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Frequent coexistence of chronic heart failure and chronic obstructive pulmonary disease in respiratory and cardiac outpatients: Evidence from SUSPIRIUM, a multicentre Italian survey

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Abstract

Background: Chronic heart failure (CHF) and chronic obstructive pulmonary disease (COPD) frequently coexist but concurrent COPD + CHF has been little investigated.

Design: This multicentre survey (SUSPIRIUM) was designed to evaluate: the prevalence of COPD in stable CHF and CHF in stable COPD; diagnostic/therapeutic work-up for concurrent COPD + CHF; clinical profile of patients with COPD + CHF; predictors of COPD in CHF and CHF in COPD.

Methods: A 5-month-long cross-sectional prospective observational survey was conducted in 10 cardiac and 10 respiratory connected outpatient units.

Results: The prevalence of CHF in the 378 surveyed COPD patients was 11.9% (95% confidence interval 8.8–16.6) and the prevalence of COPD in 375 CHF patients was 31.5% (95% confidence interval 26.8–36.4). Diagnostic tests for suspected comorbidity were prescribed in 21.6% and 22.9% of COPD and CHF patients, respectively. Patients with coexisting CHF + COPD had a higher incidence of hypertension, physical inactivity and more frequently a GOLD score of 3 or greater. Compared to CHF only, CHF + COPD patients were significantly older, more frequently smokers, at worse respiratory risk and in a higher New York Heart Association class. Conversely, hypercholesterolaemia, a family history of ischaemic heart disease, fluid retention and comorbidities were more frequent in COPD + CHF than COPD-only patients. At multivariate analysis, a GOLD score of 3 or greater in CHF strongly predicted coexistent COPD (odds ratio 8.985, $P < 0.0001$) as did a history of other respiratory diseases (5.184, $P < 0.0001$). A history of ischaemic heart disease (4.868, $P < 0.0001$), atrial fibrillation (3.302, $P < 0.0001$) and sedentary lifestyle (2.814, $P < 0.004$) predicted coexistent CHF in COPD.

Conclusion: The high prevalence of COPD + CHF calls for integrated disease management between cardiologists and pulmonologists. SUSPIRIUM identifies which cardiac/pulmonary outpatients should be screened for the respective comorbidity.

Keywords

Chronic obstructive pulmonary disease, chronic heart failure, epidemiology, survey, cardiopulmonary rehabilitation, observational research

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Introduction

The epidemiology of chronic heart failure (CHF) and chronic obstructive pulmonary disease (COPD) are well known.[1] The prevalence of COPD global initiative for chronic obstructive lung disease (GOLD) stage II or higher ranges from 5% to 10% among adults[2] with a relatively low 1-year mortality in community dwellers (3%), increasing following hospitalisation (25%).[3,4] CHF is less common, affecting 1–3% of the general population[5] but carries a worse prognosis with a 5–7% annual mortality rate in stable community dwellers while the median survival following hospitalisation is still around 2 years.[6,7] Reduced exercise tolerance and abnormal ventilation are affected by both these common conditions with consequent impact on quality of life and on the healthcare of patients.[8,9]

Through shared risk factors (e.g. smoking and advanced age) and pathophysiological mechanisms ('cardiopulmonary continuum' and low-grade systemic inflammation),[10,11] CHF and COPD frequently coexist.[12] The presence of one or other comorbidity has important clinical and prognostic implications, highlighted by several registry-based studies and *post hoc* analyses of large randomised controlled trials.[13–16] Coexistent COPD independently predicts middle and long-term mortality in CHF patients with reduced or preserved ejection fraction, also after adjustment for beta-blocker use,[17] while a study examining the prognostic implication of coexistent CHF in COPD patients documented a hazard ratio for mortality of 2.1 over a mean follow-up of 4.2 years.[18]

The presence of one syndrome in conjunction with the other also has important therapeutic implications, particularly regarding the use of adrenergic agents, e.g. beta-blockers or beta2-agonists, still considered unsafe in the real world in COPD and CHF patients, respectively. Hence, knowledge about the prevalence and management of COPD or CHF as comorbidities is clinically important. However, the two diseases have largely been investigated as separate syndromes – pooled investigations combining cardiologists and pulmonologists are surprisingly rare. We therefore conducted the Survey on Prevalence and Disease Management in Patients with Heart Failure and Chronic Obstructive Pulmonary Disease (SUSPIRIUM) through Italy's national network of cardiac and pulmonary rehabilitation centres, to investigate: the occurrence of COPD (documented, suspected, or newly diagnosed) in outpatients with stable CHF visited by cardiologists and, vice versa, of CHF (documented, suspected, or newly diagnosed) in outpatients with stable COPD visited by pulmonologists; and the routine diagnostic and therapeutic work-up applied by cardiologists and pulmonologists in the suspicion/presence of concurrent disease. Secondary objectives were: to compare the clinical profile of patients with versus without comorbidity; to identify clinical predictors of the respective comorbidity.

