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BRIEF ARTICLE

Short-term outcomes in heart failure patients with chronic obstructive pulmonary disease in the community

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Abstract

AIM: To establish the short term outcomes of heart failure (HF) patients in the community who have concurrent chronic obstructive pulmonary disease (COPD).

METHODS: We evaluated 783 patients (27.2%) with left ventricular systolic dysfunction under the care of a regional nurse-led community HF team between June 2007 and June 2010 through a database analysis.

RESULTS: One hundred and one patients (12.9%) also had a diagnosis of COPD; 94% of patients were treated with loop diuretics, 83% with angiotensin converting enzyme inhibitors, 74% with β-blockers; 10.6% with bronchodilators; and 42% with aldosterone antagonists. The mean age of the patients was 77.9 ± 5.7 years; 43% were female and mean New York Heart Association class was 2.3 ± 0.6. The mean follow-up was 28.2 ± 2.9 mo. β-blocker utilization was markedly lower in patients receiving bronchodilators compared with those not taking bronchodilators (overall 21.7% *vs* 81%, $P < 0.001$). The 24-mo survival was 93% in patients with HF alone and 89% in those with both comorbidities (P = not significant). The presence of COPD was associated with increased risk of HF hospitalization [hazard ratio (HR): 1.56; 95% CI: 1.4-2.1; $P < 0.001$] and major adverse cardiovascular events (HR: 1.23; 95% CI: 1.03-1.75; $P < 0.001$).

CONCLUSION: COPD is a common comorbidity in ambulatory HF patients in the community and is a powerful predictor of worsening HF. It does not however appear to affect short-term mortality in ambulatory HF patients.

Key words: Heart failure; Chronic obstructive pulmonary disease; Short-term mortality

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INTRODUCTION

Heart failure (HF) and chronic obstructive pulmonary disease (COPD) are major causes of presentation to both primary and secondary care in the United King-

dom National Health Service (NHS)[1,2]. Both diseases independently carry high morbidity and high mortality, alongside high health-care costs, and negative impacts on quality of life and functional status[3]. Despite most research examining each disease in isolation several studies have suggested considerable comorbidity[3-5], possibly due to shared risk factors including tobacco smoking. Recently, investigators have suggested that up to 32% of all HF patients have co-existing COPD, including 10% of all acutely hospitalized HF cases[3]. In addition, COPD patients have been found to be 4.5 times more likely to develop HF than disease-free control individuals[4], with these values suggested to be an underestimation due to the misdiagnosis of COPD[5,6].

The majority of reports examining the interaction between the two diseases have taken place in secondary care. In hospitalized patients with both HF and COPD, diagnostic challenges differentiating the cause of the acute exacerbations has been emphasized[7]. Patients with co-existence of the diseases have greater mortality and longer hospital stay than patients with chronic HF or COPD alone[8]. This has led to the suggestion that COPD is a short-term prognostic indicator of cardiovascular morbidity and mortality in secondary care[7].

However, little evidence exists on the prognosis of patients with both HF and COPD in the community and primary care setting. This study aims to establish the short-term outcomes of HF patients in the community who have concurrent COPD. The authors hypothesize that the comorbidity of HF and COPD in the community will lead to a worse prognosis than when HF alone is present due to diagnostic challenges, and challenges in effectively treating both conditions.

MATERIALS AND METHODS

The Leicestershire County and Rutland Primary Care Trust (LCRPCT) covers a fairly rural setting with a population of 750 000 according to the 2001 census. Approximately 0.8% of the population have been identified with left ventricular systolic dysfunction (LVSD). The specialist HF team comprises a group of five full-time-equivalent advanced nurse practitioners with clinical supervision by a community physician. The specialist respiratory team comprises a similar group of advanced nurse practitioners clinically supervised by a Respiratory Nurse Consultant and a General Practitioner (GP) with a special interest in Respiratory Medicine. The teams work closely with local GPs, and indeed local GPs refer patients directly to the team. The strategy of the Community Health Services of LCRPCT for delivering specialist care for long-term conditions (LTC) is to develop models of care within other chronic diseases and to centrally locate the running and administration of the service through a single point of access, known as the LTC Hub. Although clinicians will work along care pathways of the disease, they will coordinate care for all patients with comorbid conditions, ensuring that the correct clinician with the appropriate skills responds to the changing needs of the patients. A central tenet of the service is to work in an integrated manner with all clinicians who could possibly manage the patient. HF patients are referred into the service by GPs following diagnosis for case management, by secondary care physicians post-hospitalization and by other internal stakeholders within the Primary Care Trust.

