ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Higher GOLD spirometeric class (severity of airflow limitation) correlated with higher number of comorbidities

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Submission: 20-07-2023 Revision: 02-11-2023 Publication: 01-12-2023

ABSTRACT

Background: Various systemic manifestations of chronic obstructive pulmonary disease (COPD) are well known to us. One patient of COPD may have more than one associated comorbid conditions. Severity of airflow limitation is expressed as a global initiative for chronic obstructive lung disease (GOLD) spirometeric classification in patients with COPD, which has been proposed to better identify the disease severity and survival. **Aims and Objectives:** In this study, we aimed to find out correlation between GOLD spirometeric classification and comorbidities in patients. **Materials and Methods:** An observational study conducted at the Institute of Medical Science Banaras Hindu University Varanasi India. We evaluated 50 patients of COPD, containing smokers, non-smokers, and ex-smokers. The severity of airflow limitation in COPD was classified using the GOLD. The most frequent comorbidities are assessed in COPD which were cardiovascular diseases, diabetes, hypertension, osteoporosis, muscle wasting, psychological illness, and anemia. **Results:** Fifty patients were analyzed: Male 90%, mean age 68.5 years and mean forced vital capacity in 1 s 34.3%. There is an association between GOLD spirometeric classification and total number of comorbidities in patients. Subjects with higher GOLD spirometeric classification have more associated comorbid conditions, which suggest that these conditions may aggravate COPD course and increase risk of mortality. **Conclusion:** Assessment of GOLD spirometeric classification could provide information about a total number of various comorbid conditions in a patient with COPD. Patient with higher GOLD spirometeric classification has more comorbidities.

Key words: GOLD spirometric classification; Comorbidities; COPD

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v14i12.56801

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common preventable and treatable disease.[1] Global Burden of Disease studies estimated that COPD is the fourth leading cause of death globally, and it has been estimated that it is going to be third leading cause of death by the year 2020.[2] Smoking is the most important risk factor found to be associated with COPD. Other risk factors include pollution, biomass fuel exposure, and infections. Some host factors such as α1-antitrypsin deficiency and low birth weight also play a role in pathogenesis of COPD. In the present era, COPD is not just a pulmonary disease, its various systemic manifestations are well known to us.[3] The major manifestation of COPD is airflow limitation caused by reduction in forced expiratory volume in 1 s (FEV1).[1] The measurement of FEV1 alone does not explain clinical consequences, morbidities, and mortality in COPD. Hence, additional findings and parameters should be evaluated.[4]

COPD is characterized by chronic systemic inflammation. Chronic inflammation is important cause of the progression of disease and comorbidities in COPD. Various inflammatory cytokines have also widely recognized in the natural history of COPD. Inflammation in respiratory

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tract due to chronic irritant is amplified in COPD due to associated systemic inflammation.

These comorbidities contribute to the overall severity in individual patients.[3] Some previous study for evaluation cause of mortality in COPD patients suggest that these patients are more likely to die due to comorbidities than from COPD.[4-6] Global initiative for chronic obstructive lung disease (GOLD) spirometeric classification as described in GOLD is based on post-bronchodilator FEV1 in diagnosed COPD patients. Based on FEV1, it has four classes, these classes indicate severity of airflow limitation.[1] As various systemic manifestations in COPD, these are due to chronic systemic inflammation. Hence, patients with severe airflow limitation in COPD should have more systemic manifestations.[3]

Aim and objectives

We, in this study, evaluated various comorbid conditions associated with COPD. We aimed to find relationship of GOLD spirometeric classification with total number of comorbidities in a single patient. To the best of our knowledge, this is the first study evaluating this relationship.

MATERIALS AND METHODS

Study design

This study was conducted in the Department of Respiratory Medicine at the Sir Sunder Lal Hospital, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India. It was a cross-sectional observational study conducted from 2018 July to March 2023.

