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Range and Severity of Symptoms Over Time Among Older Adults With Chronic Obstructive Pulmonary Disease and Heart Failure

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Abstract

Background—Symptoms are a central component of health status; however, little is known about the full range and trajectory of symptoms experienced by persons with chronic diseases other than cancer.

Methods—Observational cohort study with interviews performed at least every 4 months for up to 2 years among community-dwelling persons 60 years or older with chronic obstructive pulmonary disease (COPD) or heart failure (HF). Seven symptoms rated as absent, mild, moderate, or severe were assessed at each interview.

Results—Among the 79 participants with COPD, at least 50% reported shortness of breath, physical discomfort, fatigue, and problems with appetite and anxiety. Among the 59 participants with HF, at least 50% reported physical discomfort, fatigue, and problems with appetite at both their initial and final interviews. Both disease-specific and non-disease-specific symptoms increased in severity over time. The prevalence of individual symptoms did not differ according to whether the participants lived or died.

Conclusions—As a potentially modifiable contributor to poor health status, the high symptom burden among older persons with COPD and HF represents a large unmet need for improved symptom assessment and treatment. This need may not be met by current disease management guidelines, which focus on a small number of symptoms except for patients at the end of life.

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Symptoms are central to patients' subjective assessment of their health status and quality of life.¹ In less severe illness, symptoms shape how patients think about and experience their illness.² In more advanced disease, symptoms may have a profound effect on patients' lives as reflected in the association between certain symptoms and both will to live³ and desire for physician-assisted suicide.⁴ Despite this importance of symptoms to patients, little is known about the trajectory of a broad range of symptoms among persons with chronic disease. Disease management guidelines for chronic obstructive pulmonary disease (COPD) and heart failure (HF), 2 of the most prevalent chronic diseases among older persons, provide detailed strategies for managing symptoms. However, these guidelines have a narrow focus on symptoms that are considered to "belong" to an individual disease. For example, the Global Initiative for Chronic Obstructive Lung Disease guideline⁵ discusses management of dyspnea, cough, and sputum production. The American College of Cardiology Foundation and the American Heart Association guideline⁶ for HF focuses on the evaluation of dyspnea and fatigue. These guidelines consider only a broader range of symptoms among persons at the very end of life.^{5,6}

This focus on disease-specific symptoms may not adequately reflect the full burden of symptoms experienced by patients with these diseases. Several cross-sectional studies have demonstrated that patients experience a broader range of symptoms.^{4,7} However, little is known about the trajectory of these symptoms, with longitudinal studies focusing on patients at the end of life⁸ and including proxy reports of symptoms, which may not accurately represent the patient's symptom experience.⁹

We examined the prevalence and severity of a range of symptoms among a cohort of community-dwelling older persons with a principal diagnosis of COPD or HF over a 24-month time period and determined whether higher symptom burden was limited to persons at the very end of life.

METHODS

PARTICIPANTS

Participants were at least 60 years of age, resided in the community, and had a primary diagnosis of COPD or HF. We defined "primary diagnosis" by selecting individuals who met at least 1 of the criteria listed in Table 1 for advanced illness and who required assistance with at least 1 instrumental activity of daily living.¹⁰ This was accomplished by screening sequential medical charts, identified according to the person's age and documentation of a COPD or HF diagnosis. Medical charts were reviewed in the subspecialty outpatient practices in the greater New Haven, Connecticut, area and in 3 hospitals: a university teaching hospital, a community hospital, and a VA hospital. Of the 17 practices approached for participation, only 1 (6%) did not permit screening of medical charts.

Of the 371 persons identified by medical chart review, 20 were not contacted because their physicians did not give permission to do so, 22 died before the telephone screening was performed, 5 could not be reached, and 12 declined the telephone screening. A total of 70 persons were excluded because they required no assistance with instrumental activities of daily living, 60 because of cognitive impairment, and 2 because they were not full-time Connecticut residents. Of the 180 persons who were eligible for participation, 33 declined participation. Nonparticipants did not differ significantly from participants according to age or sex. Only 8% of eligible persons with HF declined participation compared with 25% of those with COPD ($P<.01$).

