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Clinical research

Unrecognized heart failure in elderly patients with stable chronic obstructive pulmonary disease

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Aims To establish the prevalence of unrecognized heart failure in elderly patients with a diagnosis of chronic obstructive pulmonary disease, in a stable phase of their disease.
Methods and results In a cross-sectional study, patients ≥65 years of age, classified as having chronic obstructive pulmonary disease by their general practitioner and not known with a cardiologist-confirmed diagnosis of heart failure, were invited to our out-patient clinic. Four hundred and five participants underwent an extensive diagnostic work-up, including medical history and physical examination, followed by chest radiography, electrocardiography, echocardiography, and pulmonary function tests. As reference (i.e. 'gold') standard the consensus opinion of an expert panel was used. The panel based the diagnosis of heart failure on all available results from the diagnostic assessment, guided by the diagnostic principles of the European Society of Cardiology (ESC) for heart failure (i.e., symptoms and echocardiographic systolic and/or diastolic dysfunction). The diagnosis of chronic obstructive pulmonary disease was based on the diagnostic criteria of the Global Initiative (GOLD) for chronic obstructive pulmonary disease. Of 405 participating patients with a diagnosis of chronic obstructive pulmonary disease, 83 (20.5%, 95% CI 16.7–24.8) had previously unrecognized heart failure (42 patients systolic, 41 'isolated' diastolic, and none right-sided heart failure). In total, 244 (60.2%) patients had chronic obstructive pulmonary disease according to the GOLD criteria and 50 (20.5%, 95% CI 15.6–26.1) patients combined with unrecognized heart failure.
Conclusion Unrecognized heart failure is very common in elderly patients with stable chronic obstructive pulmonary disease. Closer co-operation among general practitioners, pulmonologists, and cardiologists is necessary to improve detection and adequate treatment of heart failure in this large patient population.

Introduction

Heart failure and chronic obstructive pulmonary disease are both common diseases in the elderly.[1,2] They have an important impact on quality of life and functional status, show high morbidity and mortality rates, and lead to considerable health-care costs. Although both diseases have been studied extensively, information about the prevalence of heart failure in stable chronic obstructive pulmonary disease patients is lacking.

The diagnosis of heart failure is fraught with difficulties, notably in the early phases of the syndrome and in the presence of certain co-morbidities. This is particularly true for chronic obstructive pulmonary disease, as recognition of heart failure in these patients is hampered by similarities in signs and symptoms. Importantly, co-existence of chronic obstructive pulmonary disease and heart failure is plausible in view of overlap in risk factors, notably smoking. Echocardiography is essential for establishing the diagnosis of heart failure. Accessibility to this diagnostic facility, however, is limited for primary care patients, and echocardiography is not part of the standard investigational protocol of pulmonologists.

It seems therefore plausible that a considerable proportion of patients with a diagnosis of chronic obstructive pulmonary disease have concomitant heart failure, which remains unrecognized by primary care physicians or pulmonologists. In addition, due to similarities in symptoms, some chronic obstructive pulmonary disease patients may be misclassified and in fact have heart failure.

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Earlier studies suggested that the use of pulmonary medication often coincides with unrecognized heart failure,[3,4] and that the prevalence of heart failure can be as high as 20–30% in those chronic obstructive pulmonary disease patients who are referred for an acute exacerbation.[5,6] However, information is lacking on the prevalence of heart failure in the much larger population of patients with stable chronic obstructive pulmonary disease.

We assessed the prevalence of unrecognized heart failure in elderly patients, who were in a stable phase of their disease, diagnosed as chronic obstructive pulmonary disease by their general practitioner.

