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Diagnosis of COPD and clinical course in patients with unrecognized airflow limitation

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Abstract: Chronic obstructive pulmonary disease (COPD) is frequently under-recognized and underdiagnosed. To determine the natural history of recognized and unrecognized COPD, we studied the rate of diagnosis, health care utilization, and mortality in patients with airflow limitation (AFL). Three hundred forty-seven outpatients at the Cincinnati Veterans Administration Medical Center performed spirometry and completed a respiratory questionnaire. Patients were followed for a minimum of 30 months and medical records were reviewed for COPD diagnosis, mortality, respiratory-related health care utilization, comorbidities, and respiratory medications. Three hundred twenty-five of 347 (94%) patients performed technically adequate spirometry and completed questionnaires. When AFL was defined by fixed ratio (FR, forced expiratory volume in 1 second [FEV_1]/forced vital capacity [FVC] < 0.7), patients with AFL and a diagnosis of COPD had a higher annual mortality rate (7.1% ± 2% versus 2.4% ± 0.8%, $P = 0.01$), more hospitalizations per year (0.2 ± 0.06 versus 0.04 ± 0.01, $P < 0.001$ mean ± standard error of the mean), increased respiratory symptoms (12.0 ± 0.9 versus 7.2 ± 0.6, $P < 0.0001$), and higher Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage compared with undiagnosed patients. Ninety-two of 137 patients with AFL (67%) had unrecognized AFL; 16 (17%) of the 92 were subsequently diagnosed. When AFL was defined by the lower limit of normal (LLN, FEV_1/FVC < LLN), 67 of 103 patients (65%) had unrecognized AFL; 12 (18%) of the 67 were subsequently diagnosed. Patients with AFL defined by FR who were subsequently diagnosed had more emergency department visits per year (0.33 ± 0.11 versus 0.11 ± 0.05, $P = 0.009$), increased respiratory symptoms (10.2 ± 1.6 versus 6.5 ± 0.7, $P < 0.05$), and higher GOLD stage, but similar mortality and hospitalizations compared with the persistently undiagnosed patients. The annual rate of documented COPD diagnosis was 7% for both FR and LLN definitions. Patients with AFL and a diagnosis of COPD have more severe disease, higher health care utilization, and mortality than undiagnosed patients. The annual rate of COPD diagnosis is 7% among individuals with unrecognized AFL. Worse AFL, increased respiratory symptoms, and ED visits are associated with a subsequent COPD diagnosis in individuals with unrecognized AFL.

Keywords: COPD, diagnosis, airflow limitation, Veterans Healthcare Administration

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Introduction

Deaths due to chronic obstructive pulmonary disease (COPD) have been increasing and COPD became the third leading cause of death in the United States in 2009.[1–8] COPD occurs commonly in the general US population and among veterans cared for by the Veterans Healthcare Administration (VHA). The Third National Health and Nutrition Examination Survey (NHANES III) estimated COPD prevalence to be 6.8%–

8.5% within the general US population.[3] Among veterans hospitalized in the VHA in 2005, COPD was the fourth most common discharge diagnosis; approximately one third of patients and one sixth of all inpatients had a diagnosis of COPD.[9] In a utilization review study from 1996 to 2001, 19% of men and 17% of women in the VHA were diagnosed with COPD.[9] We performed spirometry in a randomly selected group of veterans at the Cincinnati Veterans Administration Medical Center (VAMC) and showed that the prevalence of airflow limitation (AFL) was 33%–43% and that COPD was dramatically underdiagnosed by both health care providers and patients.[10]

Between 52%–91% of individuals with AFL are not diagnosed with COPD because individuals with minimal or no respiratory symptoms are frequently not assessed by pulmonary function testing.[11–15] Recent epidemiologic studies have shown poorer outcomes based on declines in forced expiratory volume in 1 second (FEV_1), inflammatory markers, lower respiratory tract infections, and increases in the Body-mass, airflow Obstruction, Dyspnea and Exercise (BODE) index in patients with known AFL.[15–20] However, few investigations have measured the outcomes among individuals with unrecognized AFL and the clinical factors that stimulate clinicians to make a diagnosis of COPD. Therefore, we studied the rate of COPD diagnosis, health care utilization, and mortality in patients with unrecognized AFL.

Materials and methods

Subjects were recruited from the outpatient waiting area of the Cincinnati VAMC. The waiting area provided a sample of patients awaiting primary care, mental health, and pharmacy, as well as medical and surgical subspecialty appointments. Patients were recruited in random, chronological order and spirometry was performed according to the 1994 American Thoracic Society guidelines.[21] Each participant completed a questionnaire about smoking habits, occupational exposures, respiratory diagnoses, and symptoms.[10] AFL was defined by either fixed ratio (FR), the ratio of FEV_1 to the forced vital capacity (FVC), <0.70 or lower limit of normal (LLN), $FEV_1/FVC < LLN$ as determined by NHANES III.[22] Severity of COPD was determined by the modified Global Initiative for Chronic Obstructive Lung Disease (GOLD) definitions: GOLD stage 1: pre-bronchodilator $FEV_1\% > 80\%$ of predicted; GOLD stage 2: pre-bronchodilator $FEV_1\%$ 50%–80% of predicted; GOLD stage 3: pre-bronchodilator $FEV_1\%$ 30%–50% of predicted; GOLD stage 4: pre-bronchodilator $FEV_1\% < 30\%$ of predicted.[23]