Table 1 Baseline clinical characteristics of patients with heart failure, comparing those with and without chronic obstructive pulmonary disease for June 2007 to June 2010 (SD)

Baseline features	HF patients with COPD (n = 101)	HF patients without COPD (n = 682)
Age, yr	75.8 (6.9)[b]	71.3 (4.4)
Gender (M/F, %)	58/42	56/44
LVEF, %	33.6 (10.7)[b]	38.9 (4.8)
Ischemic cause, %	64.5 (4.8)	68.9 (10.2)
Duration of HF, yr	7.2 (2.3)	5.9 (4.2)
Duration of COPD, yr	6.9 (1.6)	----
NYHA status	2.6 (1.2)	2.4 (1.4)
FEV1/FVC ratio, %	53.6 (7.4)	----
Heart rate	71.4 (12.8)	73.4 (11.8)
Blood pressure, mmHg	125 (17.2)/76 (10.1)	129 (11.4)/81 (9.3)
eGFR	57.4 (12.9)	60.2 (13.5)
BMI	23.8 (5.3)	24.6 (3.9)

HF: Heart failure; COPD: Chronic obstructive pulmonary disease; eGFR: Estimated glomerular filtration rate; LVEF: Left ventricular ejection fraction; BMI: Body mass index; FEV: Forced expiratory volume; FVC: Forced vital capacity. [b]$P < 0.01$ *vs* patients without COPD.

Patients

In the current study, we analyzed 783 patients with HF under the care of both HF and COPD teams between June 2007 and June 2010. Patient data was reviewed in an anonymized fashion through the NHS Shared Care records database operated by the primary care trust. Consequently specific patient consent forms were not required to evaluate the data. Ethical approval was not required as this was an observational study involving health services practice. The current population represented 27.2% of the total HF patients in the area under supervision. The diagnosis of HF was initially made by a secondary care physician based on the patient's history, symptoms, and physical signs, and was validated by transthoracic echocardiography. Patients were considered to have COPD if they had positive diagnostic spirometry results or if they filled > 2 prescriptions for ipratropium bromide before the index study date. In addition, oral prednisolone use in the 12 mo before the start of the study was used as a marker of the severity of pulmonary disease. The baseline characteristics of the study patients and their comorbidities are recorded in Tables 1 and 2, respectively. In brief, the mean age of the study group was 77.9 ± 5.7 years. There were slightly more males in the study group (57%). Patients were followed up during the entire study period. Cause of death and hospitalization date were ascertained using hospital

Table 2 Comorbidity in patients with heart failure, comparing those with and without chronic obstructive pulmonary disease for June 2007 to June 2010 *n* (%)

Condition	HF patients with COPD (*n* = 101)	HF patients without COPD (*n* = 682)
Cardiovascular risk factors		
Diabetes	17 (17)	136 (20)
Hypertension	43 (43)[b]	382 (56)
Dyslipidemia	24 (24)	177 (26)
Smoker	57 (57)[b]	164 (25)
Ex-smoker	31 (31)[b]	136 (20)
Cardiovascular disease		
Previous MI	27 (27)	198 (29)
Angina	49 (49)	355 (53)
Previous stroke	20 (20)	130 (19)
Atrial fibrillation	21 (21)[b]	184 (27)
Non-cardiovascular factors		
Cancer	24 (24)	177 (26)
Depression	31 (31)[b]	143 (21)

MI: Myocardial infarction; HF: Heart failure; COPD: Chronic obstructive pulmonary disease. [b]$P < 0.01$ *vs* patients without COPD.

