 individuals; prevalence 28.6% [95% CI 20.0%–37.2%]) and HF with preserved ejection fraction (12 individuals; prevalence 27.9% [95% CI 19.4–36.4]). Twenty-one (70%) of the 30 participants were newly detected cases of COPD.

Conclusion: More than a quarter of the patients with HF concomitantly have COPD, with the large majority being previously unrecognized. Coexistence of COPD should be considered more often in these patients.

Keywords: heart failure, COPD, prevalence, comorbidity, spirometry, diagnosis, primary care

Introduction

Heart failure (HF) and chronic obstructive pulmonary disease (COPD) are both common in the elderly, and often coexist.[1] Diagnosing COPD in HF is challenging because clinical features overlap, and dyspnea and fatigue are common symptoms.[1,2] Both share smoking as an important risk factor, and they have a chronic progressive disease trajectory with systemic effects, and require complex treatment regimens.[3–5] The prognosis of patients with both disorders is worse than those with only one of the diseases.[6,7] Importantly, bronchodilators may improve symptoms of COPD, but possibly cause cardiac side effects.[8,9] Under-diagnosis of one disease in the presence of another is an important issue,[10,11] but also there is a risk of over-diagnosing COPD in patients with HF if these patients are not stable and have some pulmonary congestion.[12] Pulmonary congestion is common in those hospitalized for an exacerbation of HF, and this may mimic COPD clinically, but also spirometrically. Spirometry at discharge in that situation would show – caused by pulmonary congestion – a larger reduction in forced expiratory volume in 1 second (FEV_1) than in forced vital capacity (FVC), resulting in a risk of over-diagnosing COPD.[13,14] When patients with HF are stable and euvolemic, the FEV_1/

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FVC allows to adequately detect COPD, although, both the FEV_1 and the FVC are reduced to a similar extent.[15] Diagnosing COPD at the right moment is therefore key in patients with HF.

Earlier reports on the prevalence of co-morbid COPD in HF often relied on previous documentation of COPD, or on spirometry results performed in HF patients when unstable.[10,16,17] Prevalence estimates ranged from 9% to 52%.[2] Data in a representative sample of patients with HF in a stable phase of their disease, also including patients with preserved ejection fraction (PEF), are still lacking.[1]

The aim of our study was to provide a valid prevalence estimate of COPD in a representative sample of patients with HF while in a stable condition (ClinicalTrials.gov identifier NCT01662323).

Methods

Design and study population

In a cross-sectional study we enrolled patients from 30 general practices from the vicinity of Amersfoort, the Netherlands. The study and recruitment period was from November 2010 until October 2011. In total 70,000 persons were enlisted in these practices. In the Netherlands all citizens are registered with a general practitioner (GP), irrespective of cooperative care by a hospital specialist, including those living in a home for the elderly, but excluding those living in a nursing home or hospice. Patients were eligible if they had a diagnosis of HF confirmed by an expert panel consisting of two cardiologists and a GP specializing in HF using all diagnostic information, including echocardiography. The panel based the diagnosis of HF on the criteria of the European Society of Cardiology, that is, suggestive symptoms and objective evidence of cardiac structural or functional cardiac abnormality related to ventricular dysfunction at rest detectable with echocardiography. For HF with reduced ejection fraction (HF-REF) the left ventricular ejection fraction should be $<45\%$. For HF with preserved ejection fraction (HF-PEF) the left ventricular ejection fraction should be $\geq 45\%$, in addition to diastolic dysfunction identified by echocardiography.[18] Disagreement between panel members was resolved by majority. We invited 236 patients with a confirmed diagnosis of HF for spirometry, and 121 (51.2%) consented to participate (Figure 1).

The study was approved by the Regional Medical Ethics Committee of the Meander Medical Center, Amersfoort, the Netherlands. All participants gave written informed consent.

Measurements

Between November 2010 and June 2011 baseline characteristics of the participants were extracted from the medical files of the participating GPs. Participants underwent spirometry in the primary care setting performed by trained personnel. Spirometry was performed with SPIDA software (Spida 5) and microloop. Before and after 400 micrograms of salbutamol, the FVC and FEV_1 were measured. COPD was considered present if the post-bronchodilator FEV_1/FVC ratio was below 0.7, as defined by the Global initiative for chronic Obstructive Lung Disease (GOLD) criteria.[5] Severity of pulmonary obstruction was expressed as the proportion of the predicted FEV_1 (the latter based on "normal" values as derived from the population at large with the same age, sex, and height) and derived from the forced spirometry.[19] The FEV_1 as percentage predicted was subdivided into four categories: ≥ 80, 50–79, 30–49, ≤ 30. The quality of the flow-volume curves was assessed by an experienced physician.