Sample size

The sample size was calculated by 19.4% prevalence of COPD in the available literature. The confidence interval was to be 95% and permissible error was 5%. Under these circumstances, the sample size came out to be 36. However, in this study, we have enrolled 50 COPD patients.

Ethical permission

Ethical permission was taken from the Institutional Ethical Committee of theInstitute of Medical Sciences, Banaras Hindu University, Varanasi, India. Ethical number is Dean/2013/14/EC/362. Furthermore, written informed consent was taken from patients after explaining of study in their simple language before enrolling them for the study.

Sampling method

Inclusion criteria

COPD patients were diagnosed as per the standard definition and criteria given by GOLD that is post-bronchodilator pulmonary function test confirmation (FEV1/FVC<0.7) with irreversible airway obstruction.[1] Before including in the study, all patients were screened for other causes of breathlessness such as bronchial asthma, interstitial lung diseases, and heart failure, by channeling through a detailed history, thorough physical examination, and a battery of relevant investigations. All patients were free of exacerbation for at least 3 months. Informed consent was obtained from all the patients included in the study. Diabetes was defined as prior receiving oral hypoglycemic drugs or insulin, or blood sugar fasting level above 126 mg/dL, random blood sugar above 200, on several occasions, or HbA1c level more than 7.[7] Hypertension was defined on the basis of prior receiving antihypertensive therapy or whether BP exceeds 140/90 mm Hg for at least three measurements.[8] Osteoporosis was defined according to T-score after DEXA scan as per WHO definition. To look for renal impairment serum creatinine levels and blood urea levels were measured and the Glomerular filtration rate was calculated using Cockcroft-Gault formula. Psychiatric illnesses were labeled after specialist evaluation. Muscle wasting was labeled after anthropometric measurements. For cardiac evaluation, 2D-ECHO was used. Apart from these, we also did arterial blood gas analysis, quantitative c reactive protein, lipid profiles, and hemoglobin levels.

Exclusion criteria

The following criteria were excluded from the study:

a. Patients who presented with breathlessness not due to COPD but due to other diseases such as bronchial asthma and bronchiectasis interstitial lung diseases.
b. Patient in acute exacerbation of COPD
c. Patients with multiple organ failure
d. Hemodynamic instability
e. Those patients who are not giving consent.

Now every patient included in the study was screened for any associated comorbid conditions such as diabetes, hypertension, cardiac diseases, renal impairment, osteoporosis, psychiatric illness, and muscle wasting with the help of detailed clinical assessment and necessary investigations. Total numbers of comorbidities in a single patient were noted and all patients were classified accordingly.

Statistical analysis

Obtained data analyzed with the help of statistical software (SPSS 23.0). Frequencies of various comorbidities are expressed as percentage. Pearson product-moment correlation coefficient was used to assess correlation between Gold spirometeric class and total number of comorbidities in a single patient.

RESULTS

GOLD Spirometeric classification

The classification of airflow limitation severity in COPD is shown in Table 1. Specific spirometeric cut-points are used for purposes of simplicity.[1] Spirometry should be performed after the administration of an adequate dose of at least one short-acting inhaled bronchodilator to minimize variability.

From Table 2, it found various systemic manifestations of COPD such as hypertension, diabetes, cardiac comorbidities, renal, dyslipidemia, muscle wasting, osteoporosis, and psychiatric illness. Majority of patients had comorbidities of cardiovascular and psychiatric illness in COPD.

Table 3 suggested that single patient of COPD may have more than one comorbid condition. About 34% of patients have two comorbidities individually.