Methods

Participants

Fifty-one primary care practices, located in the vicinity of Utrecht, The Netherlands, agreed to participate in this study executed between April 2001 and June 2003. In total, 14 069 subjects aged 65 or over were registered within these practices, which routinely register patient contacts electronically.[7] In this sample of primary care practices, inner-city, urban, suburban, and rural communities are represented. All patients aged 65 or over with an International Classification of Primary Care (ICPC) code R91 (chronic bronchitis) or R95 (chronic obstructive pulmonary disease or emphysema) were eligible.[8] These ICPC codes are based on symptoms (dyspnoea, cough, or sputum production) and in the case of R95, additionally on pulmonary changes on the chest radiograph.[8] Identification of eligible subjects from the computerized patient files of the general practitioners was performed by a single general practitioner (F.H.R.), using a standardized extraction form. In total, 1716 patients met these criteria. In 98 (5.7%) patients, heart failure had already been diagnosed, that is, heart failure confirmed by a cardiologist, with evidence of left ventricular dysfunction from echocardiography. Because we were interested in the prevalence of previously unrecognized heart failure, these 98 patients were excluded. Another 432 (25.2%) patients were excluded because of severe psychiatric disorders, immobility, or terminal illness. In total, 1186 patients were invited by a letter signed by their own general practitioner and 405 (34%) patients agreed to participate. The most often mentioned reasons for not participating were a recent check-up by a specialist and time involved in the diagnostic program. In none of these patients was suspected heart failure the reason for the recent specialist check-up. Of all 1716 subjects, patient characteristics were extracted anonymized from the computerized patient files of the general practitioners, with special attention for cardiovascular diseases and co-morbidity.

The Institutional Review Board of the University Medical Center Utrecht, The Netherlands, approved the study protocol and all participants gave written informed consent.

Diagnostic procedures

Each of the 405 participants was investigated during a single 3 h session at our out-patient department. A standardized questionnaire was administered to participants to obtain additional information on complaints and smoking habits. Present medication use was asked and checked (participants had to take medication boxes with them). Presence of angina pectoris and shortness of breath was assessed by means of the World Health Organisation (WHO) questionnaires.[9] Data on co-morbidities were acquired by scrutinizing the computerized data files of the participating general practitioners, including available letters from hospital specialists.

Body-mass index was calculated as weight (kg)/height (m^2). A standardized physical examination was carried out by F.H.R. A standard 12-lead electrocardiogram (ECG) was recorded and classified according to the Minnesota coding criteria,[9] by a single cardiologist (M.-J.M.C.). Postero-anterior and lateral plane chest radiographs were taken in standing position according to standard radiological criteria and described by one of three radiologists, who was blinded to clinical data. Blood samples were taken and analysed the same day, and after centrifugation specimens of serum and plasma were stored at $-70^{\circ}C$.

Cardiac function

Echocardiographic studies were performed using a Philips Sonos 5500 imaging system (Andover, MA, USA) by two cardiac sonographers. All echocardiographic images were interpreted by M.-J.M.C., who was blinded to clinical data. Parameters from Doppler analysis, M-mode echocardiography, and 2D transthoracic echocardiography were used. Where image quality was sufficient, the left-ventricular ejection fraction (LVEF) was calculated from the endocardial surface tracings in the apical four-chamber view and two-chamber view, using Simpson's rule (disc summation method).[10] Alternatively, the endocardial surface of the left ventricle was traced at end-systole and end-diastole. The ejection fraction was then calculated using the single plane area-length method.[11]

In 185 patients, ejection fraction could be assessed by one of these quantitative methods. In the remaining 219 patients, left-ventricular systolic function was assessed semiquantatively by the 2D visual estimate method ('eyeballing').[12] The accuracy of this visual method has been validated previously.[13] In 42 (10.4%) patients, echocardiographic view was of poor quality. In one patient, the image quality did not allow any estimation of LVEF. Valve regurgitation was graded semiquantitatively, and in case of aortic stenosis the pressure gradient was assessed. Left atrial volume was assessed by the biplane area–length method from apical four- and two-chamber views.[14] The normal value was indexed for body surface area. As cut-off values for normal and definitely increased left atrial volume index, 28 and 32 mL/m^2 were used, respectively.[14,15] With pulsed-wave Doppler echocardiography, mitral inflow, and pulmonary venous inflow were assessed. From the mitral inflow profile, the E- and A-wave velocity and E-deceleration time were measured and E/A velocity ratio was calculated. The flow velocities of the left or right upper pulmonary vein were recorded, and the ratio of systolic to diastolic forward flow was calculated. Diastolic function was categorized as normal, impaired relaxation (grade I), pseudonormal filling (grade II), or restrictive filling (grade III) by a combination of transmitral and pulmonary flow patterns and left atrial volume indexes.[16–18] (Appendix).