The Cincinnati VAMC utilizes a comprehensive electronic medical record (EMR) that includes a complete problem list. Patients with a diagnosis of COPD, emphysema, or chronic bronchitis in their problem list and spirometric evidence of AFL by either FR or LLN at the time of recruitment were labeled "previously diagnosed." Patients with AFL who had a diagnosis of COPD, emphysema, or chronic bronchitis entered into their problem list after the original study were termed "subsequently diagnosed," and those with AFL who were never diagnosed with COPD, emphysema, or chronic bronchitis were labeled "persistently undiagnosed." Patients with $FVC < 80\%$ of predicted without AFL were classified as "restricted." Those individuals without AFL and an $FVC \geq 80\%$ of predicted were categorized as "normal."

We reviewed patients' medical records and recorded information regarding current COPD diagnosis, active respiratory medications, BMI, cardiac comorbidities, vital status, emergency department (ED) visits, and hospital admissions caused by respiratory symptoms. Cardiac related comorbid diagnoses included atrial fibrillation, systolic or diastolic congestive heart failure, and coronary artery disease.

The date of each patient's recruitment was recorded as well as date of death where applicable. The duration of follow-up for patients who survived to the end of the study ranged from 32 to 53 months. Each patient's outcomes were normalized to determine the annual rate for each measured parameter.

Patients with no EMR notes for more than 1 year after recruitment and were not recorded as deceased were considered lost to follow-up and excluded. Patients with a diagnosis of COPD in the EMR but no AFL on spirometry were also excluded (Figure 1).

All quantitative variables are described using appropriate summary statistics (mean, median, and standard deviation); categorical variables are presented using frequency and proportions. Graphs were produced using Excel software (Microsoft Corporation, Redmond, WA, USA). Statistical analysis was performed using Fisher's and Student's *t*-tests.[24] Significance was set at $P < 0.05$.

The study protocol was approved by the Cincinnati VAMC Research and Development Committee and the University of Cincinnati Institutional Review Board. Informed consent and Health Information Portability

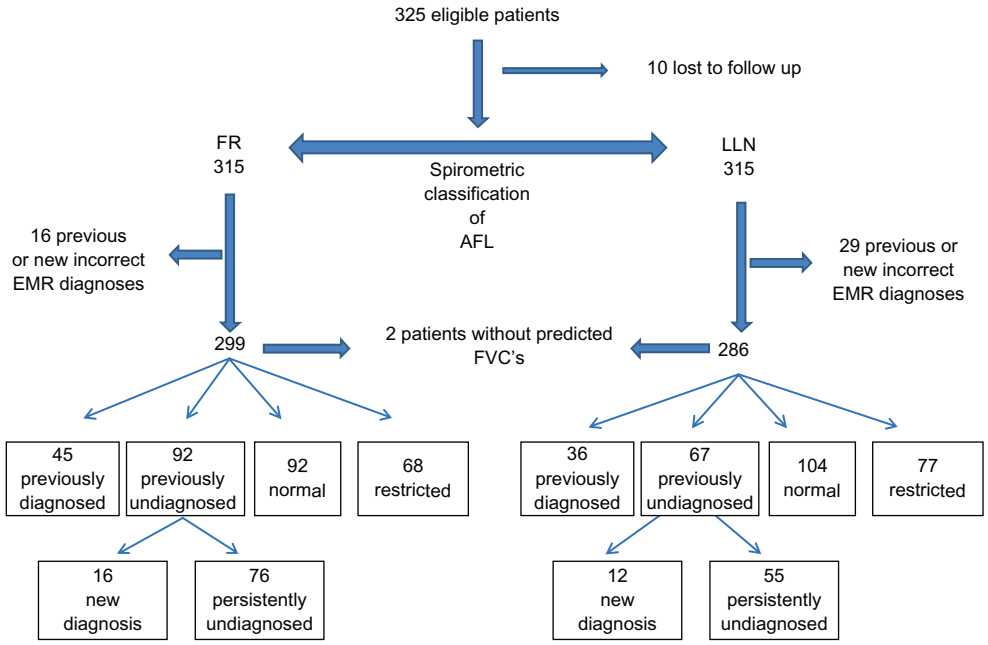

Figure 1 Flow diagram of cohort analyzed using FR ($FEV_1/FVC < 0.7$) and LLN ($FEV_1/FVC <$ LLN).
Notes: Three hundred twenty-five of the original 347 patients were eligible based on adequate spirometry. Patients were divided into subgroups based on spirometry and diagnosis of COPD recorded in the EMR problem list at time of recruitment. Patients with a COPD diagnosis in their medical record who did not have AFL based on spirometry were removed from analysis.
Abbreviations: AFL, airflow limitation; COPD, chronic obstructive pulmonary disease; EMR, electronic medical record; FEV_1, forced expiratory volume in 1 second; FR, fixed ratio; FVC, forced vital capacity; LLN, lower limit of normal.

and Accountability Authorization were obtained from all participants prior to enrollment.