Methods

The study protocol has been published elsewhere.[19] In brief, SUSPIRIUM was a cross-sectional observational prospective multicentre nationwide survey involving 20 outpatient units: 10 cardiac and 10 'sister' respiratory units from the same institution. Data were collected online. Each participating centre was asked to enroll the first two consecutive patients per week with a definite diagnosis of CHF or COPD observed in the respective outpatient department, over a 5-month period between 15 December 2013 and 15 May 2014. The systematic nature of the intermittent enrolment favours consecutiveness and safeguards against enrolment selectivity. Patients of either sex in stable condition were enrolled, irrespective of the presence or not of the comorbidity. COPD diagnosis was based on GOLD 2013 criteria[20] and CHF diagnosis on the European Society of Cardiology guidelines for the diagnosis and treatment of chronic heart failure 2012.[21] Exclusion criteria were: (a) unstable CHF defined as: previous (within last 3 months) or scheduled cardiac surgery; acute coronary syndrome within previous 3 months; percutaneous coronary or valvular intervention within the previous month; change in cardiovascular medications within the previous month; hospitalisation/emergency ward admission for cardiorespiratory causes within the previous 3 months; (b) unstable COPD defined as: hospitalization/emergency ward admission for cardiorespiratory cause within the previous 3 months; change in respiratory medications within the previous month. Patients with psychiatric disorders, cardiopulmonary congenital malformation, malignant cancer under active treatment, scheduled for heart/lung transplant, or who did not give written informed consent were also excluded.

Assessments and procedures

Electronic case report forms, accessible in a dedicated section of the Italian Association for Cardiovascular Prevention, Rehabilitation and Epidemiology website (www.iacpr.it), were used for data entry, and data were transferred via web to a central database. The data collection instrument had a multiple choice format, with jump menus or select boxes and obligatory items to reduce the risk of confounding data. Patient anonymity was ensured. The information gathered regarded only the patient's enrolment visit and subsequent diagnostic workout and included: demographic

and anthropometric characteristics, comorbidities, cardiac and respiratory risk profile (risk factors), clinical history including past cardiac or respiratory events and patient-reported or documented history of COPD or CHF, other comorbidities, functional status assessed with GOLD questionnaire, Medical Research Council (MRC) breathlessness scale and New York Heart Association (NYHA) class, and data from the physical examination and routine diagnostic, functional and therapeutic work-up applied by the cardiologist/pulmonologist. The study was conducted in accordance with legal and regulatory requirements and practice guidelines such as good clinical practice. The ethical committee of each institution approved the protocol, and informed consent was obtained from each patient.

Estimation of COPD/CHF comorbidity risk was based on suspected presence (history, symptoms, physical examination) or documented (previous pulmonary function tests, imaging, brain natriuretic peptide (BNP) measurement) or undocumented patient-reported diagnosis. All investigators were aware of the major current guidelines on both CHF and COPD and were invited to manage their patients in accordance with them. In cases of suspicion or no documentation, each specialist reported any diagnostic tests and/or functional evaluations prescribed (e.g. 6-minute walking test, cardiopulmonary exercise tests, etc.) as per their routine clinical practice to confirm or exclude the presence of comorbidity.

The survey involved no diagnostic tests, care interventions or pharmacological treatments that were not part of the routine clinical practice of each participating centre, and each physician enrolling a patient was fully responsible for his/her management. The survey was independently conducted and the data analysed under the scrutiny of the steering committee of the study.

Statistical analysis

All data collected in the online database underwent data cleaning and quality control. Enrolled patients were analysed by entry diagnosis (CHF vs. COPD) and final diagnosis (CHF vs. COPD vs. CHF + COPD). Continuous variables were expressed as mean ± standard deviation (SD) and median (range), categorical variables as number and percentage. The two enrolled patient cohorts were analysed separately, with a description of clinical characteristics and clinician's attitude and modalities of comorbidity investigations. The three final groups (COPD, CHF and CHF + COPD) were also compared. Differences between these groups were tested by the Fischer's exact test (categorical data) or Student's *t*-test. Finally, within the two original cohorts (COPD and CHF), differences in clinical characteristics between patients with single disease and those diagnosed with comorbidity were explored through univariate analysis. Variables significantly associated at univariate analysis underwent multivariate logistic (backward) analysis, and the odds ratio (OR) and respective 95% confidence interval (CI) were calculated. All computations were carried out with SAS statistical software (version 9.2; SAS Institute, Cary, NC, USA) and a P value of less than 0.05 was considered significant.