Table 3 Pharmacological treatments of patients with heart failure, comparing those with and without chronic obstructive pulmonary disease for June 2007 to June 2010 *n* (%)

Treatment	HF patients with COPD (*n* = 101)	HF patients without COPD (*n* = 682)
Cardiovascular treatment		
Beta-blocker	21 (22)[b]	555 (81)
ACE-inhibitor	49 (49)	382 (56)
Angiotensin receptor blocker	11 (11)	82 (12)
Spironolactone	54 (54)[b]	189 (28)
Loop diuretic	61 (61)[b]	525 (77)
Calcium channel blocker	31 (31)	184 (27)
Amiodarone	5 (5)	41 (6)
Aspirin	60 (60)	436 (64)
Warfarin	15 (15)[b]	130 (20)
COPD treatment		
Beta agonist	61 (61)[b]	20 (3)
Inhaled anti-muscarinic	27 (27)[b]	6 (1)
Inhaled steroid	53 (53)[b]	19 (3)
Oral steroids	24 (24)[b]	2 (0.003)

HF: Heart failure; COPD: Chronic obstructive pulmonary disease. [b]$P < 0.01$ *vs* patients without COPD.

records, death certificates and hospital autopsy records.

Statistical analysis

Statistical analysis was performed using SAS software. Statistical methods included the Chi-square test, the χ test and Fisher's exact test where appropriate for categorical data, proportions and means. Logistic regression was used to determine factors associated with COPD diagnosis. Variables were entered into the model based on clinical relevance and published predictors of COPD diagnosis. The final adjusted model included the following covariates: age, sex, year and presence of COPD, angina, previous myocardial infarction, atrial fibrillation and hypertension. Age was treated as a continuous variable. All statistical tests were two-tailed and $P < 0.001$ was considered statistically significant. To obtain the distribution curve for the survival time, an estimated value of Kaplan-Meier was calculated, and differences in survival time were analyzed using the log-rank test.

RESULTS

The data from 783 patients were analyzed. Mean follow-up was 28.2 ± 2.9 mo. The baseline characteristics of the two study groups are presented in Table 1. The crude prevalence of COPD in patients with HF in this region was 12.9%. The prevalence was slightly higher in men (n = 58, overall 7.4%). Table 2 displays the comorbidities associated with the HF patients in this study. The majority of patients with HF and COPD were recorded as current or previous smokers, as opposed to 45% of those without COPD ($P < 0.001$). Despite this, the prevalence of smoking-related cardiovascular and non-cardiovascular comorbidity was similar in the two groups (Table 2). This included a prior history of myocardial infarction, angina, stroke and cancer. The prevalence of hypertension in HF patients with COPD was significantly lower than in those without COPD (43% *vs* 56%, $P < 0.001$). The prevalence of atrial fibrillation was also significantly lower in the HF and COPD patients than in those without COPD (21% *vs* 27%, $P < 0.001$). A possible explanation for this was that on examination of the echocardiographic data, the left atrial diameter of the COPD and HF group was a mean of 5.1 (± 0.6) cm *vs* 5.6 (± 0.3) cm in the HF patients ($P < 0.001$).

Pharmacological treatment in both study groups is listed in Table 3. Only 22% of patients with HF and COPD were prescribed beta-blockers, as opposed to 81% of those without COPD ($P < 0.001$). This contrasted strikingly with the prescription of angiotensin converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers, amiodarone and antiplatelet drugs where no significant difference was noted between groups. More patients with COPD were prescribed aldosterone antagonists (54% *vs* 28%, $P < 0.001$), but on comparison they had less loop diuretics prescribed (61% *vs* 77%, $P < 0.001$). Beta agonists were the most frequent therapy for COPD (61%), followed by inhaled corticosteroids (53%) and anti-muscarinic drugs (27%).

There were 94 deaths recorded during the study period (12%). The 24-mo survival was 93% in patients with HF alone and 89% in those with both comorbidities (P = not significant; Figure 1). On univariate analysis, a baseline diagnosis of COPD did not predict the likelihood of survival, with a relative risk of death from any cause of 1.07 (95% CI: 0.89-1.54; $P = 0.428$, Table 4). After adjustment for demographic data, clinical characteristics, and medical treatment, the relation proved to be still insignificant (Table 4). To estimate the trend in risk of 2-year mortality, we employed spline functions for baseline COPD comorbidity.