We measured the peak velocity of the tricuspid regurgitant signal with continuous-wave Doppler and calculated the systolic pulmonary artery pressure with the modified Bernoulli's equation.[19]

Pulmonary function

A fixed-volume body plethysmograph (Masterlab Jaeger, Würzburg, Germany) was used to measure lung volumes and airway resistance, and a Masterscreen for measuring alveolar volume and diffusion capacity of the lung for carbon monoxide using a single-breath method. In the analysis, the choice of the best test out of three was based on the highest sum of forced expiratory volume in 1 s (FEV1) and forced vital capacity (FVC).[2] A bronchodilator reversibility test was performed by inhalation of two puffs of 20 μg ipatropium bromide by an inhalation chamber. Measurements were performed after an interval of at least 30 min. Baseline spirometric measurement was performed in all patients. In five (1.2%) patients, we were not able to perform post-dilatory spirometric measurements or body box measurements. CO-diffusion could not be assessed in 42 (10.4%) patients because of low values of FEV1.

Table 1 Characteristics of patients aged ≥65 with a general practitioner's diagnosis of chronic obstructive pulmonary disease

Characteristics	Participants ($n = 405$)	Non-responders ($n = 781$)	Excluded patients ($n = 530$)	
			Severe psychiatric disorder, immobility, or terminal illness ($n = 432$)	Documented heart failure ($n = 98$)
Mean (SD) age in years	73.0 (5.3)	74.9 (7.8)	77.5 (7.0)	76.9 (6.2)
Male	55.1	53.8	40.7	62.2
Ischaemic heart disease[a]	20.2	24.3	23.6	50.0
Hypertension	35.8	37.3	41.4	48.0
Diabetes mellitus	10.4	12.8	14.4	24.5
Stroke/TIA	5.2	7.2	13.2	14.3
Atrial fibrillation	8.4	9.1	11.6	51.0
Valvular disease	3.5	4.7	4.2	29.6
Peripheral arterial disease	6.9	6.5	6.9	15.3
Thyroid disease	3.7	5.3	4.0	6.1

Values are in per cent unless stated otherwise.
TIA = transient ischaemic attack.
[a]Ischaemic heart disease = prior myocardial infarction, angina pectoris, coronary artery bypass grafting or percutaneous coronary intervention.

Diagnostic criteria

Heart failure was assessed by an expert panel of two cardiologists, a pulmonologist, and a general practitioner. The panel used all available diagnostic information, including echocardiography and pulmonary function tests. First, the panel classified heart failure as definite, probable, or no heart failure. For those with definite or probable heart failure, the most probable cause of heart failure according to the panel was notified. As a guide, the panel used the diagnostic principles formulated by the ESC, that is, symptoms of heart failure and objective evidence of cardiac dysfunction.[1] Importantly, objective evidence of cardiac dysfunction in our study was defined as echocardiographic ventricular (systolic and/or diastolic) dysfunction. Systolic heart failure was defined as the presence of symptoms in combination with an LVEF ≤45%. 'Isolated' diastolic heart failure was defined as echocardiographic diastolic dysfunction (grade I, II, or III) (Appendix) in combination with LVEF >45%. These echocardiographic parameters had to be present in combination with (i) symptoms and signs of heart failure[20] or (ii) symptoms and a combination of two of the following items: hypertension, echocardiographic left ventricular hypertrophy, atrial fibrillation, or anginal complaints.[21] Additionally, these symptoms and/or signs should not, or insufficiently, be explained by chronic obstructive pulmonary disease.[22] Right-sided heart failure was defined as signs of right-sided heart failure, LVEF >45%, and increased right atrial pressure, estimated from the respiratory variation in diameter of the caval vein and/or right-ventricular dysfunction assessed semiquantatively by the 2D visual estimate method ('eyeballing').

Presence of definite chronic obstructive pulmonary disease was assessed by the panel according to the recent GOLD criteria.[2,23] A spirometrically assessed ratio of a post-dilatory FEV1/FVC <70% confirmed the presence of definite chronic obstructive pulmonary disease, either with or without complaints compatible with chronic obstructive pulmonary disease (cough, dyspnoea, sputum production). Other pulmonary diseases were classified by the panel, using information from patient's history, pulmonary function tests, and chest radiography.

Data analysis

We calculated age- and sex-specific prevalence of heart failure. Prevalence estimates are given for 10 year age groups, and for men and women separately. Binomial confidence intervals (95%) were calculated for prevalence estimates. Prevalence was calculated as the number of cases of heart failure divided by the number of participants. Any data with a skewed distribution were summarized as medians with interquartile ranges. Data were analysed using SPSS Windows version 11.0 (SPSS Inc., Chicago, IL, USA).

