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ORIGINAL RESEARCH ARTICLE

Clinical factors predictive of appropriate treatment in COPD: a community hospital setting

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a common respiratory disease. The appropriate treatment according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guideline was 19-60%. However, there are limited data on predictors of appropriate treatment in patients with COPD. This study aimed to evaluate risk factors of appropriate treatment in patients with COPD according to the GOLD guideline in a real-world community setting.

Methods: This is a retrospective study conducted at a community hospital. Inclusion criteria were adult patients diagnosed as COPD treated at a COPD clinic. The primary outcome was the appropriate treatment, defined by correct pharmacological treatment by the GOLD guideline according to the ABCD severity assessment. Clinical predictors of appropriate treatment were executed by stepwise multivariate logistic regression analysis.

Results: 136 patients with COPD met the study criteria. Of those, 100 patients had inappropriate treatment according to the GOLD guideline. Three factors were independently associated with the appropriate treatment including number of admissions, modified Medical Research Council (mMRC) score, and CAT score. These factors had adjusted odds ratio of 3.11, 2.86, and 1.26, respectively. Causes of inappropriate treatment were unavailability of long-acting muscarinic antagonist (LAMA) (51 patients; 79.69%), treated by inhaled corticosteroid (ICS) alone (12 patients; 18.75%), and treated with only bronchodilator (1 patient; 1.56%).

Conclusions: Appropriate COPD patients' treatment according to the GOLD guideline was 26.47% in community setting. Factors associated with severity of COPD were associated with prescribing appropriate treatments.

Keywords: CAT, hospitalization, mMRC

Introduction

Chronic obstructive pulmonary disease (COPD) is a respiratory disease mainly caused by smoking. Patients with COPD suffer from several symptoms, exacerbations, or hospitalizations leading to 2.6% of disability-adjusted life years (DALYs) and at least 3.2 million deaths globally (1). Diagnosis of COPD can be confirmed by evidence of incomplete irreversible airflow limitation without other causes. Treatment of COPD comprises both pharmacological and nonpharmacological modalities such as smoking cessation. Uncontrolled COPD may lead to COPD exacerbations and mortality (2). A study of 73,106 patients with COPD found that the mortality rate was 50% at 3.6 years after hospitalization (3), while another study found that in-hospital mortality rate was 2.6% (4).

There are several factors associated with COPD control such as COPD severity, patient compliance, correct inhaler technique, or nonpharmacological treatment (5,6). Even though patients with COPD had medication adherence of 51.0%, 85 out of 549 patients or only 15.5% were under control (7). Another factor that may be associated with COPD symptom control is appropriately prescribed medication (6,8,9). An undertreatment according to the guideline increases risk of COPD exacerbation with a coefficient of –0.179 ($p < 0.001$) (9). The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guideline recommends

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various pharmacological regimens based on COPD severity (10). In real practice, the appropriate treatment according to the GOLD guideline was 19-60% (9,11,12). However, there are limited data on predictors of appropriate treatment in patients with COPD. This study aimed to evaluate risk factors of appropriate treatment in patients with COPD according to the GOLD guideline in a real-world community setting.

Methods

This study was a retrospective study conducted at Chumpae Hospital, the largest community hospital in Khon Kaen province, Khon Kaen, Thailand. The inclusion criteria were adult patients who were diagnosed with COPD and treated at the COPD clinic. The diagnosis of COPD was made according to the GOLD guideline (10). The study period was between May and November 2019. The study protocol was approved by the institutional review board, Ministry of Public Health, Khon Kaen Branch, Thailand (61165).

Eligible patients were enrolled from clinical charts and evaluated for baseline characteristics, smoking history, risk factor for COPD, symptoms, chest x-ray, pulmonary function test, COPD type, 6-minute walk test (6MW), history of exacerbations, history of admission, and COPD assessment. History of cough was defined by the presence of cough for more than 2 weeks, while productive sputum more than 2 months was recorded. COPD assessment was evaluated by using modified Medical Research Council (mMRC), COPD Assessment Test (CAT), and COPD classification by the GOLD guideline or ABCD assessment. The primary outcome of the study was the appropriate treatment, which was defined by correct pharmacological treatment by the GOLD guideline to category A to D: a bronchodilator for group A; a long-acting bronchodilator (long-acting beta2-agonists: LABA or long-acting muscarinic antagonist: LAMA) for group B; LAMA for group C; and LAMA or LAMA plus LABA or inhaled corticosteroid (ICS) plus LABA for group D. Treatment other than this recommendation in a particular category was defined as inappropriate treatment. The inappropriate treatment was also classified as under- and overtreatment according to the recommendation for each category. Note that information retrieved for the study was at the initial therapy of each patient.

Statistical analyses

Patients were categorized into two groups by appropriateness of treatment. The studied variables were compared between both groups by descriptive statistics. For numerical variables, mean and SD was reported and compared between groups by using independent t-test or Wilcoxon Rank Sum test where appropriate. Numbers and percentages of each categorical variable were reported and compared between groups by Chi Square test or Fisher Exact test where appropriate. Clinical predictors of appropriate treatment were executed by stepwise multivariate logistic regression analysis. Those factors with a p value of less than 0.20 by univariate logistic regression were put in the subsequent multivariate logistic regression analysis. The goodness of fit of the final model was tested by Hosmer-Lemeshow method. The statistical analyses were executed by the STATA software (College Station, Texas, USA).

