



Overdiagnosis and Overtreatment of COPD in Individuals 90 Years and Older

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ABSTRACT

Background: Although prevalence of chronic obstructive pulmonary disease (COPD) increases with age, limited information about the current diagnostic and therapeutic practices in COPD is available in aged individuals. We conducted a retrospective study of adults aged 90 years and older with COPD diagnosis and compared differences in prescribed medications, and steroid or antibiotic use for respiratory symptoms during acute healthcare visits across the four subgroups: 1) without valid spirometry, 2) ratio of forced expiratory volume in one second over forced vital capacity (FEV₁/FVC) ratio ≥ 0.70 , 3) FEV₁/FVC ratio <0.70 but $>$ age-based lower limit of normal (LLN), and 4) FEV₁/FVC ratio $<$ LLN.

Methods: A single-center retrospective study of 90-years and older adults with a diagnosis of COPD. Demographics, medications, medical history, acute healthcare visits (hospitalizations, emergency and urgent care), and spirometry values were extracted. ANOVA, Kruskal Wallis, Chi-square, Fisher and logistic regression tests as appropriate were used to compare differences across the four groups.

Results: Among 166 adults with COPD diagnosis, 71 (43%) did not have a valid spirometry test, 24 (14.5%) had normal post-bronchodilator FEV₁/FVC ratio ≥ 0.70 , 28 (16.9%) had LLN \leq post-bronchodilator FEV₁/FVC ratio <0.70 , and 43 (25.9%) had post-bronchodilator FEV₁/FVC ratio $<$ LLN. There were no differences in prescribed COPD medications or steroid and antibiotic use during acute health care visits among the four groups. The proportion of patients who had unscheduled healthcare visits within one year for respiratory symptoms differed across the four groups. Individuals with FEV₁/FVC $<$ LLN had a significantly higher visit frequency compared to those without spirometry ($p < 0.05$).

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Conclusion: Over half of 90-and-older veterans were diagnosed with and treated for COPD without substantiating spirometry reports. This may lead to inappropriate prescription of COPD medications.

KEYWORDS: Aging, COPD, Drug side effects, Diagnostic errors, Spirometry

INTRODUCTION

The United States population of persons 90-and-older reached 1.9 million in 2010 [1]. As a result, those aged 90-and-older comprise 4.7% of the 65-and-older population and may reach 10% by 2050 [1]. Chronic obstructive pulmonary disease (COPD) is an inflammatory disorder of airway and lung parenchyma characterized by airflow limitation [2]. The prevalence of COPD increases with age [3,4]; however, information on the current diagnostic and therapeutic practices of COPD in aged individuals is limited [5] and age-specific practice guidelines have yet to be formulated [2-4,6,7].

Spirometry is required to establish the diagnosis of COPD [8]. A reduction in the ratio of post-bronchodilator forced expiratory volume in one second over forced vital capacity (FEV_1/FVC) is used to detect airflow limitation. Conventionally, the Global Initiative for Obstructive Lung Disease (GOLD) criteria are used to define COPD when post-bronchodilator FEV_1/FVC is <0.70 in the presence of symptoms and risk factors [2]. However, FEV_1 declines more rapidly with time than FVC, thereby leading to age-dependent reductions in the FEV_1/FVC ratio [9]. The use of a variable FEV_1/FVC ratio threshold derived from the age-adjusted lower limit of normal (LLN) from 95% confidence limits to make the diagnosis of COPD in older individuals has been proposed [4,10-12]. Using this standard, it has been estimated that the LLN intersects with the 0.70 GOLD threshold at age 50 years for men and age 60 years for women [12]. Consequently, utilization of the fixed cut-off of $FEV_1/FVC < 0.70$ proposed by GOLD may lead to inadvertent erroneous diagnosis of physiological decline as COPD, particularly in elderly individuals [2,4,6,7,13].