Results

The mean age of the participants was 73.0 (SD 5.3), and 55% were male. Participants were comparable in cardiovascular co-morbidity to eligible non-responders and to those who were excluded because of severe psychiatric disorders, immobility, or terminal illness, although participants were somewhat younger (*Table 1*). Patients who were excluded because they were known with documented heart failure had much more cardiovascular co-morbities than participants.

In 83 patients, previously unrecognized heart failure was discovered (prevalence 20.5%, 95% CI 16.7–24.8). Of these patients, 33 had heart failure only, whereas in 50, heart failure and definite chronic obstructive pulmonary disease were both present. Of the 83 heart failure patients, 42 (50.6%) had systolic, 41 (49.4%) had 'isolated' diastolic, and none had right-sided heart failure. Of those with systolic heart failure, 32 (76.2%) had an LVEF ≤40% and 10 (23.8%) had an LVEF between 40 and 45%. Another 47 (11.6%) patients were classified as having possible heart failure by the expert panel: eight patients as having systolic, 37 as having 'isolated' diastolic, and two patients as having possible right-sided heart failure. In total, 130 (32.1%, 95% CI 27.6–36.9) patients were classified as having heart failure or possible heart failure by the panel. Age- and sex-specific prevalence data of systolic and diastolic heart failure are shown in *Table 2*. The overall prevalence of heart failure was somewhat higher in men. The prevalence of heart failure increased with age in women, but not in men. Systolic heart failure was most common in younger male patients, whereas 'isolated' diastolic heart failure was most common in elderly women.

Definite chronic obstructive pulmonary disease was diagnosed in 244 (61.2%) participants. In 194 patients, only chronic obstructive pulmonary disease was present and in

Table 2 Prevalence of systolic and 'isolated' diastolic heart failure by age and sex

	Systolic heart failure ($n = 42$)	'Isolated' diastolic heart failure ($n = 41$)	All heart failure ($n = 83$)
Males			
Age (years)			
65–74 ($n = 150$)	26 [17.3% (11.6–24.4)]	11 [7.3% (3.7–12.7)]	37 [4.7% (18.0–32.4)]
≥75 ($n = 73$)	9 [12.3% (5.8–22.1)]	5 [6.8% (2.3–15.3)]	14 [19.2% (10.9–30.1)]
All ages ($n = 223$)	35 [15.7% (11.1–21.1)]	16 [7.2% (4.2–11.4)]	51 [22.9% (17.5–28.9)]
Females			
Age (years)			
65–74 ($n = 112$)	4 [3.6% (1.0–8.9)]	7 [6.3% (2.5–12.5)]	11 [9.8% (5.0–16.9)]
≥75 ($n = 70$)	3 [4.3% (0.9–12.0)]	18 [25.7% (16.0–37.6)]	21 [30.0% (19.6–42.1)]
All ages ($n = 182$)	7 [3.8% (1.6–7.8)]	25 [13.7% (9.1–19.6)]	32 [17.6% (12.3–23.9)]
All males and females			
Age (years)			
65–74 ($n = 262$)	30 [11.5% (7.9–15.9)]	18 [6.9% (4.1–10.6)]	48 [18.3% (13.8–23.5)]
≥75 ($n = 143$)	12 [8.4% (4.4–14.2)]	23 [16.1% (10.5–23.2)]	35 [24.5% (17.7–32.4)]
All ages ($n = 405$)	42 [10.4% (7.6–13.8)]	41 [10.1% (7.4–13.5)]	83 [20.5% (16.7–24.8)]

Numbers with per cent and 95% CI.
Seven females and three males were aged ≥85.