Results

Patient characteristics

The survey comprised 753 patients: 375 with CHF (302 with systolic left ventricular dysfunction – mean ejection fraction 39.1% ± 10.6, median 38.5% – and 73 with diastolic dysfunction) enrolled by cardiologists, and 378 with COPD (mean forced expiratory volume in 1 second % predicted 59.0 ± 37.6, median 54) enrolled by pulmonologists. Patients' clinical characteristics are summarised in Table 1.

The male/female ratio was similar in both groups. COPD patients were significantly older than CHF patients and had a longer history of illness. Regarding risk factors, COPD patients were more frequently current smokers (with a longer history of smoking) and had more respiratory risk factors (exposure to harmful inhalants and family history of COPD). The incidence of arterial hypertension, overweight/obesity and sedentary lifestyle was similar in the two groups, but hypercholesterolaemia and a family history of ischaemic heart disease (IHD) were significantly more frequent in patients with CHF. Comorbidities such as chronic kidney failure, diabetes mellitus, metabolic syndrome and anaemia were more frequent in CHF patients. On the other hand, COPD patients were more symptomatic for cough, sputum, fatigue and dyspnoea and had fewer signs of fluid retention than CHF patients.

Of the 366/375 CHF patients who answered unequivocally when asked if they were aware of having COPD, 98 (26.8%) responded 'yes' and 95 reported other diseases affecting the respiratory system: history of acute bronchitis/pneumonia 19.2%, obstructive sleep apnoea syndrome 5.6%, pulmonary hypertension 4.1%. Of 361/378 COPD patients who responded to the analogous question (if they were aware of having CHF), 50 (13.9%) reported a previous diagnosis of CHF and 188 reported other diseases affecting the cardiovascular system: coronary artery disease 18.8%, atrial fibrillation/flutter 10.5%.

Among patients with CHF, 87.1% were on beta-blockers and 86.8% used either an angiotensin-converting enzyme inhibitor or antagonist receptor blocker. As expected, significantly fewer patients with COPD

Table 1. Baseline characteristics of the study population.

	CHF patients, $n = 375$ (%)	COPD patients, $n = 378$ (%)
Mean age, years	68.0 ± 11.7	72.6 ± 8.5
Male/female	294/81 (78.4/21.6)	285/93 (75.4/24.6)
No. years since diagnosis	5.8 ± 6.1	10.2 ± 8.2
Previous hospitalisation	229 (70.9)	200 (61.7)
Smoking habit		
Current smokers	33 (9.0)	61 (16.4)
Past smokers (>1 year)	243 (66.2)	270 (72.4)
Years of smoking	30.7 ± 12.8	38.3 ± 12.2
Cardiac risk factors		
None	37 (10.0)	105 (29.4)
Family history of IHD	126 (34.1)	68 (19.0)
Overweight/obesity	232 (65.9)	236 (65.6)
Hypercholesterolemia	207 (56.1)	80 (22.4)
Hypertension	223 (60.4)	203 (56.9)
Sedentary lifestyle	124 (33.6)	114 (31.9)
Comorbidities		
COPD (reported by patient)	98 (26.8)	–
CHF (reported by patient)	–	50 (13.9)
Other CV disease	–	188 (51.9)
Other respiratory disease	95 (29.8)	–
CRF (≥stage II)	80 (22.5)	15 (4.2)
Diabetes mellitus	84 (23.6)	62 (17.4)
Metabolic syndrome	53 (14.9)	19 (5.3)
Chronic anaemia	22 (6.2)	5 (1.4)
Respiratory risk factors		
None	250 (79.4)	157 (51.1)
Occupational exposure D/C	47 (14.9)	112 (36.5)
Family history of COPD	17 (5.4)	53 (17.3)
Symptoms		
None	58 (15.5)	13 (3.4)
Cough	75 (20)	227 (60.1)
Sputum	64 (17.1)	213 (56.3)
Fatigue	115 (30.7)	185 (48.9)
Dyspnoea	271 (72.3)	330 (87.3)
Signs of fluid retention	71 (18.9)	35 (9.3)
Ongoing therapy		
ACE-I/ARB	315 (86.8)	179 (48%)
Beta-blockers	316 (87.1)	74 (19.8)
Diuretics	292 (80.4)	152 (40.8)
Selective beta2-agonists	22 (6.1)	291 (78)
Anticholinergics	38 (10.5)	304 (81.5)
Steroids	30 (8.3)	247 (66.2)
Oxygen	11 (3.0)	116 (31.1)

Percentages refer to the number of patients in which the data were available. In any case, the number was always greater than 90% of the total population.