However, the presence of COPD was associated with an increased relative risk for re-hospitalization on

Table 4 Association between chronic obstructive pulmonary disease diagnosis and clinical outcomes in the patient cohort for June 2007 to June 2010

Outcome	COPD and HF	HF alone	Unadjusted HR (95% CI)	*P* value	Adjusted HR (95% CI)	*P* value
HF hospitalization	36 (36)	143 (21)	1.78 (1.49-2.11)	< 0.001	1.56 (1.4-2.1)	< 0.001
All-cause mortality	29 (29)	177 (26)	1.07 (0.89-1.54)	0.428	1.02 (0.77-1.5)	0.225
Major CV events (non-fatal MI, stroke)	19 (19)	61 (9)	1.34 (1.1-1.53)	< 0.001	1.23 (1.03-1.75)	< 0.001
CV death	22 (22)	155 (23)	0.92 (0.68-1.06)	0.357	0.96 (0.77-1.13)	0.149

HF: Heart failure; COPD: Chronic obstructive pulmonary disease; HR: Hazard ratio; CV: Cardiovascular; MI: Myocardial infarction.

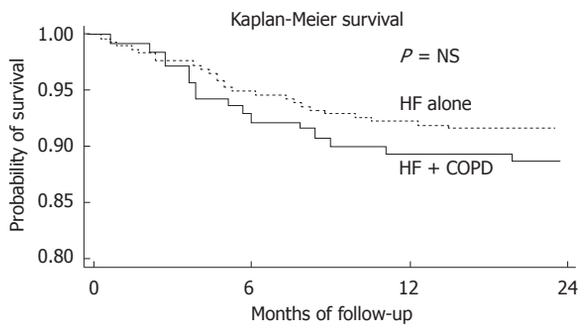

Figure 1 Kaplan-Meier survival curve in patients with heart failure, comparing those with and without chronic obstructive pulmonary disease for June 2007 to June 2010. HF: Heart failure; COPD: Chronic obstructive pulmonary disease; NS: Not significant.

univariate analysis [hazard ratio (HR): 1.78; 95% CI: 1.49-2.11; $P < 0.001$]. This association remained strongly significant after adjustment for covariates (Table 4). This association was also strongly reported in the development of major cardiovascular events such as non-fatal myocardial infarction and stroke, where the presence of COPD increased relative risk by 23% (HR: 1.23; 95% CI: 1.03-1.75; $P < 0.001$).

DISCUSSION

Chronic diseases, including cancer, cardiovascular disease, chronic respiratory diseases and metabolic syndromes (hypertension, diabetes and dyslipidemias)[9], are increasing in the developed world and result in a substantial economic and social burden[10]. This cost increases exponentially when chronic diseases co-exist in patients[8-11]. Patients with two or more long-term conditions account for only one-quarter of the population of all elderly people (> 65 years old) but for > 50% of the overall costs[10-12].

This is the first study we know of which examined the epidemiology and outcomes of patients with HF (LVSD) and co-existent COPD in the community. Prior reports have involved epidemiology and management of these patients hospitalized with worsening HF[13], attending specialized HF clinics[14] or enrolled in clinical trials[15,16], and there is one report of Scottish community patients[17]. We describe several key findings. The presence of COPD was associated with increased risk of HF hospitalization and major adverse cardiovascular events. However, it did not affect short-term mortality outcomes in these patients.

Remarkably, very few reports describe the prevalence of COPD in HF patients. The prevalence in our study was 12.9% and was similar to that observed in a community HF clinic in Hull, United Kingdom (12.1%)[18]. CHARM-Overall reported a rate of 8.9%[19], but they included both preserved and lowered ejection fraction HF patients. The co-existence of both these diseases should not be a surprise, as both diseases share smoking as the most common risk factor. In our sample, nearly 50% had a history of smoking in the development of HF and this rose to nearly 80% in patients who suffered both HF and COPD. Cigarette smoking is associated with a 45% higher risk of HF in men and an 88% higher risk of development of HF in women after adjustment for other known risk factors for HF, including coronary heart disease[20,21].

The prognosis of these patients may well be linked to both conditions sharing the same pathogenetic features. Chronic inflammation is present in both HF and COPD. It has been hypothesized that, as a consequence of mutual mechanisms of systemic cellular and humoral inflammation, HF and COPD occur more commonly in the presence of each other[22]. It is this common inflammatory pathway that has been the target of research and drug development in recent years. However, there has been conflicting reports in the COPD literature to suggest that this common pathway may not be the only mechanism involved. Interestingly, Simon-Tuval *et al*[23] recently reported that the severity of airflow restriction in COPD patients, and hence a marker for increasing inflammation, does not necessarily predict outcomes of COPD patients in terms of exacerbations or hospitalizations. Other common mechanisms are the renin-angiotensin-aldosterone system and sympathetic nervous system. In HF, there is no doubt that neurohormonal blockers have a beneficial effect[24], whilst in COPD, adequately designed trials are distinctly lacking[25].