Table 3 Baseline characteristics of 405 patients with a GP's diagnosis of chronic obstructive pulmonary disease

Characteristics	All patients ($n = 405$)	HF only ($n = 33$)	HF + COPD ($n = 50$)	COPD only ($n = 194$)	Neither ($n = 128$)
Demographic data					
Mean (SD) age in years	73.0 (5.3)	74.0 (5.9)	73.7 (5.3)	73.3 (5.0)	71.8 (5.6)
Male	55.1	45.5	72.0	67.5	32.0
Median (25th–75th percentile) pack years of smoking	14.5 (0.0–37.8)	9.6 (0.0–30.3)	27.0 (0.6–53.7)	22.7 (1.4–43.9)	0.75 (0.0–27.1)
History					
Ischaemic heart disease[a]	20.5	27.3	38.0	19.1	14.1
Hypertension	35.8	51.5	36.0	28.9	42.2
Diabetes mellitus	10.4	15.2	14.0	7.2	12.5
Signs and Symptoms					
Dyspnoea	96.5	97.0	100	98.5	92.2
Orthopnoea or PND	26.7	33.3	28.0	24.2	28.1
Fatigue	62.2	75.8	72.0	64.4	60.9
Heart rate (beats/minute)	76.5 (14.1)	76.5 (17.2)	82.4 (14.8)	76.0 (12.9)	74.9 (14.2)
BMI (kg/m^2)	26.7 (4.2)	29.3 (4.0)	27.2 (3.6)	25.6 (3.9)	27.4 (4.3)
Systolic blood pressure (mmHg)	151.7 (18.3)	153.2 (16.1)	150.1 (24.0)	150.9 (17.4)	153.2 (17.7)
Diastolic blood pressure (mmHg)	83.5 (10.4)	86.6 (8.7)	83.2 (13.0)	82.0 (10.2)	85.0 (9.5)

Values are in per cent, mean values (SD), or median (25th–75th percentile). COPD, chronic obstructive pulmonary disease; HF, heart failure; PND, paroxysmal nocturnal dyspnoea.
[a]Ischaemic heart disease: prior myocardial infarction, angina pectoris, coronary artery bypass grafting or percutaneous coronary intervention.

50 patients concomitant heart failure was present. Therefore, the prevalence of heart failure in definite chronic obstructive pulmonary disease was 20.5% (95% CI 15.6–26.1). Of the patients with neither heart failure nor chronic obstructive pulmonary disease, the following pulmonary diagnoses were established by the panel: persisting asthma (20 patients), bronchiectasis (four patients), scarring on chest radiograph due to tuberculosis (four patients), prior pulmonary embolism (two patients), and alveolitis (one patient).

In *Table 3*, demographic details are provided for participants with heart failure only, heart failure plus chronic obstructive pulmonary disease, chronic obstructive pulmonary disease only, or neither heart failure nor chronic obstructive pulmonary disease. Chronic obstructive pulmonary disease patients were more often males, with a higher

Table 4 Results of additional investigations of 405 patients with a general practitioner's diagnosis of chronic obstructive pulmonary disease

Additional measurements	All patients ($n = 405$)	HF only ($n = 33$)	HF + COPD ($n = 50$)	COPD only ($n = 194$)	Neither ($n = 128$)
Cardiothoracic ratio	0.48 (0.05)	0.52 (0.04)	0.49 (0.05)	0.46 (0.05)	0.49 (0.05)
Pulmonary fluid[a]	2.7%	9.1%	4.0%	1.0%	3.1%
Abnormal ECG[b]	35.3%	60.6%	64.0%	26.8%	30.5%
Myocardial infarction	31 (7.7%)	2 (6.1%)	13 (26.0%)	12 (6.2%)	4 (3.1%)
Left bundle branch block	63 (15.6%)	9 (27.3%)	18 (36.0%)	20 (10.3%)	16 (12.5%)
LVH	24 (5.9%)	1 (3.0%)	7 (14.0%)	10 (5.2%)	6 (4.7%)
Atrial fibrillation	22 (5.4%)	3 (9.1%)	5 (10.0%)	11 (5.7%)	3 (2.3%)
ST and/or T-wave changes	92 (22.7%)	14 (42.4%)	17 (34.0%)	33 (17.0%)	28 (21.9%)
Sinus tachycardia	9 (2.2%)	2 (6.1%)	4 (8.0%)	0 (0%)	3 (2.3%)
LVEF	57.2 (9.8)	48.9 (12.8)	45.1 (14.7)	59.6 (6.3)	60.6 (5.1)
FEV1/FVC ratio[c]	64.4 (14.2)	77.3 (5.4)	57.4 (10.4)	55.0 (10.8)	78.0 (6.0)

Values are in *n* (%), mean (SD). Cardiothoracic ratio, four missings (due to lobectomy); left ventricular ejection fraction one missing.

[a]Pulmonary fluid: pleural fluid, interlobular, alveolar or interstitial fluid, or redistribution on chest radiograph.