ACE-I/ARB: angiotensin-converting enzyme inhibitors/angiotensin-receptor blockers; CHF: chronic heart failure; COPD: chronic obstructive pulmonary disease; CRF: chronic renal failure; CV: cardiovascular; D/C: dusts/chemicals; IHD: ischaemic heart disease.

Table 2. Physical examination and functional evaluation.

	CHF patients, $n = 375$	COPD patients, $n = 378$
MRC breathlessness scale, n (%)		
1–2	184 (68.4)	127 (38.9)
3	55 (20.4)	115 (35.3)
4–5	30 (11.2)	84 (25.8)
NYHA class, *n* (%)		
I	65 (17.6)	61 (17.4)
II	248 (67.2)	179 (51.0)
III	56 (15.2)	94 (26.8)
IV	–	17 (4.8)
GOLD questionnaire, *n* (%)		
≤2	210 (57.2)	180 (48.9)
≥3	157 (42.8)	188 (51.1)
Blood pressure during the visit		
Systolic mmHg	118.4 ± 16.2	128.8 ± 13.3
Diastolic mmHg	71.7 ± 8.9	75.1 ± 8.0
≥140 ≥ 90 mmHg at visit (%)	59 (15.7)	83 (22.0)
Heart rate during the visit	67.2 ± 10.9	76.2 ± 13.2
Body mass index	27.5 ± 5.0	27.7 ± 6.3

CHF: chronic heart failure; COPD: chronic obstructive pulmonary disease; GOLD: global initiative for chronic obstructive lung disease; MRC: Medical Research Council; NYHA: New York Heart Association.

received these cardiovascular medications. At physical examination (Table 2), 61.1% of COPD patients were grade 3 or more on the MRC breathlessness scale, whereas 84.8% of CHF patients (evaluated by the cardiologist) were in NYHA class I/II. All patients were assessed also with a GOLD questionnaire and 42.8% of CHF patients had a high risk of COPD (score ≥ 3). In COPD patients, 351/378 underwent NYHA classification by the pulmonologist and 111 (31.6%) resulted in NYHA class III/IV.

Prevalence of CHF in COPD patients

Of 378 COPD patients, 27 (7.1%) had a documented diagnosis of CHF, while in 92 (24.3%) CHF was excluded as a comorbidity by previous diagnostic assessment; 25 patients (6.6%) reported having CHF without documentation and 234 (61.9%) had never undergone diagnostic assessment (Figure 1(a)). In the 259 (68.5%) patients who were without available information on CHF comorbidity, the pulmonologist prescribed diagnostic tests (alone or in combination) in 56 (21.6%) patients (echocardiogram in 53.6%,

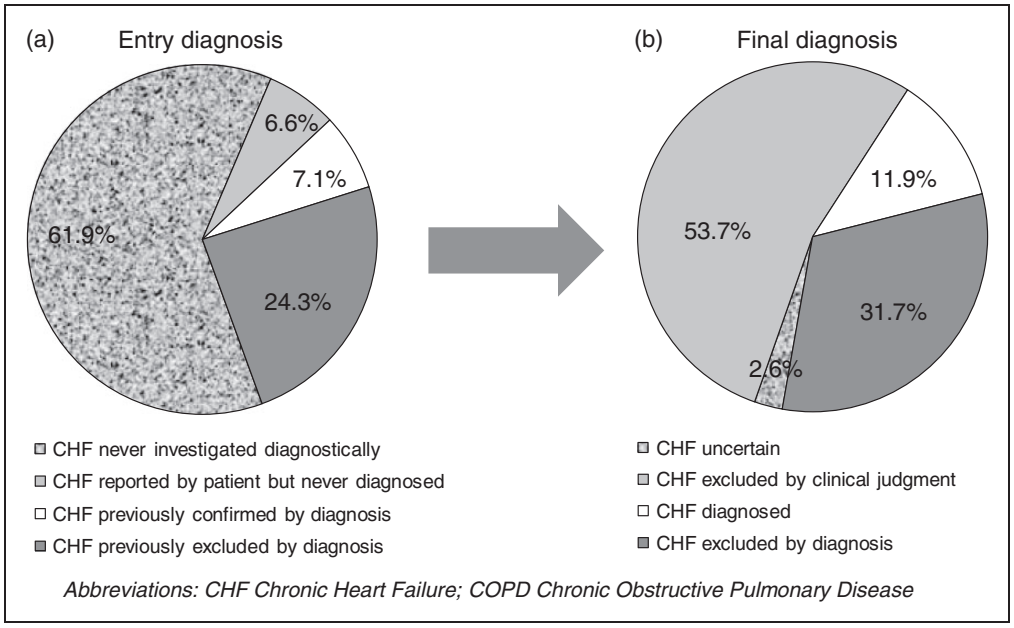

Figure 1. Presence of CHF as a comorbidity in COPD patients (a) before and (b) after diagnostic assessment ($N = 378$). CHF: chronic heart failure; COPD: chronic obstructive pulmonary disease.