Of the 147 initial participants, 4 (3%) refused further participation after the baseline interview, 6 (4%) died after the baseline interview and before any additional information could be

obtained, 3 (2%) were too impaired to participate after the baseline interview, and 1 (1%) had missing symptom data at follow-up. These 14 participants (10%) were excluded from the present study, resulting in a cohort of 133 participants. Of the surviving 104 participants at the end of the first year of the study, 93 consented to a second year of participation, without any further losses to follow-up. Enrollment occurred from December 1999 to December 2000; follow-up was completed in December 2002. The human investigations committee of each site approved the study protocol. All participants provided written informed consent.

DATA COLLECTION

Skilled research nurses interviewed participants in the participant's home every 4 months for up to 24 months. A monthly telephone call screened for changes in health status that occurred after the completion of the previous interview. If a participant reported 1 of the following changes in status, a follow-up interview was performed immediately: (1) a new disability in an activity of daily living such as bathing, grooming, dressing, eating, transferring from a bed to chair, toileting, or walking across a room¹¹; (2) a hospitalization of at least 7 days or resulting in a discharge to nursing home or rehabilitation facility; or (3) initiation of hospice services. This strategy was designed to balance the burden associated with frequent interviews with the ability to interview participants as their illness worsened. The death of a participant was ascertained from a proxy during the monthly telephone call.

OUTCOME VARIABLES

Participants were asked to rate the severity of their symptoms using the Edmonton Symptom Assessment Scale,¹² a validated instrument for the assessment of symptoms in seriously ill persons.¹³ This scale asks participants to rate the intensity of 10 symptoms (physical discomfort, pain, fatigue, problems with appetite, feelings of depression, anxiety, shortness of breath, nausea, limited activity, and lack of well-being) during the previous 24 hours. We modified the original visual analog scale to a 4-point scale (not present, mild, moderate, or severe), thereby allowing participants to provide verbal rather than written responses.¹⁴ We solicited verbal responses because visual analog scales can be difficult for older persons to complete and verbal symptom measurements have been shown to correlate well with visual analog scale measurements.^{15,16}

We limited our analyses to the smallest number of potentially modifiable symptoms that retained the same information as the full set of symptoms. We excluded limited activity and lack of well-being because (1) they may not be modifiable and (2) they are more complex constructs that are the result of symptoms rather than symptoms in and of themselves. We also excluded nausea because 83% of the participants who reported nausea also reported problems with appetite, but only 15% of participants who reported problems with appetite also reported nausea. The prevalence of the remaining 7 symptoms was based on symptoms reported as mild, moderate, or severe. We created a composite measure of symptom burden by assigning values of 0, 1, 2, and 3 to the ratings of not present, mild, moderate, and severe, respectively, for each symptom at each participant interview, and summing these scores.

DESCRIPTIVE VARIABLES

Sociodemographic variables, health and functional status variables, and health care utilization were assessed at the baseline interview as obtained by participant self-report.

Sociodemographic variables included age, sex, and race or ethnicity. Health and functional status variables included self-rated health¹⁷ and activity of daily living status.¹¹ Health care utilization included number of hospitalizations in the prior 12 months. Comorbidity was determined by review of the participant's outpatient medical record for documentation of illnesses included in the Charlson Comorbidity Index¹⁸ other than primary diagnosis.

STATISTICAL ANALYSIS

We described participant characteristics, the prevalence of symptoms, and the severity of symptoms at baseline and in the final interview using univariate statistics. The final interview was defined as the last interview provided prior to the close of the study for survivors and the last interview provided prior to death for decedents. Using the McNemar test for paired data, we determined whether the prevalence of symptoms increased from baseline to final interview. We used the Bowker test for symmetry to compare the severity of symptoms at baseline and at the final interview. For these analyses, we combined the categories of symptoms rated as moderate and as severe. We used the χ^2 test to compare the prevalence of symptoms reported by survivors with the prevalence reported by decedents at the baseline interview.

Linear mixed-effects models, using the MIXED procedure in SAS statistical software (version 8.2; SAS Institute Inc, Cary, North Carolina), were used to examine the association among total symptom burden score and time, vital status, and comorbidity burden (measured as the total number of comorbidities) using data collected at each interview. These models were adjusted for age, sex, race, and number of hospitalizations in the year prior to enrollment.