[b]Abnormal ECG: abnormal Q-waves fitting in the diagnosis of (prior) myocardial infarction, left bundle branch block (complete or incomplete), left ventricular hypertrophy (LVH), atrial fibrillation, ST and/or T-wave changes (non-specific or suggestive for myocardial ischaemia), and sinus tachycardia. More than one electrocardiographic diagnosis per patient is possible.

[c]FEV1/FVC ratio are post-dilatory values of the ratio of forced expiratory volume in 1 s and forced vital capacity. In five cases with missing post-dilatory values, pre-dilatory values were used.

number of pack years of smoking, although a history of ischaemic heart disease, hypertension, and diabetes mellitus were more prevalent in heart failure patients. Most participants in all four categories reported dyspnoea and fatigue. Apart from increased cardiothoracic ratio and decreased LVEF, ~60% of the patients with heart failure showed abnormalities on ECG (i.e. abnormal Q-waves, left bundle branch block, left ventricular hypertrophy, ST and/or T-wave changes, or sinus tachycardia). These ECG abnormalities were more common in heart failure patients than in those with chronic obstructive pulmonary disease only (*Table 4*). Of all participants, 148 (36.5%) patients had a normal ECG, whereas 16 (19.3%) patients with heart failure had a normal ECG. The 33 patients who were wrongly classified by their general practitioner as having chronic obstructive pulmonary disease, but were actually suffering from heart failure, were more often female than heart failure patients with concomitant chronic obstructive pulmonary disease. Half of these 33 patients had hypertension, and a third reported complaints of orthopnoea or paroxysmal nocturnal dyspnoea. They also reported less pack years of smoking and prevalence of chest radiographic abnormalities when compared with heart failure patients with concomitant chronic obstructive pulmonary disease.

According to the panel, ischaemic heart diseases were the most prominent possible causes for systolic heart failure, whereas hypertension, left ventricular hypertrophy, and atrial fibrillation were the most common possible causes for 'isolated' diastolic heart failure (*Table 5*). The number of patients with heart failure due to clinically significant valvular disease (3.6%) was low. Most heart failure patients were in New York Heart Association (NYHA) functional class II and III (*Table 5*).

Discussion

To our knowledge, this is the first study to show that unrecognized heart failure is very common (20.5%) in elderly patients with a general practitioner's diagnosis of chronic obstructive pulmonary disease, in a stable phase of their disease. Also, in patients with definite chronic obstructive pulmonary disease according to the GOLD-criteria [244 patients (61.2%)], the prevalence rate of unrecognized heart failure is 20.5%. None of the heart failure patients had right-sided heart failure, only two (0.5%) patients had possible right-sided heart failure. Inclusion of patients with established heart failure (who were not invited to participate) would yield an estimate of heart failure of 26% in unselected primary care chronic obstructive pulmonary disease patients in a stable phase of their disease. The prevalence of heart failure in stable chronic obstructive pulmonary disease patients is therefore about four times as high compared with subjects aged 65 or over in the population at large.[24]

Presence of chronic obstructive pulmonary disease is generally considered a complicating factor in the diagnostic assessment of patients suspected of having heart failure, but chronic obstructive pulmonary disease patients are not considered a high risk group for developing heart failure.[1] The reasons for the high prevalence of heart failure among chronic obstructive pulmonary disease patients we found in our study remain speculative, but the increased prevalence rates of atherosclerosis found in chronic obstructive pulmonary disease patients and the impressive smoking status of these patients are likely to be important, as both smoking and atherosclerosis are known risk factors for development of ischaemic heart disease and heart failure. Chronic obstructive pulmonary disease can also lead to (periods of) hypoxaemia and hypercapnia and to (periods of) pressure changes in the right ventricle and therefore increased wall stress in the interventricular septum, which may further promote heart failure. The lack of right-sided heart failure in our study is probably attributable to the fact that right ventricular contractility remains relatively normal in chronic obstructive pulmonary disease, even in the presence of pulmonary

Table 5 Possible causes of heart failure and NYHA classification according to the panel in 83 heart failure patients[a]