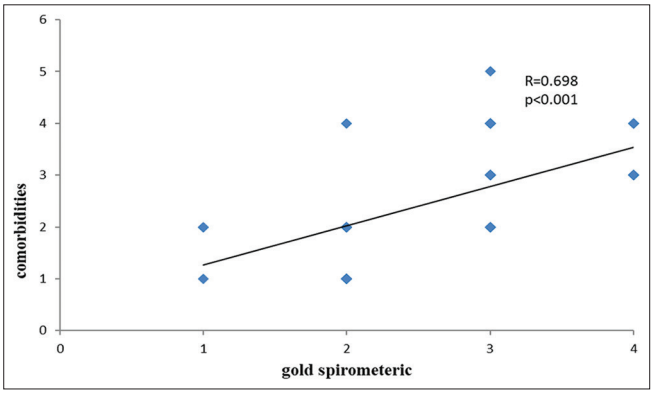
Table 4 concluded that 36% of patients have GOLD-2 (FEV1 range 51–80%) and GOLD-3 (FEV1 range 30–50%) airflow limitation in pulmonary function test.

Graph 1 demonstrated that a positive correlation between GOLD spirometeric class and total number of comorbidities in a single patient. We got Pearson product-moment correlation coefficient (r)=0.661. The correlation was highly statically significant (P≤0.001).

DISCUSSION

This study demonstrated that patient with COPD has various comorbid conditions. Cardiac and psychiatric illness were among more frequently found conditions. Yin et al., also found that similar finding in their study.[9] Systemic inflammation, weak adherence of medication, and smoking factor in COPD manifested as cardiovascular disease.[10] Systemic inflammation in COPD is the key determinant of endothelial dysfunction and vascular alteration.[11] Hypoxia and Oxidative stress in COPD also impaired vasodilatory mechanism.[11] Smoking caused dyslipidemia which is an independent factor that could explain increase risk of cardiovascular comorbidities.[12]

COPD is progressive disease and it is associated with poor quality of life.[13] Van Manen et al., demonstrated that the



Graph 1: Correlation between global initiative for chronic obstructive lung disease spirometeric classification and number of comorbidities

Table 1: GOLD spirometeric classification

GOLD-1	Mild	FEV_1>80% of predicted
GOLD-2	Moderate	50<FEV_1<80% of predicted
GOLD-3	Severe	30<FEV_1<50% of predicted
GOLD-4	Very severe	FEV_1<30% of predicted

GOLD: Global initiative for chronic obstructive lung disease, FEV_1: Forced expiratory volume in 1 s

Table 2: Frequency table showing various comorbidities of COPD

Comorbid disease	All subjects (n=50)	
	Frequency	Percentage
Hypertension	24	48
Coronary artery disease	06	12
Pulmonary hypertension	12	24
Left ventricular hypertrophy	07	14
Arrhythmias	05	10
Serum creatinine level (>1.2 mg/dL)	18	36
Serum urea level (>50 mg/dL)	15	30
GFR (<30 mL/min/1.73 m^2)	04	08
Diabetes	12	24
Dyslipidemia	12	24
Muscle wasting	13	26
Osteoporosis	21	42
Psychiatric illness	23	46

COPD: Chronic obstructive pulmonary disease

Table 3: Frequency table showing comorbidities distribution

Total number of comorbid conditions in single patients	Number of patients	Percentage
1	9	18
2	17	34
3	15	30
4	8	16
5	1	2

Table 4: Frequency table showing FEVI

FEV1 (%)	Frequency	Percentage
<30	11	22.0
30–50	18	36.0
51–80	18	36.0
>80	3	6.0
Total	50	100.0

FEV1: Forced expiratory volume in 1 s

prevalence of depression in COPD was around 20 to 60 % depending on stage of COPD. COPD with comorbidities is better associated with poor quality of health-related life. Due to repeated episodes of exacerbation and hospital readmission in COPD lead to psychiatric illness among patients.[14]

We showed that Gold spirometeric class was associated with a total number of comorbidities in a single patient. COPD patients having higher Gold spirometeric class have a higher number of comorbid conditions. This shows systemic nature of disease. Therefore, there is a great need to take into special account the incidence and severity of comorbid conditions in a course of comprehensive assessment and treatment of COPD patients.