Results

There were 136 patients with COPD who met the study criteria. Of those, 100 patients (73.53%) were with inappropriate treatment according to the GOLD guideline. Between those with appropriate and inappropriate treatment groups, there were two significant factors in terms of baseline characters including cough and sputum production (Tab. I). The appropriate treatment group had higher proportions of patients with cough and sputum production than the inappropriate treatment group (77.78% vs. 54.00%; and 80.56% vs. 60.00%, respectively).

TABLE I - Baseline characters of patients with chronic obstructive pulmonary diseases (COPD) categorized by receiving appropriate treatment

Factors	Inappropriate n = 100	Appropriate n = 36	p value
Mean (SD) age, years	64.51 (8.83)	63.47 (10.51)	0.566
Male sex, n (%)	94 (94.00)	35 (97.22)	0.675
Occupation: agricultural, n (%)	93 (93.00)	31 (86.11)	0.412
Diabetes mellitus, n (%)	8 (8.00)	7 (19.44)	0.060
Hypertension, n (%)	42 (42.00)	17 (47.22)	0.588
Dyspnea, n (%)	100 (100.00)	37 (100.00)	NA
Cough, n (%)	54 (54.00)	28 (77.78)	0.012
Sputum, n (%)	60 (60.00)	29 (80.56)	0.026
Smoking history, n (%)			0.992
None	9 (9.00)	3 (8.33)	
Ex-smoker	72 (72.00)	26 (72.22)	
Current smoker	19 (19.00)	7 (19.44)	
Mean (SD) pack-year of smoking	21.49 (15.40)	26.82 (29.24)	0.498
Exposure to noxious particles, n (%)	6 (6.00)	2 (5.56)	0.999
Mean (SD) BMI (kg/m^2)	21.17 (3.69)	21.90 (3.95)	0.446

BMI = body mass index; NA = not available.

Between these two groups, the appropriate treatment group had shorter 6MW test (328.05 vs. 353.49 m) and lower mMRC (1.83 vs. 0.96) than the inappropriate treatment group significantly (Tab. II). But the average CAT score (15.88 vs. 7.22), average number of exacerbation (2.83 vs. 1.13 times), and average number of admissions (2.83 vs. 1.13 times) were significantly higher in the appropriate treatment group than the inappropriate treatment group (Tab. II) while the post-bronchodilator FEV1/FVC was significantly lower in the appropriate treatment group than the inappropriate treatment group (53.19 vs. 57.32; p = 0.033). COPD class D

TABLE II - Laboratory results and disease status of patients with chronic obstructive pulmonary diseases (COPD) categorized by receiving appropriate treatment

Factors	Inappropriate n = 100	Appropriate n = 36	p value
CXR, n (%)			
Normal, n (%)	53 (53.00)	19 (52.78)	0.982
Hyperinflation, n (%)	36 (36.00)	13 (36.11)	0.990
Post-bronchodilator FEV1, mL	66.86 (17.40)	60.30 (19.11)	0.061
Post-bronchodilator FEV1, %	6.02 (7.00)	6.80 (7.21)	0.602
Post-bronchodilator FEV1/FVC	57.32 (9.17)	53.19 (9.99)	0.033
COPD type, n (%)			0.999
Chronic bronchitis	3 (3.00)	1 (2.78)	
Emphysema	5 (5.00)	1 (2.78)	
Mixed	92 (92.00)	34 (94.44)	
Mean (SD) 6MW, meters	353.49 (72.91)	328.05 (87.16)	0.222
mMRC, n (%)	0.96 (0.66)	1.83 (0.88)	<0.001
0	22 (22.00)	1 (2.78)	
1	62 (62.00)	13 (36.11)	
2	14 (14.00)	14 (38.89)	
3	2 (2.00)	7 (19.44)	
4	0	1 (2.78)	
Mean (SD) CAT	7.22 (5.31)	15.88 (5.04)	<0.001
Exacerbation, n (%)	1.13 (2.40)	2.83 (2.09)	<0.001
Admission, n (%)	0.26 (0.75)	1.22 (1.17)	<0.001
Category, n (%)			<0.001
A	42 (42.00)	0	
B	30 (30.00)	0	
C	25 (25.00)	0	
D	3 (3.00)	36 (100.00)	

6MW = 6-minute walk test; CAT = COPD Assessment Test; mMRC = modified Medical Research Council dyspnea questionnaire; COPD category by the GOLD guideline.

was also found more in the appropriate treatment group than the inappropriate treatment group (100.00% vs. 3.00%).