	Systolic heart failure ($n = 42$)	'Isolated' diastolic heart failure ($n = 41$)	All heart failure ($n = 83$)
Possible causes of heart failure			
Prior myocardial infarction	14 (33%)	2 (4.9%)	16 (19%)
Other ischaemic heart disease[b]	17 (41%)	7 (17%)	24 (29%)
Hypertension	13 (31%)	27 (66%)	40 (48%)
Left ventricular hypertrophy	2 (4.8%)	7 (17%)	9 (11%)
Atrial fibrillation	4 (9.5%)	6 (15%)	10 (12%)
Valvular disease	1 (2.4%)	2 (4.9%)	3 (3.6%)
NYHA Class			
NYHA I	1 (2.4%)	0 (0%)	1 (1.2%)
NYHA II	17 (40%)	12 (29%)	29 (35%)
NYHA III	18 (43%)	24 (49%)	42 (51%)
NYHA IV	6 (14%)	4 (9.8%)	10 (12%)

[a]The panel could adjudge more than one possible cause.
[b]Other ischaemic heart disease: angina pectoris, coronary artery bypass grafting or percutaneous coronary intervention.

hypertension,[25] and right-ventricular dysfunction may only occur in end-stage chronic obstructive pulmonary disease.[26]

A recent subgroup analysis of the Breathing Not Properly-study revealed a remarkably similar prevalence of previously unrecognized heart failure of 20.9% for patients (mean age 62) with a history of chronic obstructive pulmonary disease or asthma.[6] However, these patients were experiencing an exacerbation of their chronic obstructive pulmonary disease or asthma, urging them to visit an Emergency Department with acute dyspnoea. Moreover, the assessment of heart failure differed from our study. The diagnosis of heart failure was established by two cardiologists, using the Framingham and NHANES score as reference standard,[27] with echocardiographic information available only in 29% of the patients.

In our study, ~50% of all heart failure patients had 'isolated' diastolic heart failure, with higher prevalence rates in elderly women. These findings are comparable with findings in population-based studies.[28,29] Our findings that a history of myocardial infarction or other ischaemic heart disease were most often mentioned as possible cause for systolic heart failure, whereas hypertension, left ventricular hypertrophy, and atrial fibrillation were more often implicated in 'isolated' diastolic heart failure were in concordance with other studies.[1]

Because our study was restricted to elderly patients, we had to consider changes in echocardiographic parameters associated with ageing such as reduced early diastolic filling, increased late diastolic filling, and reduced myocardial diastolic velocities.[30,31] Also, we had to consider that Doppler measurements of diastolic function are influenced by loading conditions of the heart.[32] Because we studied patients in stable conditions, however, echocardiographic results were possibly less hampered by loading conditions. To optimize classification of 'isolated' diastolic heart failure, we added a combination of relevant clinical parameters to echocardiographic signs of diastolic dysfunction.[33] This may have influenced the expert panel in their allocation of the possible cause for heart failure in the individual patient.

Work-up bias (verification bias) was eliminated from our study, since all subjects underwent all diagnostic tests necessary to classify heart failure and chronic obstructive pulmonary disease. To prevent work-up bias, we also choose not to use clinical data of non-participants to establish presence or absence of heart failure, because these data were available in a minority of non-participants only.

The presence of heart failure was established by consensus evaluation, using all available diagnostic information.[29,34] This is an established method as reference standard, since a true 'gold' standard is lacking for assessing heart failure.[34] Moreover, earlier studies have shown that panel diagnosis in establishing heart failure was highly reproducible.[35] This method seems more valid than more easily applicable reference standards such as the Framingham score,[27] Boston score,[36] or NHANES score,[37] because these scores are only based on diagnostic information from signs and symptoms, ECG, and chest radiography, and do not include information from echocardiography. Because of overlapping signs and symptoms,[38,39] these scores may lead to an overestimation of the prevalence of heart failure in chronic obstructive pulmonary disease patients. The panel was guided by the ESC principles of heart failure (i.e. symptoms and objective evidence of cardiac dysfunction). Importantly, however, objective evidence of cardiac dysfunction was defined in our study as echocardiographical ventricular (systolic and/or diastolic) dysfunction. Therefore, patients with, for example, dyspnoea and atrial fibrillation or valvular disease, but with a normal ventricular function on echocardiography were not considered as heart failure patients in our study.