Data analysis

We compared HF patients who decided to participate with nonparticipants. In the participants we compared those with and without COPD. In those with COPD, we compared "already known" with "newly detected". Finally, we compared patients with HF-REF and HF-PEF. Differences between groups were assessed with the chi-square or Fisher's exact tests for categorical variables, and independent student's *t*-test for continuous variables. The prevalence of COPD was calculated with the binominal 95% confidence intervals (95% CIs). All data were analyzed with SPSS version 20.0.

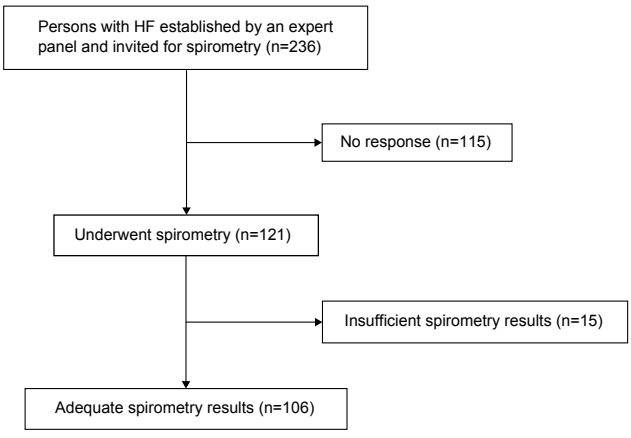

Figure 1 Flow diagram.
Abbreviation: HF, heart failure.

Results

Two-hundred and thirty-six patients with established HF were invited for spirometry. Baseline characteristics of the participants (n=121) were not significantly different from the nonparticipants (n=115) (Table S1). In 15 patients spirometry results were of insufficient quality, leaving 106 for this analysis (Figure 1). The mean age of the 106 participants was 76.0 (standard deviation [SD] 11.9) years, and 57% were male. The prevalence of COPD was 28.3% (95% CI 19.7%–36.9%), with similar rates for those with a REF (28.6% [95% CI 20.0%–37.2%]) and PEF (27.9% [95% CI 19.4%–36.4%]).

Table 1 shows patient characteristics of all 106 patients. On average, patients with COPD were older than those without COPD. Mean FEV_1 % predicted was 65.8 (SD 19.5) and 73.9 (SD 10.9) for those with newly detected COPD and without COPD, respectively. Seventy percent of the subjects with COPD was previously undiagnosed by their GP. None of the patients with COPD had a history of asthma. Table 2 shows the patient characteristics of newly detected cases vs HF patients without COPD. In Table 3 we compared patients with HF-REF and HF-PEF. The mean post-dilator FEV_1 % predicted was approximately 80% for both HF-REF and HF-PEF patients. Patients with HF-REF were more often male than those with HF-PEF.

Discussion

In our study among stable community-dwelling HF patients the prevalence of COPD was 28.3%, and in 70% this was a new diagnosis of COPD. Prevalence rates were comparable for the subgroups of HF-REF and HF-PEF.

Table 1 Characteristics of the 106 patients with established heart failure divided into those with and without newly detected, or already known COPD