Results

Ninety-four percent of patients performed adequate spirometry and completed questionnaires. The charts of these patients were reviewed and only ten patients (3%) were lost to follow-up. One patient who had AFL by both FR and LLN had an accurate diagnosis of COPD deleted from the medical record and was removed from the analysis. In addition, 16 patients were misdiagnosed with COPD using FR and 29 patients were misdiagnosed by LLN. These patients with a chart diagnosis of COPD that was not supported by AFL on spirometry were excluded. Additionally, two patients without AFL were eliminated from analysis because they did not have predicted FVC values (Figure 1).

The percentage of patients defined as normal, restricted, previously diagnosed, subsequently diagnosed, and persistently undiagnosed were similar regardless of whether the FR or LLN definition of AFL was used. The demographics, respiratory symptoms, health care utilization, and mortality for these groups are presented in Table 1 and Figures 2–5.

When AFL was defined by FR, patients with AFL and a diagnosis of COPD had a higher annual mortality rate, more annual hospitalizations, increased respiratory symptoms, and higher GOLD stage compared with those who did not have a COPD diagnosis (Table 1). Respiratory medications were more frequently prescribed for individuals with AFL and a diagnosis of COPD than for those who were not diagnosed with COPD (Table 1). Similar findings were present when AFL was defined by LLN.

A similar percentage of patients with AFL as defined by FR or LLN were previously undiagnosed with COPD; and a similarly low percentage of patients with AFL as defined by FR or LLN (17% and 18%, respectively) were subsequently diagnosed with COPD. The annual COPD diagnostic rate was 7% regardless of which AFL definition was used. Those individuals with AFL who were subsequently diagnosed with COPD had more respiratory symptoms, greater proportion of GOLD stage 3 and 4, higher respiratory medication use, and more ED visits than those who were persistently undiagnosed (Table 1).

Table 2 compares the persistently undiagnosed group to the normal patients included in this study. The persistently undiagnosed group was older and had more respiratory symptoms and lower FEV_1 than the normal population. However, despite these initial differences, there were no differences in subsequent health care utilization or mortality.

Table 1 Comparisons of all subsets of diseased patients by age, BMI, baseline pulmonary data, and prescription medications, as well as clinical outcome data using health care utilization and mortality

	AFL definition										
	FR						LLN				
	COPD diagnosed	COPD not diagnosed	*P*-value	COPD subsequently diagnosed	COPD persistently undiagnosed	*P*-value	COPD diagnosed	COPD not diagnosed	*P*-value	COPD subsequently diagnosed	COPD persistently undiagnosed	*P*-value
n	45	92		16	76		36	67		12	55	
Age (mean ± SEM)	66.1 ± 1.7	62.1 ± 1.16	0.05	58.9 ± 3	62.8 ± 1.25	0.2	64.9 ± 1.8	59.6 ± 1.3	0.02	56.6 ± 3	60.2 ± 1.4	0.28
Symptom score (mean ± SEM)	12.0 ± 0.9	7.15 ± 0.64	<0.001	10.2 ± 1.6	6.5 ± 0.7	0.03	12.5 ± 1.0	8.1 ± 0.8	0.001	11.1 ± 2.1	7.45 ± 0.8	0.07
BMI (mean ± SEM)	26.5 ± 1.0	28.3 ± 0.7	0.01	30.2 ± 2.4	27.9 ± 0.7	0.22	25.4 ± 1.1	28.9 ± 0.9	0.02	31.2 ± 3.1	27.9 ± 0.8	0.14
FEV_1 (mean ± SEM)	1.7 ± 0.09	2.27 ± 0.06	<0.001	2.1 ± 0.16	2.3 ± 0.07	0.24	1.5 ± 0.09	2.2 ± 0.08	<0.001	2.0 ± 0.18	2.24 ± 0.08	0.9
Modified GOLD class (n [%])												
1	3 (6)	22 (24)	0.017	2 (13)	20 (26)	0.34	1 (3)	14 (21)	0.02	2 (17)	12 (21)	1.0
2	22 (48)	57 (62)	0.2	8 (50)	49 (64)	0.40	15 (42)	42 (63)	0.06	5 (42)	37 (65)	0.11
3	14 (30)	12 (13)	0.02	6 (38)	6 (7.9)	0.006	13 (36)	10 (15)	0.02	5 (42)	5 (9)	0.01
4	7 (15)	1 (1)	0.002	0	1 (1.3)	1.0	7 (19)	1(1)	0.003	0	1 (2)	1.0
Cardiovascular disease	17 (37)	29 (32)	0.56	4 (25)	25 (33)	0.77	15 (42)	21 (31)	0.39	3 (25)	18 (32)	0.74
Medications (n [%])												
SABA	35 (78)	21 (23)	<0.001	8 (50)	13 (17)	0.008	29 (81)	18 (27)	<0.001	7 (58)	11 (19)	0.01
LABA	15 (33)	6 (7)	<0.001	5 (31)	1 (1)	<0.001	13 (36)	6 (9)	0.001	5 (42)	1 (2)	<0.001
SA antichol	22 (49)	10 (11)	<0.001	3 (19)	7 (9)	0.37	18 (50)	8 (12)	<0.001	2 (17)	6 (11)	0.63
LA antichol	6 (13)	4 (4)	0.35	4 (25)	0	<0.001	5 (14)	4 (6)	0.27	4 (33)	0	<0.001
ICS	12 (27)	2 (3)	<0.001	0	2 (3)	1.0	12 (33)	2 (3)	<0.001	0	2 (4)	1.0
Health care utilization												
ED visits/pt/yr (mean ± SEM)	0.26 ± 0.06	0.15 ± 0.03	0.07	0.33 ± 0.11	0.11 ± 0.05	0.009	0.21 ± 0.06	0.17 ± 0.04	0.57	0.31 ± 0.15	0.13 ± 0.04	0.11
Admissions/pt/yr (mean ± SEM)	0.2 ± 0.06	0.04 ± 0.01	<0.001	0.04 ± 0.04	0.04 ± 0.02	1.0	0.24 ± 0.07	0.05 ± 0.02	0.001	0.06 ± 0.05	0.04 ± 0.14	0.95
Annual mortality (% dead/yr ± SEM)	7.1 ± 2	2.4 ± 0.8	0.01	1.8 ± 2.4	2.6 ± 0.9	0.72	9.1 ± 2.3	1.9 ± 0.8	<0.001	2.1 ± 2	1.9 ± 0.9	0.93