We conducted a retrospective study of individuals 90 years and older with physician-diagnosed COPD. The aim was to compare prescribed COPD medications across the following four groups: 1) spirometry not available; 2) $FEV_1/FVC \geq 0.70$; 3) $FEV_1/FVC < 0.70$ but $>$ age-based LLN; and 4) $FEV_1/FVC < LLN$. Additionally, we compared prescription of corticosteroids and antibiotics for respiratory symptoms during unscheduled healthcare visits across these four groups.

MATERIALS AND METHODS

This study was a retrospective, single center cohort conducted at the Jesse Brown VA Medical Center (JBVAMC), Chicago, Illinois, USA. The study protocol was approved by JBVAMC IRB (protocol #1455698-1).

Patients 90 years and older with a diagnosis of COPD by ICD-10 codes: J44.0, J44.1, J44.9, were identified through review of electronic medical records. The initial inquiry on August 5, 2016 revealed 179 subjects. A subsequent inquiry on July 28, 2018 increased the total number of subjects to 211. Forty-five subjects were excluded due to absent documentation of COPD in available physician notes. Demographic data (i.e., age, sex, race/ethnicity) were collected. Other subject characteristics collected included smoking history, co-morbidities including other lung related diseases (i.e., asthma, emphysema, pulmonary fibrosis, obstructive sleep apnea, deep venous thrombosis and/or pulmonary embolism) and cardiac disease (i.e. atrial fibrillation, heart failure with preserved or reduced ejection fraction, coronary artery disease, and hypertension).

Information on short acting beta2-agonists, long-acting beta2-agonists, long-acting muscarinic antagonists, and inhaled corticosteroids was obtained and will hereafter be referred to as COPD medications. Additionally, home oxygen prescription status was retrieved. Unscheduled healthcare visits for respiratory symptoms within one year of inquiries were identified. Unscheduled health care visits included visits to the emergency room or urgent care, and hospitalization. Use of oral or intravenous corticosteroids and antibiotics during these visits was abstracted.

Spirometry was considered valid and recorded values derived when a post-bronchodilator spirometry was performed [2]. The most recent spirometry values within 20 years of inquiry were collected. A $FEV_1/FVC < 0.70$ was used based on the GOLD criterion (4). A LLN FEV_1/FVC of 0.627 for men and 0.635 for women were chosen as the upper cut-off of LLN FEV_1/FVC ratio based on the NHANES III data [9]. Individuals with spirometry tests were classified into 3 groups based on post-bronchodilator FEV_1/FVC : 1) $FEV_1/FVC \geq 0.70$; 2) $FEV_1/FVC < 0.70$ but $>$ LLN; and 3) $FEV_1/FVC < LLN$.

Statistical analyses were performed using SPSS Statistics version 27. Kruskal-Wallis, ANOVA, chi-square, or Fisher's exact tests were used as appropriate to compare differences across the subgroups. Logistic regression was used to compare steroids and antibiotics use during unscheduled healthcare visits. $P < 0.05$ (two-tailed) was considered statistically significant.

RESULTS

The study cohort was composed of predominantly men (n=162, 96%); 88 (52%) subjects were Black (Table 1). Of the 166 subjects with physician-diagnosed COPD, 95 (57.2%) had spirometry reports in their medical records. At the time of spirometry, most subjects (N=92, 97%) were 80 years and older; 2 (2%) were 79 years, and one (1%) was 76 years. Based on post-bronchodilator FEV₁/FVC ratio, 24 (25%) had FEV₁/FVC ≥ 0.70, 28 (29%) had FEV₁/FVC ≥ LLN but <0.70, and 43 (45%) had FEV₁/FVC <LLN.

There were no significant differences in age, sex, smoking history, prevalence of co-morbid conditions, and prescribed COPD medications across the four groups. The number of White was significantly higher in the no spirometry or normal spirometry groups (p<0.05). The proportion of patients who had unscheduled healthcare visits within one year for respiratory symptoms differed across the four groups. Individuals with FEV₁/FVC <LLN had a significantly higher visit frequency compared to those without spirometry (p<0.05). There were no significant differences in corticosteroid or antibiotic prescriptions during these visits across the four groups.