RESULTS

DESCRIPTION OF POPULATION

At baseline, the 133 participants had a mean (SD) age of 73 (7) years. There were 74 participants with a primary diagnosis of COPD and 59 with a primary diagnosis of HF. More than 90% of the participants were white, 44% were female, and more than 30% died. Participant characteristics according to diagnosis are presented in Table 2. Among participants with COPD, the median length of follow-up for survivors was 22 months (inter-quartile range [IQR], 12–24) and 8 months (IQR, 5–12) for decedents. The median length of follow-up among participants with HF was 22 months (IQR, 21–24) for survivors and 8 months (IQR, 4–15) for decedents.

SYMPTOM PREVALENCE

In the final interview, virtually all participants with COPD reported shortness of breath, physical discomfort, and fatigue. Four additional symptoms (problems with appetite, anxiety, pain, and feelings of depression) were reported by approximately one-half of participants with COPD. With the exception of fatigue ($P<.001$) and depression ($P<.001$), which both increased significantly over time, all symptoms were equally prevalent in the initial and final interviews.

Among participants with HF, most reported physical discomfort and fatigue in the final interview. An additional 3 symptoms (shortness of breath, problems with appetite, and pain) were reported by approximately two-thirds of participants. Between one-third and one-half of participants reported anxiety and feelings of depression in the final interview. The percentage of participants reporting shortness of breath ($P=.03$), fatigue ($P=.02$), pain ($P=.003$), and feelings of depression ($P=.003$) increased significantly over time ($P<.05$). The remaining symptoms were as prevalent in the initial interview as they were in the final. The prevalence of symptoms at the baseline interview among those who survived throughout the study period did not differ significantly from the prevalence among those who died (see Table 3 for P values).

SYMPTOM SEVERITY AND BURDEN OVER TIME

In addition to being highly prevalent, many symptoms were rated as moderate or severe by substantial percentages of participants, at both the baseline and final interviews (Table 4). Among participants with COPD, fatigue showed the greatest increase in severity over time; 19% reported mild fatigue and 50% reported severe fatigue at the initial interview, whereas

30% reported mild fatigue and 62% reported moderate or severe fatigue at the final interview ($P=.001$). Among participants with HF, pain showed the greatest increase in severity over time. The percentage of participants reporting mild pain did not differ at the initial and final interviews, but the percentage reporting moderate or severe pain increased from 20% to 42% ($P=.02$).

We examined the association among total symptom burden and months in the study, count of comorbidities, and whether the participant lived or died using linear mixed-effects models. For participants with COPD, symptom burden increased significantly over time ($\beta=0.06$ [95% CI, 0.01–0.10]; $P=.008$) (CI indicates confidence interval), with the mean symptom burden higher among those who died, although this failed to reach statistical significance ($\beta=1.34$ [95% CI, –0.15 to 2.84]; $P=.08$). Symptom burden was not associated with number of comorbidities. For participants with HF, symptom burden increased over time ($\beta=0.04$ [95% CI, –0.01 to 0.09]; $P=.15$) and with greater number of comorbidities ($\beta=0.52$ [95% CI –0.17 to 1.21]; $P=.14$), although these failed to reach statistical significance. Symptom burden was not associated with whether the participant died.

COMMENT

In this cohort of community-dwelling older persons with advanced COPD and HF followed for up to 2 years, the prevalence of both symptoms considered to be disease specific, such as shortness of breath, and symptoms not considered to be disease specific, such as pain and physical discomfort, was extremely high among both those who lived and those who died. Although the prevalence of certain symptoms increased over time, many symptoms were as highly prevalent at the beginning as at the end of the study period. Both disease-specific and non-disease-specific symptoms increased in severity over time.

We previously reported the burden of symptoms in this cohort of persons with advanced disease as assessed at the time of participants' enrollment into the study.⁷ This prior cross-sectional analysis showed that the symptom burden was high, but the full nature of patients' experience with symptoms could be delineated only by following participants over time. Because the eligibility criteria for participation are associated with limited life expectancy, we could not know at the beginning of the study that we had in fact enrolled a heterogeneous group of patients in terms of where they were in the trajectory of their illness. The findings that the prevalence of symptoms did not differ according to whether the patient died and that many of the symptoms were as highly prevalent at the start of the study as at a point 2 years later in the course of the patient's illness highlight the conclusion that the experience of a diverse range of symptoms is not limited to those patients who are at the end of their lives but rather is a part of patients' disease course over longer periods of time.