Notes: AFL as defined by FR: FR = FEV_1/FVC < 0.70. AFL as defined by LLN: (FEV_1/FVC)/LLN < 1.0. Statistical analysis was performed using Fisher's and Student's *t*-test.

Abbreviations: AFL, airflow limitation; BMI, body mass index; COPD, chronic obstructive pulmonary disease; ED, emergency department; FEV_1, forced expiratory volume in 1 second; FR, fixed ratio; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; ICS, inhaled corticosteroid; LA antichol, long acting anticholinergic; LABA, long acting beta agonist; LLN, lower limit of normal; pt, patient; SA antichol, short acting anticholinergic; SABA, short acting beta agonist; SEM, standard error of the mean; yr, year.

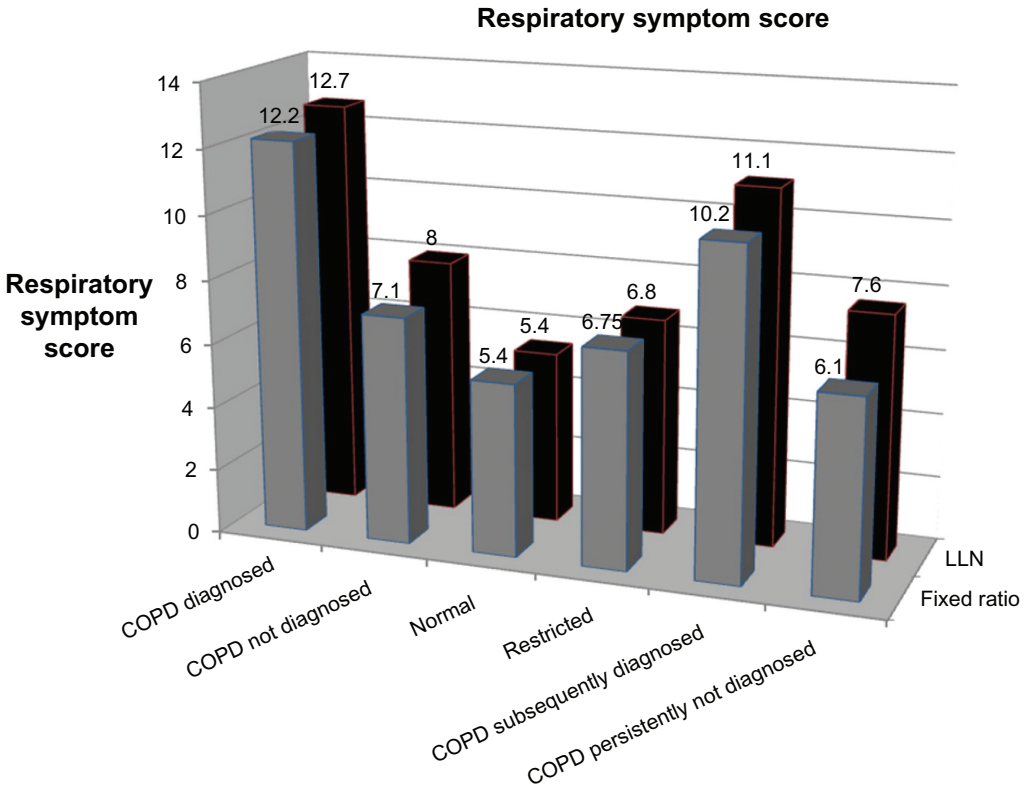

Figure 2 Mean symptom scores of study subjects showing spirometric classification, and diagnostic status.
Abbreviations: COPD, chronic obstructive pulmonary disease; LLN, lower limit of normal.