	No post-BD test (N=11) & No spirometry (N=60)	FEV ₁ /FVC ratio		
		≥ 0.70	≥ LLN, < 0.70	< LLN
	N=71	N=24	N=28	N=43
Age	93.4 ± 2.7	93.2 ± 3.1	93.3X ± 2.2	92.4 ± 1.6
Gender				
Male	69 (97%)	23 (96%)	28 (100%)	42 (98%)
Female	2 (3%)	1 (4%)	0 (0%)	1 (2%)
Race/Ethnicity*				
Black	22 (31%)	18 (75%)	20 (71%)	28 (65%)
White	41 (58%)	5 (21 %)	7 (25%)	14 (33%)
Other	8 (11%)	1 (4 %)	1 (4%)	1 (2%)
Smoking				
Active	3 (4%)	0 (0%)	2 (7%)	2 (5%)
Former	60 (85%)	21 (88%)	25 (89%)	36 (84%)
Never	8 (11%)	3 (12%)	1 (4%)	5 (12%)
Co-morbid conditions				
Asthma	8 (11%)	4 (17%)	3 (11%)	6 (14%)
Emphysema	23 (32%)	11 (46%)	12 (43%)	23 (53%)
Interstitial lung disease	6 (8%)	2 (8%)	4 (14%)	1 (2%)
Obstructive sleep apnea	7 (%)	3 (%)	6 (21%)	7 (16%)
Lung cancer	2 (3%)	1 (4%)	1 (4%)	3 (7%)
Deep venous thrombosis & Pulmonary embolism	9 (13%)	3 (13%)	4 (14%)	8 (19%)
Hypertension	65 (92%)	21 (88%)	27 (96%)	42 (98%)
Atrial fibrillation	22 (31%)	7 (29%)	11 (39%)	10 (23%)
Coronary artery disease	26 (37%)	6 (25%)	9 (32%)	15 (35%)
Heart failure				
Preserved ejection fraction	29 (41%)	12 (50%)	14 (50%)	25 (58%)
Reduced ejection fraction	8 (11%)	4 (17%)	3 (11%)	4 (9%)
Pulmonary hypertension	8 (11%)	2 (8%)	6 (21%)	12 (28%)
Diabetes mellitus	13 (18%)	6 (25%)	8 (29%)	8 (19%)

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Dementia	8 (11%)	8 (33%)	9 (32%)	8 (19%)
Pulmonary function test				
Age at spirometry	87.4 ± 4.5	85.5 ± 5	87.8 ± 3.4	86.9 ± 3.1
Post bronchodilator % FEV ₁ *	---	74.7 ± 20.2	75.0 ± 17.1	59.5 ± 16.1
Post bronchodilator FEV ₁ /FVC ratio*	---	76.5 ± 6.1	66.3 ± 1.9	51.1 ± 7.5
COPD treatment				
Short acting beta-agonist	60 (85%)	19 (79%)	23 (82%)	40 (93%)
Long acting muscarinic-antagonist	34 (48%)	9 (38%)	13 (46%)	27 (63%)
Inhaled corticosteroids	35 (49%)	9 (38%)	13 (46%)	29 (67%)
Oxygen	12 (17%)	5 (21%)	7 (3%)	12 (28%)
Emergency room visit/hospitalization within 12 months				
Respiratory complaints*	13 (18%)	8 (33%)	7 (25%)	19 (44%)
Steroid use	5 (38%)	4 (50%)	3 (43%)	11 (58%)
Antibiotics use	11 (85%)	6 (75%)	5 (71%)	11 (58%)
*p<0.05 across the groups				
BD: Bronchodilator; COPD: Chronic Obstructive Pulmonary Disease; FEV ₁ : Forced Expiratory Volume in one second; FVC: Forced Vital Capacity, LLN: Lower Limit of Normal				
Chi-square test, Fisher exact test, ANOVA, or Kruskal Wallis test, as appropriate, were used to compare differences among the groups.				
Logistic regression model was used to compare differences in steroid or antibiotics use with emergency room or hospitalizations as a covariate.				