There are at least 2 explanations for the range of symptoms experienced by this cohort. One is that COPD and HF produce a broader range of symptoms than presently addressed in disease management guidelines, and the second is that the symptoms are a result of participants' multiple coexisting conditions. It is likely that both explanations contributed to the symptom burden of participants in this study. Prior cross-sectional studies of persons with COPD⁷ and HF⁷ have demonstrated that these individuals experience many symptoms in addition to the dyspnea and cough that are the focus of guidelines, including depression, anxiety, and fatigue. Although the association between number of comorbidities and total symptom burden among persons with HF did not reach statistical significance, the present study provides preliminary evidence for a relationship between comorbidities and symptoms.

It could be argued, given the association between time and increasing total symptom burden, that symptoms are an inevitable part of the disease process and progression. However, each of

the symptoms examined is potentially modifiable. Prior progress in the recognition and treatment of symptoms effectively illustrates the improvements that can be achieved through the use of targeted interventions. In the case of pain, for example, consensus-based guidelines outline approaches to treatment¹⁹ that can effectively relieve the pain of most patients with cancer.²⁰ Although a substantial proportion of patients with cancer continue to experience pain, the principle guiding responses to this finding is that pain represents an unmet need rather than an inevitable and untreatable part of the disease. Research has focused on determining modifiable barriers to effective pain management, including inadequate pain assessment and treatment,²¹ and interventions providing standardized approaches to assessment and treatment have been shown to improve cancer pain control.²² Although currently there are fewer effective therapeutic options for symptoms other than pain for patients with noncancer diagnoses, this lack of interventions may reflect the inadequate attention paid to developing therapies for these symptoms²³ rather than the impossibility of treating these symptoms. One small study²⁴ demonstrated the effectiveness of a consultative team providing formal symptom assessment and intervention in reducing shortness of breath and anxiety among patients with advanced HF, COPD, and cancer. In addition, the finding that symptoms tend to occur in clusters suggests that successful treatment of one symptom may also help to improve additional symptoms.²⁵ Taken together, such findings argue that the symptom burden demonstrated in this population is a measure of participants' unmet need for improved symptom control.

There are several limitations related to the study population and its measures. Our ability to detect meaningful differences in symptom prevalence and severity may have been limited by our small sample size, despite using repeated measures. In addition, the small number of non-white participants enrolled may limit the generalizability of our results. Moreover, the ascertainment of comorbidities did not include those illnesses that, although they may not be highly associated with mortality, may be highly symptomatic, such as osteoarthritis. When such diseases have been included in prior studies, the burden of comorbidity was higher than what is described in the current study.⁸ This may have limited our ability to detect an association between comorbidities and symptom burden.

The results of this study, demonstrating that large proportions of patients with COPD and HF have a broad range of symptoms over an extended time period, suggest that current individual disease management guidelines, which include only a narrow range of symptoms except for persons at the end of life, may not be sufficient to address this symptom burden. Symptoms provide an integrated, clinically relevant measure of a person's health status as it is affected by multiple diseases and interventions. However, unless investigations include a range of symptoms, the associations between less-studied symptoms and health outcomes may not become apparent. We previously reported that physical discomfort and feelings of depression were associated with important health outcomes, namely, self-rated health, functional disability, and quality of life.¹ Thus, physicians may need to adopt an expanded treatment approach to achieve improved symptom palliation for persons with chronic disease. Moreover, further research is warranted to determine the effect of interventions designed to address a wider range of symptoms on health outcomes for persons with COPD and HF.

The broad range of symptoms experienced by older patients with HF and COPD over an extended period of time calls for a research agenda to determine modifiable barriers to effective symptom management in chronic disease. Modeled on the research performed among patients with cancer, this agenda would include investigation of the frequency and nature of symptom assessment among older persons with chronic disease, use of existing strategies to address symptoms, and development of new strategies. Concomitant with this effort, utilization of the existing evidence for effective assessment and treatment of symptoms needs to become an integral component of the care of all older persons with chronic diseases.