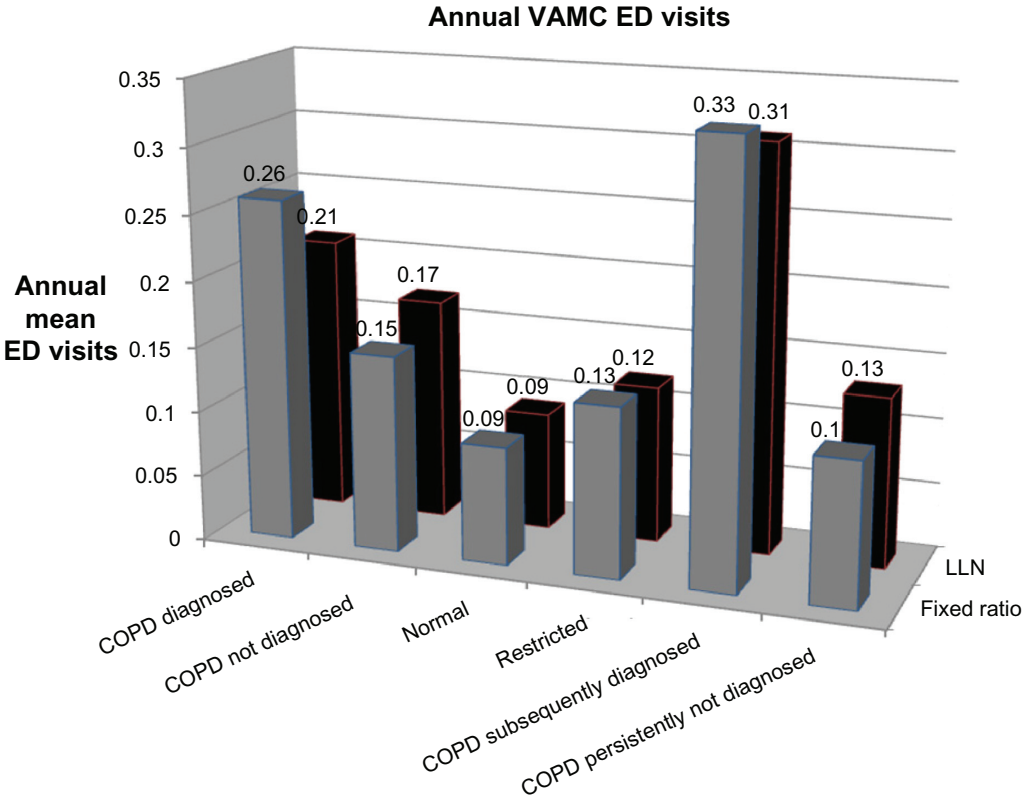

Figure 3 Mean number of annual emergency department visits per patient.
Abbreviations: COPD, chronic obstructive pulmonary disease; ED, emergency department; LLN, lower limit of normal; VAMC, Veterans Administration Medical Center.