Characteristics	Total (n=106)	Newly detected COPD (n=21)	Known COPD (n=9)	No COPD (n=76)
Mean age in years (SD)	76.0 (11.9)	76.9 (11.7)	76.4 (10.9)	75.8 (12.2)
Male sex	60 (56.6)	14 (66.7)	9 (100.0)	37 (48.7)
HF-REF	63 (59.4)	12 (57.1)	6 (66.7)	45 (59.2)
HF-PEF	43 (40.6)	9 (42.9)	3 (33.3)	31 (40.8)
Mean FVC as % predicted (SD)	86.4 (21.0)	83.5 (16.8)	95.6 (14.5)	86.3 (24.0)
Mean FEV_1 as % predicted (SD)	79.6 (22.1)	65.8 (19.5)	73.9 (10.9)	88.9 (22.8)
Mean FEV_1/FVC (SD)	74.5 (11.8)	60.2 (9.8)	58.0 (5.7)	78.3 (14.3)
Smoking*				
Current	43 (47.3)	8 (47.1)	1 (14.3)	34 (50.8)
Former	37 (40.7)	9 (52.9)	5 (71.4)	23 (34.3)
Never	11 (12.0)	0 (0.0)	1 (14.3)	10 (14.9)
Co-morbidities				
Hypertension	55 (51.9)	12 (57.1)	4 (44.4)	39 (51.3)
Diabetes mellitus	28 (26.4)	2 (9.5)	2 (22.2)	24 (31.6)
Prior myocardial infarction	35 (33.0)	9 (42.9)	4 (44.4)	22 (28.9)
Cardiovascular medication				
Diuretics	75 (70.8)	13 (61.9)	5 (55.6)	57 (75.0)
ACE-i or ARB	67 (63.2)	15 (71.4)	4 (44.4)	49 (63.6)
β-blockers	55 (51.9)	11 (52.4)	6 (66.7)	38 (50.0)
Mineralocorticoid receptor antagonists	35 (33.0)	2 (9.5)	1 (11.1)	32 (42.1)
Pulmonary medication:				
Inhaled beta-mimetics				
Short-acting	9 (8.4)	4 (19.0)	1 (11.1)	4 (5.3)
Long-acting	13 (12.1)	3 (14.3)	4 (44.4)	6 (7.9)
Inhaled anticholinergics				
Short-acting	10 (9.3)	1 (4.8)	2 (22.2)	7 (9.2)
Long-acting	3 (2.8)	0 (0.0)	3 (33.3)	0 (0.0)
Corticosteroids				
Oral	3 (2.8)	1 (4.8)	2 (22.2)	0 (0.0)
Inhaled	14 (13.1)	4 (19.0)	4 (44.4)	6 (7.9)

Notes: Numbers are cases (%) unless mentioned otherwise. *Data on smoking were missing in 15 patients.

Abbreviations: COPD, chronic obstructive pulmonary disease; SD, standard deviation; HF-REF, heart failure with reduced ejection fraction; HF-PEF, heart failure with preserved ejection fraction; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 second; ACE-i, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker.

Our results are in line with previous studies reporting prevalence rates of 9%–52% in patients with HF.[2] These previous studies were performed in hospitalized patients with an over-representation of HF-REF, and spirometry was performed while these patients were recently pulmonary fluid overloaded. We could therefore provide a more valid point estimate of the COPD prevalence of the HF population at large than previous studies. A recent study among 118 elderly patients with stable HF and a smoking history of ≥10 pack years also showed a prevalence rate of 30% of COPD, similar to our study, and also a similarly high number of newly detected cases of COPD (64%).[20] In this study COPD was also defined according to the GOLD criteria. Moreover, patients were investigated while stable, approximately 3 months after being hospitalized for HF. Separate prevalence rates for HF-REF and HF-PEF, however, were lacking.[20]

The prevalence of COPD in patients with HF in our study is approximately 1.5 times higher than the expected estimate of 20% in elderly from the population at large.[21]

We found that the post-bronchodilator FEV_1 in patients with HF was on average 80% of predicted in patients with the same age and length. This is in line with a previous study showing that HF in the absence of COPD may cause a reduction in FEV_1 of approximately 20%, caused by HF itself.[15] Thus, classifying severity of COPD based on FEV_1 % predicted may overestimate the severity of obstruction in patients with HF. Because both FVC and FVC as % predicted are reduced approximately 20%, the ratio FEV_1/FVC is not affected.[15]

Table 2 Characteristics of the patients with heart failure and a new diagnosis of COPD vs those without COPD

Characteristics	Newly diagnosed COPD (n=21)	No COPD (n=76)	*P*-value
Mean age	76.9 (11.7)	75.8 (12.2)	0.71
Male sex	14 (66.7)	37 (48.7)	0.14
HF-REF	12 (57.1)	45 (59.2)	0.87
HF-PEF	9 (42.9)	31 (40.8)	0.87
Smoking			
Current	8 (47.1)	34 (50.8)	0.59
Former	9 (52.9)	23 (34.3)	0.28
Never	0 (0)	10 (14.9)	0.79
Cardiovascular medication			
Diuretics	13 (61.9)	57 (75.0)	0.24
ACE-i or ARB	15 (71.4)	48 (63.2)	0.48
β-blocker	11 (52.4)	38 (50.0)	0.85
Mineralocorticoid receptor antagonist	2 (9.5)	32 (42.1)	0.006

Notes: Numbers are cases (%) unless specified otherwise. Data on smoking were missing in 13 patients.

Abbreviations: COPD, chronic obstructive pulmonary disease; HF-REF, heart failure with reduced ejection fraction; HF-PEF, heart failure with preserved ejection fraction; ACE-i, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker.