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Table 1**Eligibility Criteria**

Disease	Criteria
COPD	Bed-to-chair functional status Hospitalization within the past 6 months with breathlessness, respiratory failure, or mental status change as the main reason for hospital admission and $PO_2 \leq 60$ and $PCO_2 \geq 50$ (or oxygen saturation $\leq 90\%$) if patient is breathing room air or $PCO_2 \geq 50$ if patient is receiving supplemental oxygen Having any 2 of the following $PCO_2 \geq 45$ or oxygen saturation $\leq 90\%$ if breathing room air Cor pulmonale Forced expiratory volume in 1 s < 0.5 L Polycythemia (hematocrit $> 53\%$)
HF	NYHA class III or IV and use of at least 2 of the following classes of medications: diuretics, inotropics, ACE inhibitors, or other vasodilators Left ventricular ejection fraction $\leq 20\%$ and use of at least 2 of the same classes of medications Hospitalization and NYHA class IV at the time of hospital admission or intensive care unit transfer manifested by baseline dyspnea at rest, systolic BP ≤ 100 , or hypotension that excluded use of cardiac medications

Abbreviations: ACE, angiotensin-converting enzyme; BP, blood pressure; COPD, chronic obstructive pulmonary disease; HF, heart failure; NYHA, New York Heart Association; PCO_2 , carbon dioxide pressure; PO_2 , oxygen pressure.

Table 2Baseline Description of 133 Participants^a

Characteristic	COPD Group (n = 74)	HF Group (n = 59)
Age, mean (SD), y	72 (7)	75 (8)
Education, mean (SD), y	11 (3)	12 (3)
Female, %	50	37
White	92	90
Married	53	54
≥1 ADL disability	43	34
≥2 Hospitalizations in prior 12 mo	51	61
Comorbidity count		
0	55	17
1	27	32
2	16	27
3	1	19
4	0	5
Comorbidities		
COPD	NA	31
HF	19	NA
Diabetes mellitus	10	42
Myocardial infarction	5	32
Cancer	18	17
Peripheral vascular disease	4	17
Stroke	3	12
Renal disease	0	7
Peptic ulcer disease	0	5
Liver disease	0	2
Deceased at end of study	39	46

Abbreviations: ADL, activity of daily living; COPD, chronic obstructive pulmonary disease; HF, heart failure; NA, not applicable.

^aData are given as percentages unless indicated otherwise.

Table 3
Symptom Prevalence in the Baseline Interview According to Whether the Participant Died During Follow-up^a

Symptom	COPD			HF		
	Survivors (n = 45)	Decedents (n = 29)	P Value	Survivors (n = 32)	Decedents (n = 27)	P Value
Shortness of breath	93	100	.16	44	48	.74
Physical discomfort	78	79	.88	75	70	.69
Fatigue	69	69	.99	69	74	.65
Problems with appetite	47	55	.48	59	63	.78
Anxiety	44	55	.37	28	11	.11
Pain	49	41	.53	44	48	.74
Feelings of depression	29	31	.84	22	19	.75

Abbreviations: COPD, chronic obstructive pulmonary disease; HF, heart failure.

^aData are given as percentages.

Table 4
Participants With Mild and Moderate to Severe Symptoms at Baseline and Final Interview^a

Symptom	COPD			HF		
	Baseline	Final	P Value	Baseline	Final	P Value
Shortness of breath						
Absent	4	5		54	37	
Mild	30	19		27	34	
Moderate or severe	66	76	.36	19	29	.08
Physical discomfort						
Absent	22	16		27	19	
Mild	36	46		44	47	
Moderate or severe	42	38	.39	29	34	.72
Fatigue						
Absent	31	8		29	14	
Mild	19	30		27	39	
Moderate or severe	50	62	.001	44	47	.13
Problems with appetite						
Absent	50	43		39	39	
Mild	41	38		49	42	
Moderate or severe	9	19	.16	12	19	.57
Anxiety						
Absent	51	46		80	69	
Mild	16	31		19	19	
Moderate or severe	32	23	.02	2	12	.06
Pain						
Absent	54	51		54	31	
Mild	19	28		25	27	
Moderate or severe	27	20	.26	20	42	.02
Feelings of depression						
Absent	70	45		80	58	
Mild	14	38		14	31	
Moderate or severe	16	18	.003	7	12	.03

Abbreviations: COPD, chronic obstructive pulmonary disease; HF, heart failure.

^aData are given as percentages unless indicated otherwise.