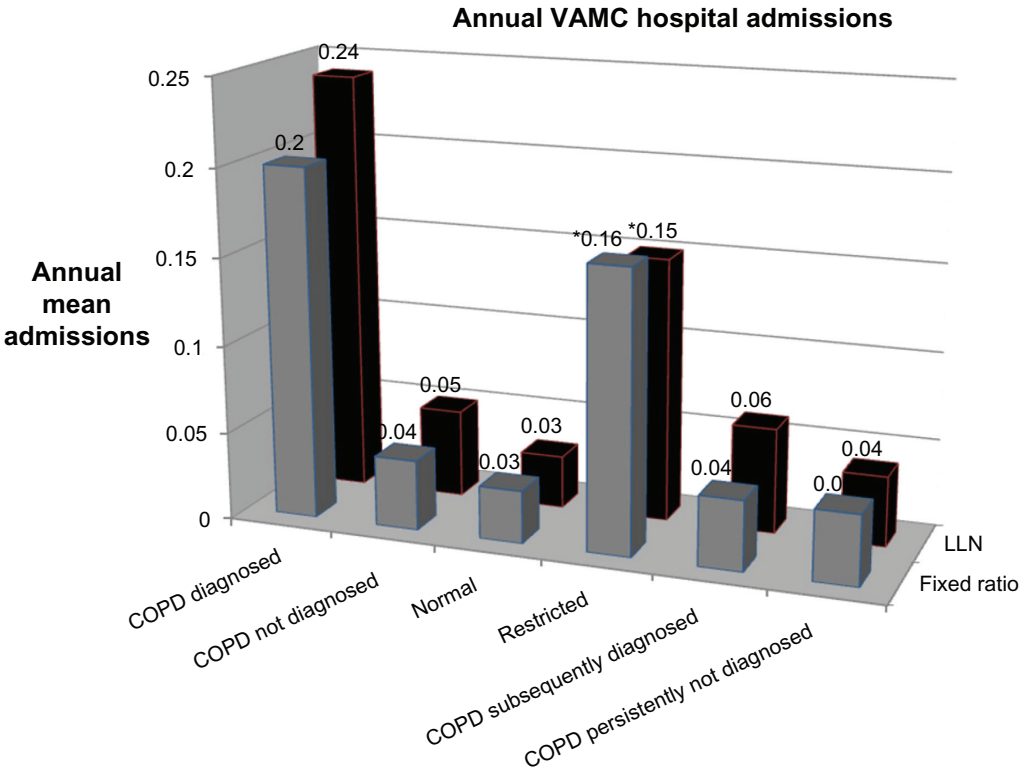

Figure 4 Mean number of annual hospitalizations per patient.
Notes: *One patient had four admissions during the 6 months after the recruitment period prior to his death, contributing half of all admissions for the entire group. Data presented for completeness; without this outlier the restricted population values are similar to that of the normal population.
Abbreviations: COPD, chronic obstructive pulmonary disease; LLN, lower limit of normal; VAMC, Veterans Administration Medical Center.

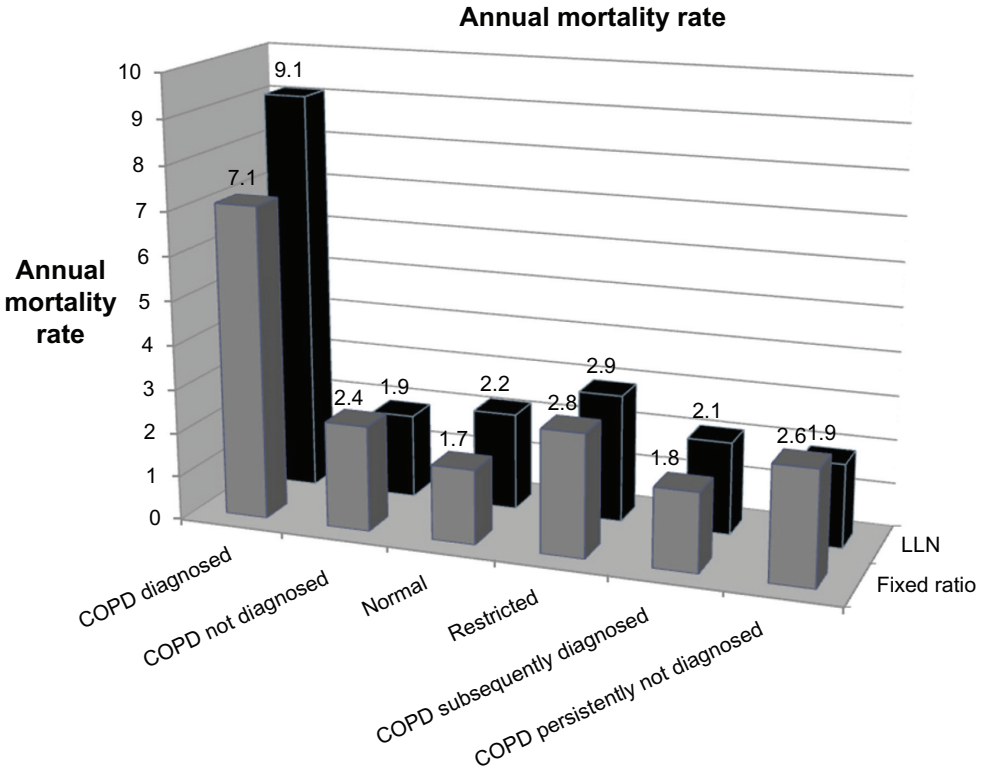

Figure 5 Annual mortality rate during study period.
Abbreviations: COPD, chronic obstructive pulmonary disease; LLN, lower limit of normal.

Table 2 Comparisons of diseased patients without a documented diagnosis of COPD and patients with normal spirometry