Table 3 Characteristics and spirometry results of the 106 patients with established HF, divided in those with HF-REF and HF-PEF

Characteristics	HF-REF (n=63)	HF-PEF (n=43)	*P*-value
Mean age in years (SD)	73.1 (13.0)	80.4 (8.4)	0.001
Male sex	38 (60.3)	22 (51.2)	0.35
Confirmed COPD	18 (28.6)	12 (27.9)	0.94
Spirometry results			
Mean FVC as % predicted	85.9 (SD 22.9)	87.3 (SD 21.4)	0.77
Mean FEV_1 as % predicted	79.2 (SD 21.4)	80.3 (SD 23.7)	0.82
FEV_1 as % predicted			
≥80	7 (11.1)	3 (7.0)	0.48
50–79	9 (14.3)	7 (16.3)	0.78
30–49	2 (3.2)	2 (4.7)	0.70
<30	0 (0)	0 (0)	1.0
Cardiovascular medication			
Diuretics	41 (65.1)	34 (79.1)	0.12
ACE-i or ARB	45 (71.4)	22 (51.2)	0.03
β-blockers	35 (55.6)	20 (46.5)	0.36
Mineralocorticoid receptor antagonists	20 (31.7)	15 (34.9)	0.73

Note: Numbers are cases (%) unless specified otherwise.

Abbreviations: HF, heart failure; COPD, chronic obstructive pulmonary disease; SD, standard deviation; HF-REF, heart failure with reduced ejection fraction; HF-PEF, heart failure with preserved ejection fraction; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 second; ACE-i, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker.

A strength of our study is the inclusion of a representative sample of patients with HF in a stable phase of their disease, and we could present prevalence rates for patients with HF-REF and HF-PEF separately.

A limitation is the relatively small sample size and the lack of body box measurements. Measurements of the total lung capacity and the residual volume would have been helpful to refine the diagnosis of COPD, especially in cases with spirometry results around the critical cut-off point of FEV_1/FVC 0.7.[22] Importantly, however, previous studies reporting on the prevalence of COPD in HF did not apply pulmonary function tests other than spirometry. Recently, some authors advocated age- and sex-related thresholds for the FEV_1/FVC lower limit of normal to define COPD.[19] We did not use one of the suggested lower limit of normal methods, because application in our study would reduce the possibility to compare our results with previous studies. Finally, some COPD cases may in fact represent persistent asthma, or "mixed cases", however, none of the COPD cases in earlier years had been labeled with asthma by the GP. We therefore preferred to use the GOLD-definition for COPD (a FEV_1/FVC <0.7). Knowledge of co-morbid COPD in patients with HF has clinical implications because for the management of breathlessness there is room for pulmonary inhalation drugs. We have, however, realized that some

authors suggest that both beta-mimetics and anti-muscarinic agents may harm the heart. HF drugs may be prescribed in patients with COPD, including cardio selective β-blockers. It is, however, important to uptitrate slowly.[23]

Conclusion

COPD is common in patients with HF, both HF-REF and HF-PEF, and remains undetected in the majority of patients. Selective screening of patients with HF when in a stable phase of their disease should be considered.

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Author contributions

FHR conceived the study idea. AWH, FHR, AM, and MJV designed the study. MJV did the data acquisition, and MJV, BDB, and NPZ did the statistical analysis. MJV, and BDB drafted the manuscript and all authors contributed to the revision of the manuscript. FHR supervised the study and is guarantor of the study.

Disclosure

The authors report no conflicts of interest in this work.

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Supplementary material

Table S1 Characteristics of the 236 patients with established heart failure who were invited for spirometry, divided into participants and nonparticipants

	Participants (n=121)	Nonparticipants (n=115)	*P*-value
Male sex	46.3	55.7	0.15
Mean age in years (SD)	77.0 (11.4)	76.6 (11.9)	0.91
Hypertension	56.7	53.0	0.63
Diabetes mellitus	30.6	26.1	0.44
Prior myocardial infarction	33.1	32.2	0.89
Angina pectoris	22.3	13.0	0.06
Atrial fibrillation	54.5	50.4	0.53
eGFR <60 mL/m^2	38.8	37.4	0.82
Medication			
Diuretics	84.3	73.0	0.03
ACE-i	54.5	52.2	0.72
β-blocker	59.9	52.2	0.29
Digoxin	24.0	21.7	0.68

Note: Numbers are cases (%) unless specified otherwise.

Abbreviations: SD, standard deviation; eGFR, estimated glomerular filtration rate according to the modification of diet in renal diseases formula; ACE-i, angiotensin converting enzyme inhibitor.