electrocardiogram in 42.8%, cardiologist evaluation in 39.3%, BNP/N-terminal-proBNP in 17.9%). After the diagnostic workout, an additional 18 patients with COPD + CHF were identified. In the remaining patients ($n = 203$) the clinical judgement was deemed sufficient to exclude the comorbidity. Therefore, the overall prevalence of CHF as a comorbidity in COPD was 11.9% (95% CI 8.8–16.6) (Figure 1(b)). Of note, nine out of 17 patients who reported having CHF in the absence of documentation had the diagnosis confirmed. In 18 COPD patients in whom CHF was diagnosed, four were already taking beta-blockers. In no patient in whom the comorbidity was newly diagnosed did the specialist modify the therapy.

Prevalence of COPD in CHF patients

Of the 375 CHF patients assessed by cardiologists, 76 (20.3%) had a documented diagnosis of COPD, while in 59 (15.7%) COPD as a comorbidity was excluded by previous diagnostic assessment; 21 patients (5.6%) reported having COPD but without documentation and 219 (58.4%) had never undergone diagnostic assessment (Figure 2(a)).

Out of the 240 patients (64.0%) without available information on COPD comorbidity, the cardiologist prescribed diagnostic tests (alone or in combination) in 55 (22.9%) patients (spirometry in 85.5%, pulmonologist evaluation in 18.2%, other examinations in 12.7%). At the end of the diagnostic workout 42 additional patients with CHF + COPD were identified. In the remaining patients ($n = 185$) the clinical judgement was considered adequate to exclude the presence of comorbidity. Therefore, the overall prevalence of COPD as a comorbidity in CHF was 31.5% (95% CI 26.8–36.4) (Figure 2(b)). Of note, after the diagnostic investigation, the diagnosis was confirmed in 14/17 patients who reported having COPD but without documentation. In 42 CHF patients in whom COPD was diagnosed, seven were already taking bronchodilators/inhaled steroids. Again, in no patient in whom the comorbidity was newly diagnosed did the specialist modify the therapy.

Clinical profile of the patients with coexisting disease

The only differences observed between patients with coexisting disease and patients with isolated CHF or isolated COPD (Table 3) were a higher incidence of a history of arterial hypertension and physical inactivity and a more frequent classification of a GOLD score of 3 or greater. In comparison to patients with isolated CHF, patients with CHF + COPD were significantly older, more frequently smokers, had a worse respiratory risk, were more symptomatic for cough, sputum and fatigue and consequently in a higher NYHA class (III/IV). Conversely, hypercholesterolaemia, a family history of IHD, fluid retention and comorbidities were more frequent in patients with COPD + CHF than in isolated COPD.