BODE index is prognostic marker of COPD. BODE index included airway limitation (FEV1), dyspnea scale, exercise capacity, and body mass index. In that study, Gold spirometeric classification is based on FEV1.[15] Gold spirometeric classification is directly affect mortality and prognosis.[16]

Medication in COPD also contributes in comorbidities. Anticholinergic and beta-agonist drugs used as bronchodilator in COPD caused tachyarrhythmias and tremors. They might have cardiovascular effects. Inhaled corticosteroids may increase risk of pneumonia, osteoporosis, and cataracts. Kidney, liver, and heart comorbidities lead to changes in pharmacokinetic effect of drugs and caused unfavorable side effect.[17]

Evidence from previous studies suggests that multiple factors can be associated with mortality in COPD. It is now becoming clear from a number of observational studies that treatment of comorbid diseases may have some unexpected benefit on COPD mortality and health-care resource utilization.[18] In the previous study, a relation between spirometeric classification and risk of exacerbation has been found so it can also be used to predict future risk of exacerbations.[19]

It was suggested that therapy for COPD with existing medications targeting only lungs may not be enough to improve outcomes.[18] We consider that early preventive therapeutic interventions for various comorbid conditions may decrease mortality and morbidity in patients with COPD.

Limitations of the study

This study is single center and the sample size is small. COPD is a heterogeneous disease. Phenotypes of COPD become confounding factor in analysis of relation between comorbidities and GOLD spirometeric classification. We need a multicenter and large sample size study. Stratification and standardization of different groups of COPD needed to prevent confound bias.

CONCLUSION

Our study revealed that assessment of GOLD spirometeric classification could provide information about a total number of various comorbid conditions in patient with COPD. Patient with higher GOLD spirometeric classification has more comorbidities. Hence, patient with more severe airflow limitation should evaluate in detail with the help of clinical examination and relevant investigations about associated comorbid conditions.

ACKNOWLEDGMENT

None.

REFERENCES

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for Prevention, Diagnosis and Management of COPD; 2023 Report. Available from: https://goldcopd.org/2023-gold-report-2 [Last accessed on 2014 Sep 25].
2. World Health Organization. Chronic Obstructive Pulmonary Disease (COPD); 2011. Available from: https://www.who.int/respiratory/copd [Last accessed on 2014 Sep 25].
3. Barnes PJ and Celli BR. Systemic manifestations and comorbidities of COPD. Eur Respir J. 2009;33(5):1165-1185. https://doi.org/10.1183/09031936.00128008
4. Anthonisen NR, Connett JE, Enright PL, Manfreda J and Lung Health Study Research Group. Hospitalizations and mortality in the Lung Health Study. Am J Respir Crit Care Med. 2002;166(3):333-339. https://doi.org/10.1164/rccm.2110093
5. Vilkman S, Keistinen T, Tuuponen T and Kivelä SL. Survival and cause of death among elderly chronic obstructive pulmonary disease patients after first admission to hospital. Respiration. 1997;64(4):281-284. https://doi.org/10.1159/000196687
6. McGarvey LP, John M, Anderson JA, Zvarich M, Wise RA and TORCH Clinical Endpoint Committee. Ascertainment of cause-specific mortality in COPD: Operations of the TORCH Clinical Endpoint Committee. Thorax. 2007;62(5):411-415. https://doi.org/10.1136/thx.2006.072348
7. Forouzanfar MH, Liu P, Roth GA, Ng M, Biryukov S, Marczak L, et al. Global burden of hypertension and systolic blood pressure of at least 110 to 115 mm Hg, 1990-2015. JAMA. 2017;317(2):165-182. https://doi.org/10.1001/jama.2016.19043
8. Mancini GB, Etminan M, Zhang B, Levesque LE, FitzGerald JM and Brophy JM. Reduction of morbidity and mortality by statins, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers in patients with chronic obstructive pulmonary disease. J Am Coll Cardiol. 2006;47(12):2554-2560. https://doi.org/10.1016/j.jacc.2006.04.039
9. Yin HL, Yin SQ, Lin QY, Xu Y, Xu HW and Liu T. Prevalence of

comorbidities in chronic obstructive pulmonary disease patients: A meta-analysis. Medicine (Baltimore). 2017;96(19):e6836.
https://doi.org/10.1097/MD.0000000000006836