An interesting historical aspect is also the so-called "prejudice" against β-blocker use in HF patients with co-existent COPD. This is clearly borne out in our sample of patients where only one-fifth of the patients with both conditions were prescribed such medication. Differentiating asthma from COPD and assessing airflow obstruction is well within the remit of a GP. Indeed the ability to do this has become a part of the remuneration package provided to GPs within the United Kingdom under their current funding structure (The Quality and

Outcomes Framework of the GP contract)[26]. Withholding life-saving therapy with β-blockers to patients with concomitant HF and COPD should thus become a practice of the past. Sadly, as our study demonstrates, there is work to be done to promote this key intervention within community settings.

More recently, a large retrospective study of COPD prescribing in primary care in Italy showed that the breakdown of medications were as follows: inhaled β-agonist 37.4%, inhaled antimuscarinics 61.6%; inhaled corticosteroids 15.3%; and combination inhalers (β-agonist and corticosteroids) 32%[27]. Although clearly there may be differences in the medication trends between European countries both the European Respiratory Society and Global Initiative of Obstructive Lung Disease guidelines[28,29] provide consensus internationally for the prescribing of medications for COPD. The blend of medications for the COPD and HF group in our study showed comparable percentages for inhaled β-agonists (61%) but much lower percentages for inhaled antimuscarinics (21%). Our figures for inhaled corticosteroids included both those given singly or in combination with an inhaled long-acting β-agonist, and thus were also comparable with the Italian study. This suggests that the treatment could have been optimized with antimuscarinics for these patients. Whether this would have aided in improving cardiovascular outcomes in these patients is unknown and possibly a question for further research.

Boudestein *et al*[30] also recently suggested that the presence of a diagnosis of HF is a strong independent predictor of all-cause mortality in patients with a diagnosis of COPD. Unfortunately, our study did not concur with those results for the short term, possibly due to the time limit constraint, with the Dutch study lasting twice as long.

This study has implications for the management of patients with the comorbidities of HF and COPD. Based on our study and previous research, it would appear that each of these conditions may have potentially independent adverse effects on the disease progression of each condition individually. Although beyond the scope of this study, the need for a combined and integrated approach to managing these comorbidities within the community would seem an appropriate strategy.

COMMENTS

Background

Heart failure (HF) and chronic obstructive pulmonary disease (COPD) are common co-morbidities. The combination presents diagnostic challenges and has been linked with worse prognosis in patients admitted to hospital. There is hardly any prognostic data in patients with both co-morbidities in the community.

Innovations and breakthroughs

HF and COPD independently carry high morbidity and high mortality, alongside high health-care costs, and negative impacts on quality of life and functional status. However, these co-morbidities are increasingly common in patients and their impact on these parameters have not been well documented in the primary care setting. This study aims to establish the short term outcomes of HF patients in the community who have concurrent COPD. The authors hypothesise that the comorbidity of HF and COPD in the community will lead to a worse prognosis than when HF alone is present due to diagnostic challenges and challenges in effectively treating both conditions.

Applications

This study has implications for the management of patients with the co-morbidities of heart failure and COPD. Based on the study and previous research, it would appear that each of these conditions may have potentially independent adverse effects on the disease progression of each condition individually.

Terminology

HF: A chronic disease state of the heart that results in specific cardiac symptoms (breathlessness and fluid overload/lethargy) and signs. The disease is incurable and has a poor long term prognosis; COPD: A chronic condition of bronchial inflammation caused primarily by smoking. Characterized by breathlessness and lethargy as well.

Peer review

The authors evaluated the prevalence and prognostic impact of chronic obstructive pulmonary disease in 783 patients with systolic heart failure managed in the community between June 2007 - June 2010. The prevalence of COPD was 12.9% and it was associated with increased heart failure hospitalization, major cardiovascular events but not mortality.

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