There were five factors remaining in the final model predictive of appropriate treatment in patients with COPD (Tab. III). Of those, three factors were independently associated with the appropriate treatment including number of admissions, mMRC score, and CAT score. These factors had adjusted odds ratio of 3.11, 2.86, and 1.26, respectively. The final model had the Hosmer-Lemeshow chi-square of 10.72 (p = 0.218), indicating goodness of fit of the model. Causes of inappropriate treatment were unavailability of LAMA

TABLE III - Factors predictive of appropriate treatment in chronic obstructive pulmonary diseases (COPD) treated at community hospital

Factors	Unadjusted odds ratio (95% confidence interval)	Adjusted odds ratio (95% confidence interval)
Age	0.99 (0.95, 1.03)	0.94 (0.89, 1.01)
Diabetes	2.77 (0.93, 8.31)	3.10 (0.46, 20.84)
Admission	3.73 (2.02, 6.88)	3.11 (1.39, 6.97)
mMRC	4.47 (2.41, 8.30)	2.86 (1.18, 6.94)
CAT	1.32 (1.19, 1.47)	1.26 (1.13, 1.42)

Factors in the model included sex, smoking, cough, sputum, body mass index, chest x ray, 6-minute walk test, post-bronchodilator FEV1, post-bronchodilator FEV1/FVC, and exacerbation.
CAT = COPD Assessment Test; mMRC = modified Medical Research Council dyspnea questionnaire.

(51 patients; 79.69%), treated by ICS alone (12 patients; 18.75%), and treated with only bronchodilator (1 patient; 1.56%). Categorized by COPD category, overtreatment was found in categories A, B, and C, while undertreatment was reported in categories B, C, and D (Tab. IV).

TABLE IV - Proportions of under- or overtreatment by chronic obstructive airway disease category (n = 100)

Treatment	A (n = 42)	B (n = 30)	C (n = 25)	D (n = 3)
Undertreatment	0	6 (20.00)	2 (8.00)	3 (100.00)
Overtreatment	42 (100.00)	24 (80.00)	23 (92.00)	0

Discussion

This study showed that the appropriate treatment for patients with COPD was 26.47%: in category D at 100.00% (Tab. II). Compared with other three previous studies, this study had appropriate treatment rate comparable with the study at VA hospital in the US (27.2% vs. 18.7%) and lower than two studies from tertiary hospitals. In this community hospital setting, patients with category D had highest appropriate treatment rate than others at 100.00% (Tab. II). This pattern was also found in other studies which may indicate that severe cases of COPD tend to follow the GOLD guideline as they may have severe symptoms and required appropriate and several pharmacological therapies (10,13).

This study also found another similar pattern on appropriate treatment: low appropriate treatment rate in categories A, B, and C. First, we found that inhaled corticosteroid alone was used in 12 patients or 18.75%. The study from Italy also found that inhaled corticosteroid was overused despite the GOLD guideline that does not recommend it as shown in Table V (11). But, the attending physicians believe that it is more effective. A study from Sweden also found that inhaled corticosteroid was used inappropriately in 45.5% of patients with COPD regardless of categories: A 33.6%; B 46.2%;

TABLE V - Appropriate treatment in ABCD severity assessment in patients with chronic obstructive pulmonary disease

Study, year	Country	Setting	Total	A	B	C	D
Palmiotti, 2018	Italy	Pulmonologists	419/693 (60.5%)	57/142 (40.1%)	110/238 (46.2%)	18/41 (43.9%)	234/272 (86.0%)
Foda, 2017	USA	VA and University Hospital	164/878 (18.7%)	30/86 (34.9%)	19/379 (5.0%)	73/292 (25.0%)	42/121 (34.7%)
Chan, 2017	Hong Kong	Tertiary Hospital	262/450 (58.2%)	1/5 (20.0%)	7/164 (1.6%)	0/8 (0%)	254/273 (56.4%)
This study	Thailand	Community Hospital	36/136 (26.47%)	0/42 (0%)	0/30 (0%)	0/25 (0%)	36/39 (92.31%)

C 54.8%; and D 71.0% (14). An inappropriate use of inhaled corticosteroid was also found in 50% of patients with COPD in the UK (15). Another limitation for community hospital in this study is lack of LAMA in 79.69%: it may be due to unavailability and cost of LAMA.

Not surprisingly, factors predictive for appropriate treatments were factors indicating severe COPD including hospital admissions, mMRC, and CAT score (Tabs. II and III). Among these three factors, admissions and mMRC had higher adjusted odds ratios than the CAT score. These may imply that the two factors are slightly stronger predictors for severe COPD than the CAT score (9,10,13). Additionally, hospitalizations may remind physicians to prescribe more proper medications for the patients as they may have more times to assess the patients than in the outpatient setting (16).

This study had some limitations. First, we did not evaluate association of COPD such as obstructive sleep apnea (OSA) or asthma which may result in overprescription of corticosteroids (17-21). Second, the study population was community hospital. The results of this study may not be applied for more complicated COPD patients. Second, there was no follow-up data on long-term outcomes. Finally, inappropriate treatment of not using LAMA was due to unavailability. Other causes of inappropriate treatment were treatment with only ICS (18.75%) or bronchodilator alone (1.56%).

Conclusion

Appropriate treatment of patients with COPD according to the GOLD guideline was 26.47% in community setting. Factors associated with severity of COPD were associated with prescribing of appropriate treatments.

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Disclosures

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