10. Curkendall SM, DeLuise C, Jones JK, Lanes S, Stang MR, Goehring E Jr., et al. Cardiovascular disease in patients with chronic obstructive pulmonary disease, Saskatchewan Canada cardiovascular disease in COPD patients. Ann Epidemiol. 2006;16(1):63-70.
https://doi.org/10.1016/j.annepidem.2005.04.008
11. Tudorache E, Fira-Mladinescu O, Traila D, Marc M, Rajnoveanu RM, Tofolean DE, et al. Endothelial dysfunction: The possible link between cardiovascular comorbidities and phenomenon of inflammaging from COPD. Medicine (Baltimore). 2022;101(33):e30078.
https://doi.org/10.1097/MD.0000000000030078
12. Gallucci G, Tartarone A, Lerose R, Lalinga AV and Capobianco AM. Cardiovascular risk of smoking and benefits of smoking cessation. J Thorac Dis. 2020;12(7):3866-3876.
https://doi.org/10.21037/jtd.2020.02.47
13. Ahmed MS, Neyaz A and Aslami AN. Health-related quality of life of chronic obstructive pulmonary disease patients: Results from a community based cross-sectional study in Aligarh, Uttar Pradesh, India. Lung India. 2016;33(2):148-153.
https://doi.org/10.4103/0970-2113.177438
14. Van Manen JG, Bindels PJ, Dekker FW, IJzermans CJ, van der Zee JS and Schadé E. Risk of depression in patients with chronic obstructive pulmonary disease and its determinants. Thorax. 2002;57(5):412-416.
https://doi.org/10.1136/thorax.57.5.412
15. Khan NA, Daga MK, Ahmad I, Mawari G, Kumar S, Kumar N, et al. Evaluation of BODE index and its relationship with systemic inflammation mediated by proinflammatory biomarkers in patients with COPD. J Inflamm Res. 2016;9:187-198.
https://doi.org/10.2147/JIR.S108783
16. Lee SJ, Yun SS, Ju S, You JW, Cho YJ, Jeong YY, et al. Validity of the GOLD 2017 classification in the prediction of mortality and respiratory hospitalization in patients with chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis. 2019;14:911-919.
https://doi.org/10.2147/COPD.S191362
17. Salpeter SR. Bronchodilators in COPD: Impact of beta-agonists and anticholinergics on severe exacerbations and mortality. Int J Chron Obstruct Pulmon Dis. 2007;2(1):11-18.
https://doi.org/10.2147/copd.2007.2.1.11
18. Hillas G, Perlikos F, Tsiligianni I and Tzanakis N. Managing comorbidities in COPD. Int J Chron Obstruct Pulmon Dis. 2015;10:95-109.
https://doi.org/10.2147/COPD.S54473
19. Faganello MM, Tanni SE, Sanchez FF, Pelegrino NR, Lucheta PA and Godoy I. BODE index and GOLD staging as predictors of 1-year exacerbation risk in chronic obstructive pulmonary disease. Am J Med Sci. 2010;339(1):10-14.
https://doi.org/10.1097/MAJ.0b013e3181bb8111

Author's Contribution:
MB- Definition of intellectual content, literature survey, prepared the first draft of a manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation, and submission of article; **AJ**- Concept, design of the study, clinical protocol, manuscript preparation, editing, and manuscript revision; **SD**- Statistical analysis and interpretation; and **AK**- Coordination and manuscript revision.

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Source of Support: Nil, **Conflicts of Interest:** None declared.