	Definition of AFL					
	FR			LLN		
	Normal	COPD persistently undiagnosed	*P*-value	Normal	COPD persistently undiagnosed	*P*-value
n	92	76		104	55	
Age (mean ± SEM)	55.1 ± 1.22	62.8 ± 1.25	<0.001	56.6 ± 1.2	60.2 ± 1.4	0.07
Symptom score (mean ± SEM)	4.9 ± 0.55	6.5 ± 0.7	0.07	4.8 ± 0.54	7.45 ± 0.8	0.006
BMI (mean ± SEM)	30.4 ± 0.67	27.9 ± 0.7	0.01	30 ± 0.6	27.9 ± 0.8	0.04
FEV_1 (mean ± SEM)	3.3 ± 0.06	2.3 ± 0.07	<0.001	3.24 ± 0.06	2.24 ± 0.08	<0.001
Cardiovascular disease	15 (16)	25 (33)	0.02	16 (15)	18 (32)	0.015
Health care utilization						
ED visits/year (mean ± SEM)	0.09 ± 0.04	0.11 ± 0.05	0.75	0.09 ± 0.03	0.13 ± 0.04	0.43
Hospitalizations/year (mean ± SEM)	0.03 ± 0.02	0.04 ± 0.02	0.73	0.03 ± 0.02	0.04 ± 0.14	0.92
Annual mortality (% dead/year ± SEM)	1.7 ± 0.7	2.6 ± 0.9	0.42	2.2 ± 0.8	1.9 ± 0.9	0.82

Notes: AFL as defined by FR: FR = $FEV_1/FVC < 0.70$. AFL as defined by LLN: $(FEV_1/FVC)/LLN < 1.0$.
Abbreviations: AFL, airflow limitation; BMI, body mass index; COPD, chronic obstructive pulmonary disease; ED, emergency department; FEV_1, forced expiratory volume in 1 second; FR, fixed ratio; FVC, forced vital capacity; LLN, lower limit of normal; SEM, standard error of the mean.

Although hospital admissions occurred most frequently in patients with a diagnosis of COPD, ED visits were greatest among those individuals who were subsequently diagnosed with COPD (Figures 3 and 4). The annual mortality rate was greatest for those patients with a previous diagnosis of COPD: 7.1% for FR and 9.1% for LLN (Figure 5).

Fifty-four percent of the participants did not have AFL by FR and 63% did not have AFL by LLN. Of the patients without AFL, 43% had an FVC < 80% of predicted,

Table 3 Comparisons of patients with decreased FVC (restricted) and normal spirometry

	Definition of AFL					
	FR			LLN		
	Normal	Restriction	*P*-value	Normal	Restriction	*P*-value
n	92	68		104	77	
Age (mean ± SEM)	55.1 ± 1.22	64.1 ± 1.4	<0.001	56.6 ± 1.2	64.9 ± 1.3	<0.001
Symptom score (mean ± SEM)	4.9 ± 0.55	6.4 ± 0.7	0.09	4.8 ± 0.54	6.1 ± 0.64	0.12
BMI (mean ± SEM)	30.4 ± 0.67	31 ± 0.9	0.6	30 ± 0.6	30.9 ± 0.82	0.37
FVC (mean ± SEM)	4.3 ± 0.08	3.0 ± 0.07	<0.001	4.3 ± 0.08	3.0 ± 0.07	<0.001
FEV_1 (mean ± SEM)	3.3 ± 0.06	2.3 ± 0.06	<0.001	3.24 ± 0.06	2.29 ± 0.06	<0.001
Cardiovascular disease	15 (16)	29 (43)	<0.001	16 (15)	35 (45)	<0.001
Health care utilization						
ED visits/year (mean ± SEM)	0.09 ± 0.04	0.13 ± 0.03	0.45	0.09 ± 0.03	0.12 ± 0.03	0.49
Hospitalizations/year (mean ± SEM)	0.03 ± 0.02	0.16 ± 0.12	0.22	0.03 ± 0.02	0.15 ± 0.11	0.22
Annual mortality (% dead/year ± SEM)	1.7 ± 0.7	2.8 ± 1	0.35	2.2 ± 0.8	2.89 ± 1	0.59

Notes: AFL as defined by FR: FR = $FEV_1/FVC < 0.70$. AFL as defined by LLN: $(FEV_1/FVC)/LLN < 1.0$.
Abbreviations: AFL, airflow limitation; BMI, body mass index; ED, emergency department; FEV_1, forced expiratory volume in 1 second; FR, fixed ratio; FVC, forced vital capacity; LLN, lower limit of normal; SEM, standard error of the mean.

regardless of the AFL definition, and were categorized as restricted. Patients with restriction were older and had a greater prevalence of cardiovascular disease than patients with normal spirometry (Table 3).

Discussion

Most studies have measured the diagnosis of COPD among patients at risk or with known comorbidities, but our study provides a unique opportunity to determine the rate of COPD diagnosis in a group of undiagnosed patients with AFL.[25–27] Approximately 7% of patients with AFL were diagnosed with COPD annually and these patients had greater respiratory symptoms, used more respiratory medications, and visited the ED more often than those individuals with AFL who were not diagnosed with COPD. Review of the Lung Health Study suggests that smokers with lower lung function have accelerated rates of FEV_1 decline and increased mortality.[28]

Although still controversial, recent investigations increasingly suggest benefits for the early detection and treatment of COPD.[29–31] Smoking cessation is the primary intervention for the prevention and treatment of COPD and may be more beneficial for smokers with fewer respiratory symptoms and minimal AFL than those with diagnosed COPD.[32,33] The effect of undiagnosed COPD on quality of life and patient health is poorly studied, but undetected AFL may impair daily activities with subsequent loss of physical conditioning and erosion of social interactions.[34]