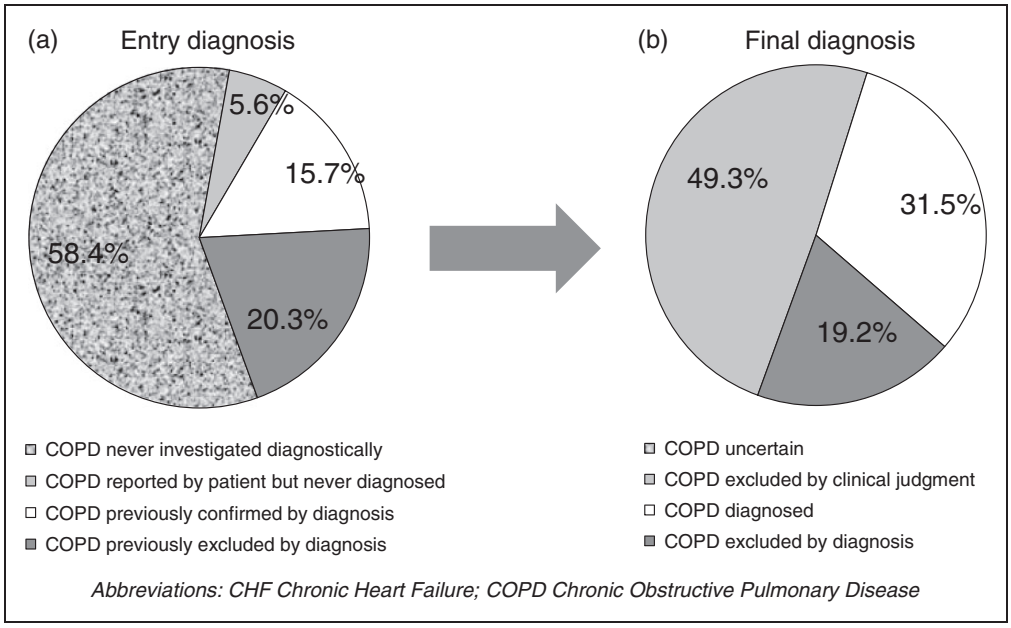

Figure 2. Presence of COPD as a comorbidity in CHF patients (a) before and (b) after diagnostic assessment ($N = 375$). CHF: chronic heart failure; COPD: chronic obstructive pulmonary disease.

Clinical predictors of the comorbidity

Table 4(a) shows the regression analysis for the risk of COPD in CHF patients. The variables included in the univariate analysis were age, hypertension, obesity, current/past smoking habit, years of smoking, GOLD score of 3 or greater and other respiratory disease. Only age, smoking habit, GOLD score of 3 or greater and other respiratory disease were predictive. At multivariate analysis backward selection, a GOLD score of 3 or greater was highly predictive (OR 8.985, 95% CI 4.613–7.499; $P < 0.0001$) of COPD, as well as a history of other respiratory diseases (OR 5.184, 95% CI 2.630–10.219, $P < 0.0001$).

Table 4(b) shows the regression analysis for the risk of CHF in COPD patients. At univariate analysis, all variables considered (age, obesity, presence of one or more cardiovascular risk factor, history of arterial hypertension, hypercholesterolaemia, smoking habit, sedentary lifestyle, history of IHD and atrial fibrillation) had predictive potential except smoking habit and hypercholesterolaemia. At multivariate analysis backward selection, a history of IHD (OR 4.868, 95% CI 2.374–9.983; $P < 0.0001$), the presence of atrial fibrillation (OR 3.302, 95% CI 1.347–8.091; $P < 0.0001$) and sedentary lifestyle (OR 2.814, 95% CI 1.347–5.754; $P < 0.004$) were predictive of CHF in COPD patients.

Discussion

SUSPIRIUM is, to our knowledge, the first study to analyse the occurrence, clinical features and predictors of coexisting CHF + COPD in cardiac and respiratory outpatient centres, i.e. two specific real-life settings that routinely follow patients with an established diagnosis of either CHF or COPD alone. The overall occurrence of documented COPD in patients with stable CHF was much higher than that of documented CHF in patients with stable COPD (i.e. 31.5% vs. 11.9%), despite the fact that the percentage of patients screened for the presence of the comorbidity was similar. The occurrence of COPD in CHF observed in SUSPIRIUM was much higher than expected based on estimates in the general population adjusted for age and sex.[2] However, the prevalence of concurrent disease reported in the literature varies considerably according to the specialist care setting (pulmonology or cardiology), the patient regime (outpatient vs. in-hospital), cohort selection, diagnostic criteria and the measurement tools applied. In studies evaluating pulmonary function in stable CHF outpatients using standardised criteria, the observed prevalence of COPD ranges from 27.6%[22] to 44%.[23] In a recent prospective study[24] of 118 consecutive patients with stable CHF in which all had spirometry data, the mean occurrence of COPD was similar (30%, 95% CI 24–37) to that observed in SUSPIRIUM. Similar results, all in stable outpatients, were found by Minasian et al. (32%),[25] Beghé et al. (34%)[26] and Macchia et al. (37%).[27]

Studies are fewer regarding the prevalence of unrecognised CHF in COPD outpatients, which ranges from 11.4%[28] (patient self-reported diagnosis) to 17%[27] (in highly selected cohorts in which diagnosis was adjudicated retrospectively) to 19%[29] (administrative data) to

Table 3. Characteristics of the CHF, COPD and CHF + COPD patient groups.