Table 1: Characteristics of patients 90 years and older by subgroups defined by post-bronchodilator FEV₁/FVC.

CONCLUSION

The new finding of this study is that more than half (53%) of 166 patients who are 90 years or older had a physician-diagnosed COPD without spirometric evidence of COPD using both FEV₁/FVC <0.70 and LLN criteria. Prescribed COPD medications were independent of presence of spirometry or post-bronchodilator FEV₁/FVC ratio. Our findings raise concerns regarding possible overtreatment of COPD in the elderly population in the absence of spirometry testing.

Previous studies have advocated the use of LLN of FEV₁/FVC for diagnosis of COPD in elderly adults rather than fixed FEV₁/FVC ratio, due to concern of overdiagnosis using the fixed FEV₁/FVC ratio criterion [2,4,6,7,13]. We were unable to identify significant differences in COPD medications used across groups defined by LLN or fixed ratio for diagnosis of COPD. Additional studies are warranted to identify potential health impact of different COPD diagnostic criteria based on post-bronchodilator FEV₁/FVC, LLN, and fixed FEV₁/FVC in older old individuals.

Overtreating older old individuals with COPD medications could be associated with serious adverse events, given the altered pharmacokinetics and polypharmacy in this age group [14,15]. For instance, the incidence of pneumonia and bone fractures due to these medications is relatively high in these persons [14,16]. In a large cross-sectional study in the United Kingdom (N=502,640), patients with COPD were more likely to have other comorbid medical conditions and polypharmacy, and were at increased risk for adverse drug reactions such as fall, urinary retention and central nervous system depression, from prescribed medications [17]. Our findings underscore the potential for indiscriminate and non-evidence-based use of COPD medications which may cause significant negative impact on the health, although the impact of overtreatment needs to be further studied in a prospective fashion.

Several studies have examined the incidence and characteristics of presumed COPD related hospitalizations in the elderly. Notably, a cohort of 172 patients with severe COPD exacerbation requiring mechanical ventilation, mean

age 71.3 years, demonstrated that upon hospital admission 29.1% had pulmonary embolism rather than COPD exacerbation [18]. Further evidence from a postmortem analysis of 43 subjects (median age 70 years) who were admitted for COPD exacerbations and died within 24 hours of admission highlights that only a relatively small percentage of death was attributed to respiratory failure due to progression of COPD (14%), whereas death caused by other etiologies, including heart failure, pneumonia and pulmonary thromboembolism, was considerably more common (86%) [19]. Stone et al. [20] reviewed the management of hospitalized patients with COPD exacerbations between age 27 to 102 and found that those over 80 years were less likely to be seen by and discharged under care of pulmonary physician. Taken together, this suggests that older old individuals are likely to be misdiagnosed with COPD and less likely to be referred to pulmonary physicians for further evaluation and disposition. This, in turn, may have a negative impact on health outcomes of these individuals.

The limitations of this study should be noted, including retrospective design in a single center and male predominance, that limiting generalizability of the results. Although all available outside medical records were thoroughly reviewed, it is possible that we may not have captured all pertinent data associated with health care provided at outside institutions. Our strengths are the relatively large sample size and the predominance of Black race/ethnicity 90 years and older, an underrepresented group in previous studies [2]. Collectively, these data add to the paucity of medical literature on COPD management in older old patients.

In summary, we found no significant differences in prescribed COPD medications among 90 years and older patients who met or did not meet established international guidelines of diagnosis and treatment of COPD. Conceivably, this could raise concern about harmful effects of prescribed COPD medications in elderly patients without proper diagnosis of COPD. Clearly, further prospective, multi-center studies are indicated to determine the prevalence of COPD and its treatment among individuals 90 years and older.

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