In a study of the medical costs of undiagnosed COPD, Mapel[35] and coworkers showed that the average total costs were higher by US$1282 in the 24 months prior to COPD diagnosis and US$2489 greater in the year before diagnosis. The average incremental medical and pharmaceutical cost for undiagnosed COPD is estimated to be $2527 and increases with time, rising precipitously in the month before diagnosis.[36] In Sweden, the average annual direct and indirect costs of COPD were $1128 for individuals with a physician diagnosis of COPD compared with $2207 for those who did not have a physician diagnosis.[37] Thus, despite estimates that half to two thirds of individuals with COPD are not diagnosed and increasing evidence that early diagnosis of COPD is beneficial and profoundly affects health care utilization and cost, our study suggests that less than 10% of individuals with occult AFL will be diagnosed with COPD each year without a proactive screening or detection program.

The diagnostic process that stimulates a clinician to make a diagnosis of COPD is not well studied. Patients who were initially diagnosed with COPD were older, had more symptoms, and greater physiologic impairment than undiagnosed individuals (Table 1). The subsequently diagnosed group had higher symptom scores and used the ED more frequently than the persistently undiagnosed group (Table 1). Although the mean FEV_1 of the group that was subsequently diagnosed was not different from that of the group that was persistently undiagnosed, 38% of the subsequently diagnosed group were classified as GOLD stage 3 or 4, whereas only 9% of the persistently undiagnosed group were classified as GOLD stage 3 or 4 (Table 1). Respiratory symptoms, including breathlessness, cough, and sputum production are critical elements of most COPD screening questionnaires.[37–39]

The role of health care utilization, especially ED visits and hospitalizations, in the diagnosis of COPD has not been defined. Patients who were subsequently diagnosed with COPD had more ED visits than those who were previously diagnosed and more than twice as many ED visits as the persistently undiagnosed patients (Figure 3), suggesting a possible role of ED visits in the diagnostic process. Since we could not determine who entered the diagnosis of COPD into the medical record, it was not possible to determine whether there was an increased rate of COPD diagnosis by ED providers or if primary care providers entered a COPD diagnosis after the ED visit. Thus, it is not known which elements of the patient's clinical history prompt clinicians to establish a COPD diagnosis. ED visits for respiratory complaints may be one stimulus that provokes providers to diagnose COPD.

Recent large, longitudinal studies demonstrated poor quality of life, accelerated FEV_1 decline, and increased exacerbation rates and mortality in individuals with mild COPD.[14,16,41–44] Consistent with these studies, the persistently undiagnosed patients had significantly more symptoms than individuals with normal spirometry, but less than those who were subsequently diagnosed (Figures 2–5). Although the persistently undiagnosed group received fewer respiratory medications, this study was not structured to determine whether the increased symptoms and health care utilization were due to lack of COPD treatment in the undiagnosed group or whether the lack of treatment was due to underdiagnosis.

The spirometric definition of AFL remains a controversial issue.[19,41,45] To mitigate this issue we employed both the FR and LLN definitions of AFL. The prevalence of AFL at the Cincinnati VAMC is much higher than the general population and approximately two thirds of affected patients are not diagnosed with COPD. The prevalence of AFL at the Cincinnati VAMC is much higher than the general population and approximately two thirds of those affected patients are not diagnosed with COPD.[10] All of our patients with AFL by LLN also met FR criteria and nine (20%) patients had COPD by FR

alone. Those nine patients had predominantly GOLD stage 2 disease and did not contribute significantly to the differences between the groups. Similarly, larger studies have looked at differences between these two definitions and shown differences in quality of life but not in exacerbations or outcomes.[41]

Recent studies by Mannino and the MESA study group have begun to define a "restricted" lung pathology based on FVC < 80% of predicted and no spirometric evidence of AFL.[19,41] These studies found increased mortality in those individuals with restriction compared to those with normal lung function. Our study did not demonstrate survival differences but there were also no differences in respiratory symptoms, BMI, or health care utilization. This study was not originally designed to study this population and a longer follow up period with more participants may be necessary to detect any significant differences. Restrictive lung function occurs in up to 37% of individuals misdiagnosed with COPD and the risk of misclassification was 2.66 fold greater among those who were overweight or obese.[46]

This study has several limitations. Participants were recruited from a single center and were predominantly older, male smokers. Another limitation is that we only measured ED visits or hospitalizations that were recorded in the VHA EMR; less severe exacerbations that were treated as outpatients or occurred in non-VHA facilities were missed. Consequently, this study likely underestimates health care utilization.

Conclusion

Unprompted clinicians diagnose COPD in only 7% of patients with unrecognized AFL annually. Increased respiratory symptoms and greater frequency of ED visits are associated with the subsequent diagnosis of COPD among patients with unrecognized AFL. Further studies of the factors that stimulate clinicians to recognize and diagnose COPD are needed.

Acknowledgments

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Disclosure

The authors report no conflicts of interest in this work.

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