	CHF $n = 200$	COPD $n = 321$	CHF + COPD $n = 163$	CHF + COPD vs. CHF	CHF + COPD vs. COPD
Mean age, years	67.3 ± 12.2	72.1 ± 8.7	72.3 ± 10.3	<0.0001[a]	ns[a]
Male/female	152/48 (76.0/24.0)	237/84 (73.8/26.2)	134/29 (82.2/17.8)	ns	0.0412
Smoking habit					
Current smokers	14(7.2)	55(17.4)	24(14.9)	<0.0001	ns
Past smokers (>1 year)	122(62.9)	224(70.9)	118(73.3)		
Years of smoking	28.8 ± 13.0	37.8 ± 12.7	34.7 ± 12.1	ns	ns
Cardiac risk factors					
None	21 (10.7)	99 (32.8)	11 (6.9)	ns	<0.0001
Family history of IHD	68 (34.5)	44 (14.6)	56 (35.0)	ns	<0.0001
Overweight/obesity	119 (64.3)	202 (65.4)	111 (74)	ns	ns
Hypercholesterolaemia	109 (55.3)	65 (21.5)	85 (53.1)	ns	<0.0001
Hypertension	111 (56.3)	162 (53.6)	112 (70.0)	0.0085	0.0007
Sedentary lifestyle	57 (28.9)	88 (29.1)	77 (48.1)	0.0003	<0.0001
Respiratory risk factors					
None	137 (83.0)	136 (52.3)	90 (64.7)	0.0120	0.0092
History of exposure to D/C	19 (11.5)	100 (38.5)	33 (23.7)	0.0058	0.0037
Family history of COPD	8 (4.8)	38 (14.6)	19 (13.7)	0.0083	ns
Comorbidities					
CRF (≥stage II)	42 (21.6)	9 (3.0)	34 (22.5)	ns	<0.0001
Diabetes mellitus	47 (24.2)	48 (15.8)	36 (23.8)	ns	0.05070
Metabolic syndrome	30 (15.5)	16 (5.3)	23 (15.2)	ns	ns
Chronic anaemia	12 (6.2)	5 (1.7)	8 (5.3)	ns	0.0393
Symptoms					
None	35 (17.5)	11 (3.4)	16 (9.8)	0.0477	0.0058
Cough	21 (10,5)	192 (59.8)	77 (47.2)	<0.0001	0.0091
Sputum	19 (9.5)	188 (58.6)	58 (35.6)	<0.0001	<0.0001
Fatigue	52 (26.0)	152 (47.4)	71 (43.6)	0.0005	ns
Dyspnoea	141 (70.5)	277 (86.3)	125 (76.7)	ns	0.0101
Signs of fluid retention	32 (16.0)	21 (6.5)	36 (22.1)	ns	<0.0001
NYHA class					
I/II	169 (82.2)	213(71.3)	121 (77.1)	0.0353	ns
III/IV	27 (13.8)	86 (27.7)	36(22.9)		
GOLD score					
≤2	150 (76.1)	160 (51.3)	45 (28.5)	<0.0001	<0.0001
≥3	47 (23.9)	152 (48.7)	113 (71.5)		
BMI	27.5 ± 5.0	27.7 ± 6.3	28.5 ± 5	ns[a]	ns[a]

BMI: body mass index; BP: blood pressure; CHF: chronic heart failure; COPD: chronic obstructive pulmonary disease; CRF: chronic renal failure; CV: cardiovascular; D/C: dusts/chemicals; GOLD: global initiative for chronic obstructive lung disease; HR: heart rate; IHD: ischaemic heart disease; NYHA: New York Heart Association.

[a]Student's *t*-test. All other tests: Fisher's exact test.

20.5%[18] in a general practitioner cohort. In two studies including stable COPD patients who underwent echocardiography, left ventricular systolic dysfunction was found in 13.8% (and isolated diastolic dysfunction in 3.2%)[27] and in 10.4%,[30] respectively, percentages not so different from the CHF occurrence observed in our real-world survey.

The proportion of patient-reported comorbidity subsequently confirmed was higher in CHF patients (82.3%) than in COPD patients (52.9%) as well as the proportion of patients not reporting the comorbidity but diagnosed as comorbid: 22.4% in CHF patients vs. 3.9% in COPD patients. Apostolovic et al. reported similar findings: out of 174 stable CHF outpatients they

Table 4. Logistic regression analysis.

Univariate analysis				Multivariate analysis (backward selection)		
(a) for predictors of COPD in CHF patients						
Variable	Odds ratio	95% CI	*P* value	Odds ratio	95% CI	*P* value
Age	1.151	1.043–1.276	0.0061			
Smoking habit	3.107	1.642–5.878	0.0005			
GOLD Q. ≥3	10.282	5.980–17.680	<0.001	8.985	4.613–7.499	<0.0001
Other resp. disease	6.573	3.753–11.514	<0.001	5.184	2.630–10.219	<0.0001
(b) for predictors of CHF in COPD patients						
Variable	Odds ratio	95% CI	*P* value	Odds ratio	95% CI	*P* value
Age	1.302	1.069–1.609	0.0110			
Obesity	2.156	1.102–4.218	0.0248			
CV risk factors (≥1)	3.804	1.454–9.950	0.0065			
Hypertension	2.061	1.038–4.092	0.0388			
Sedentary lifestyle	2.633	1.402–5.059	0.0028	2.814	1.376–5.754	0.0046
History of IHD	5.243	2.711–10.139	0.0001	4.868	2.374–9.983	<0.0001
Atrial fibrillation	3.747	1.691–8.303	0.0011	3.302	1.347–8.091	0.0090