The response rate (34%) in our study may seem modest, but was only slightly lower than in population-based studies assessing heart failure in the elderly.[28,40] Because we invited diseased elderly patients in a stable phase of their disease (i.e. patients with a diagnosis of chronic obstructive pulmonary disease), and only excluded patients with severe psychiatric disease, immobility or terminal illness, lower response rates could be expected because many elderly patients with rather high levels of disability were invited. Although we, inevitably, studied a selection of available chronic obstructive pulmonary disease patients, selection bias in our prevalence estimates of unrecognized heart failure seems limited, because relevant and known

cardiovascular risk factors for heart failure and co-morbidities of participants were only slightly lower in participants than in non-responders and patients who were excluded because of severe psychiatric disorder, immobility, or terminal illness. Patients who were excluded because they were known with documented heart failure, however, had clearly increased cardiovascular co-morbidity compared with participants in our study. Because we were interested in the prevalence of unrecognized heart failure, differences in patient characteristics between patients excluded because of documented heart failure and participants, however, do not bias our prevalence estimation. In all, owing to this patient selection, the prevalence of unrecognized heart failure in the population of elderly chronic obstructive pulmonary disease patients at large is even somewhat higher than our estimate. Importantly, the clinical applicability of our results is high, we studied those patients who were able to undergo the relevant diagnostic investigations, and therefore, we studied those chronic obstructive pulmonary disease patients in whom treatment is likely to be initiated in everyday practice.

Although inadequate echocardiographic views can hamper diagnostic assessment especially in chronic obstructive pulmonary disease patients because their large thoracic cavities filled with air,[4] the image quality in our study was poor in only ~10% of the patients, and an estimation of LVEF was impossible in one single patient.

The high prevalence of unrecognized heart failure in stable chronic obstructive pulmonary disease patients in our study provides some evidence in favour of screening of this large group of patients. Although performing echocardiography in all elderly chronic obstructive pulmonary disease patients is not feasible, more easily applicable tests such as natriuretic peptide measurements could be helpful in the diagnostic assessment of stable chronic obstructive pulmonary disease patients. Natriuretic peptide measurements have already shown to be useful in the diagnostic assessment of patients suspected of heart failure,[34] in patients with acute dyspnoea,[41] and in patients with a history of pulmonary disease who experience acute dyspnoea.[6] However, the exact role of these measurements in the diagnostic process in stable chronic obstructive pulmonary disease patients, in addition to other easily available diagnostic information such as history, physical examination, and ECG, remains to be determined. We aim to study the additional diagnostic value of natriuretic peptides in our patient population, by analysing stored serum and plasma samples, but these data are not yet available.

In 32% of the patients, neither heart failure nor chronic obstructive pulmonary disease could explain the patient's complaints. This rather large proportion was due to the fact that our study focused on detecting heart failure and chronic obstructive pulmonary disease and not on investigating all possible causes for the complaints in these patients. Moreover, some of these patients had possibly heart failure, and 31 (7.7%) patients had other pulmonary diseases rather than chronic obstructive pulmonary disease, notably persisting asthma.

In conclusion, our findings support the view that unrecognized heart failure is very common in elderly patients with stable chronic obstructive pulmonary disease. Adequate treatment of heart failure, in particular in its early stages, may alleviate symptoms, delay progression, and improve prognosis.[1] Closer co-operation between general practitioners, pulmonologists, and cardiologists is necessary to optimize management of this large population of patients.

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Appendix

Doppler echocardiographic criteria used for classification of diastolic function

	Normal (elderly adults)	Impaired relaxation (grade I)
E/A (cm/s)	$0.75 < E/A < 1.5$	$E/A \leq 0.75$
DT (ms)	$150 < DT < 240$	≥ 240
IVRT (ms)	$60 < IVRT < 110$	≥ 110
S/D	≥ 1	≥ 1
LA volume Index (mL/m^2)	≤ 28	28–32
	Pseudonormal filling (grade II)	**Restrictive filling (grade III)**
E/A (cm/s)	$0.75 < E/A < 1.5$	$E/A \geq 1.5$
DT (ms)	$150 < DT < 240$	$DT \leq 150$
IVRT (ms)	$60 < IVRT < 110$	$IVRT \leq 60$
S/D	< 1	< 1
LA volume Index (mL/m^2)	≥ 32	≥ 32

E/A, early-to-atrial left ventricular filling ratio; DT, deceleration time; IVRT, isovolumetic relaxation time; S/D, systolic-to-diastolic pulmonary venous flow ratio; LA volume index, left atrial volume indexed for body surface area.

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