CHF: chronic heart failure; COPD: chronic obstructive pulmonary disease; GOLD Q: global initiative for chronic obstructive lung disease questionnaire; resp.: respiratory; CI: confidence interval; CV: cardiovascular; IHD: ischaemic heart disease.

found COPD, previously unrecognised, in 48 (27.6%).[22] This may suggest that in CHF patients (younger, less often smokers and with a shorter history of smoking) the GOLD definition of airway obstruction could overestimate COPD.[23] However, there is also the converse possibility of under-diagnosis of CHF in COPD patients in routine clinical practice, given that echocardiography or BNP measurements are under-used in respiratory patients, as symptoms are often believed to be well explained by the main diagnosis. Furthermore, the power of diagnostic tests for CHF in COPD patients is lower for frequently ambiguous responses (e.g. diastolic dysfunction not adequately evaluated, or borderline values of natriuretic peptides). The same attitude is also confirmed by the apparent inertia concerning therapy. In fact, surprisingly, newly diagnosed comorbidity did not lead to any change in the cardiac (beta-blocker) or respiratory (bronchodilator) therapy prescriptions. One possible hypothesis about the cause for this behaviour is that the final therapeutic strategy depends on the specialist who is in charge of the patient: so it is always the primary target disease (and its specialist) that governs the treatment. Added to this is the lack of confidence of the cardiologist and pulmonologist with drugs, respectively, for COPD and CHF.

Actually, neither symptoms nor signs are unique to either condition, and patients with confirmed COPD + CHF are not easily distinguishable from those with single disease. Their clinical profile is intermediate between that of isolated CHF and isolated COPD. Pulmonary function tests in euvolaemic CHF patients are of great diagnostic value for concurrent COPD[16] as are sequential BNP testing and echocardiography in COPD patients, whose combination may counter the inherent limitations of peptides or echocardiography alone in pulmonary disease for a diagnosis of CHF. As there is no available evidence showing the efficacy and cost-effectiveness of systematic screening, the multivariate regression analysis of SUSPIRIUM data may pinpoint those patients in whom such screening would be most appropriate, namely CHF patients with a GOLD score of 3 or greater plus a history of other respiratory disease, and COPD patients with a history of IHD plus the presence of atrial fibrillation.

Study limitations and strengths

Our study has several limitations. First, the comorbidity occurrence observed in SUSPIRIUM cannot be taken as an equivalent of 'prevalence' because, according to the pure observational design of the study, only patients clinically found to be suspect by the specialist underwent diagnostic tests. Notwithstanding, the comorbidity occurrence observed in SUSPIRIUM was comparable to the prevalence observed in studies in which the comorbidity was systematically investigated in stable patients. Another limitation is that the patients recruited for SUSPIRIUM were seen by specialists of a rehabilitation hospital/university clinic and may not represent the general population of CHF and COPD outpatients; however, it is unlikely that they

differ from the outpatients with the same diseases who are referred to acute care hospitals. A further limitation is the underrepresentation of female patients, similar, however, to all studies in the literature.

The originality of SUSPIRIUM is that this survey was designed and conducted as a parallel study in the two outpatient settings (cardiology and pulmonology) with common definitions and goals, and managed by the same coordinating committee (which also controlled patient selection).

Conclusion

SUSPIRIUM provides significant new information on the coexistence of COPD and CHF in cardiac and respiratory outpatients. Given the progressive aging of the population, comorbidities now represent a key challenge to specialists, who often mostly focus on the diseases of their core competence, in isolation. A unique feature of our study is that we involved both cardiologists and pulmonologists in a single, parallel study with common definitions and goals. We confirmed the high prevalence of heart and lung comorbidities in clinical practice, and consistently found – regarding both cardiologists and pulmonologists – that no therapeutic adjustment was made when comorbidity was diagnosed. Such 'tunnel vision' on the part of specialists calls for integrated chronic disease management strategies. A systematic diagnostic screening may also be warranted, and research is needed to explore the efficacy and cost-effectiveness of such. Meanwhile, SUSPIRIUM has indicted which cardiac and pulmonary outpatients should be the targets for screening for the respective comorbidity.

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Author contribution

RG, AS, PLT, PF and LT contributed to the conception or design of the work. MC, GM and NA contributed to the acquisition, analysis, or interpretation of data for the work. RG, LT and PLT drafted the manuscript. AS, PF, MC, GM and NA critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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Declaration of conflicting interests

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