ORIGINAL ARTICLE

A Cross-sectional Study on Assessment of Estimated Glomerular Filtration Rate in Patients with Stable Chronic Obstructive Pulmonary Disease

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a systemic disease with several extrapulmonary comorbidities. However, studies to find out the relationship between COPD and renal impairment are scarce. This study aimed to assess the relationship of estimated glomerular filtration rate (eGFR) with chronic obstructive pulmonary disease assessment test (CAT) score, modified medical research council (mMRC) scale, 6-minute walking test (6MWT), and postbronchodilator forced expiratory volume (FEV_1) in COPD and to compare the reduction of eGFR in different GOLD stages.

Materials and methods: A total of 240 stable COPD patients attending the outpatient department (OPD) were randomly selected between November 2019 and October 2020. Participants had spirometry, Global Initiative for Chronic Obstructive Lung Disease (GOLD) staging, CAT score, mMRC grading, and 6MWT. Serum creatinine was obtained and eGFR was calculated. The interpretation was made by comparing the results of the eGFR and GOLD stages with different parameters.

Results: In patients with normal eGFR, the mean mMRC score was 2.00 ± 0.86, 6MWD was 324.98 ± 47.08 m, and CAT score was 14.23 ± 6.09. With reduced eGFR, the mean mMRC score was 2.32 ± 1.17, 6MWD was 278.30 ± 75.98 m, and CAT scoring was 19.38 ± 9.05. These were statistically significant ($p = 0.0145$, $p < 0.0001$, and $p < 0.0001$, respectively). A negative correlation was found between eGFR vs GOLD stages; the Pearson correlation coefficient (r) was −0.014.

Conclusion: Reduction of eGFR was seen in stable COPD patients with higher GOLD stages. Patients with reduced eGFR had higher mMRC grade, increased CAT score, and reduced 6MWD. So, routine estimation of eGFR in patients of stable COPD is advocated to assess renal involvement.

Keywords: Chronic obstructive pulmonary disease, Estimated glomerular filtration rate, Global Initiative for chronic obstructive lung disease stage, Renal involvement.

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Abbreviations used in this Article

CAT = Chronic obstructive pulmonary disease assessment test; CKD = Chronic kidney disease; CKD–EPI = Chronic kidney disease–epidemiology collaboration; COPD = Chronic obstructive pulmonary disease; CRF = Chronic renal failure; CRP = C-reactive protein; CVA = Cerebrovascular accident; eGFR = Estimated glomerular filtration rate; FEV = Forced expiratory volume; GERD = Gastroesophageal reflux disease; GOLD = Global Initiative for Chronic Obstructive Lung Disease; IHD = Ischemic heart disease; IL = Interleukin; mMRC = Modified medical research council; 6MWT = 6-minute walking test; OSA = Obstructive sleep apnea; QoL = Quality of life; TNF-α = Tumor necrosis factor-alpha.

Introduction

Chronic obstructive pulmonary disease (COPD) presents with progressive persistent shortness of breath and cough due to obstruction of airways and pathology of the alveolus.[1] The chronic airway limitation that is characteristic of COPD is caused by a mixture of small airway disease and parenchymal destruction (emphysema). Extrapulmonary comorbidities such as ischemic heart disease (IHD), heart failure, arrhythmias, peripheral vascular disease, gastroesophageal reflux disease (GERD), obstructive sleep apnea (OSA) and cerebrovascular accident (CVA) are very common in these patients.[2] These comorbidities significantly affect the quality of life (QoL) and health outcomes in COPD. In fact, COPD patients die mainly of nonrespiratory diseases such as cardiovascular disease (25%) and lung carcinoma (20–33%). Chronic kidney disease (CKD) is dysfunction of the kidney for 3 months or more, with health issues.[3]

To stage CKD, an estimated glomerular filtration rate (eGFR) is preferred over serum creatinine concentration. In this work, the

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chronic kidney disease–epidemiology collaboration (CKD–EPI) equation was utilized to calculate eGFR.

The renal involvement is often seen in COPD patients and is usually attributable to smoking and old age but the correlation between renal involvement and COPD is not well established and is a relatively neglected topic. Furthermore, COPD is a proposed cause of reduced eGFR and early detection of CKD in COPD patients will lead to early intervention with a subsequent significant decrease in morbidity and mortality. However, there is a paucity of publications showing a co-relation between eGFR and COPD in both national and international journals.

So, this study was conducted to estimate the eGFR among patients with stable COPD and to find out the correlation between eGFR and chronic obstructive pulmonary disease assessment test (CAT) Score, modified medical research council (mMRC) dyspnea scale, 6-minute walking distance (6MWD) and postbronchodilator forced expiratory volume (FEV_1) among them.

Materials and Methods

It was a hospital-based observational descriptive study conducted among the patients with COPD attending the outpatient department (OPD) of the department of respiratory medicine in a tertiary care hospital in Kolkata, West Bengal, India from November 2019 to May 2021. A total of 240 patients were randomly selected. Patients of more than 18 years of age with a confirmed diagnosis of COPD (Symptoms, Risk Factor, and Post Bronchodilator FEV_1/FVC < 0.7 as per GOLD guideline) were included in the study. Patients with diabetes, hypertension, systemic lupus erythematosus (SLE), known intrinsic renal disease, age more than 75 years, and patients presenting with acute exacerbation of COPD or a history of acute exacerbation of COPD within the last 1 month were excluded from the study. An informed consent was taken prior to taking history and clinical examination. The severity of dyspnea was assessed with mMRC grading. Six-minute walking test (6MWT) was performed on each patient. The severity of COPD was assessed by GOLD staging and CAT score. A 5 mL of venous blood was collected in a sterile procedure and serum creatinine was estimated with an automated biochemistry analyzer Indiko™ Plus (Thermo Fisher Scientific, Inc., Waltham, Massachusetts, USA). Using the CKD–EPI equation eGFR was calculated from serum creatinine level. The CKD–EPI equation, a single equation, is GFR = $141 \times \min(Scr/\kappa, 1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018$ (if female) – 1.159 (if black), where Scr is serum creatinine, κ is 0.7 for females and 0.9 for males, α is −0.329 for females and −0.411 for males, "min" indicates the minimum of Scr/κ or 1, and "max" indicates the maximum of Scr/κ or 1. Normal eGFR was taken as an eGFR value of more than 90 mL/minute/1.73 m^2. Reduced eGFR was taken as less than 89 mL/minute/1.73 m^2.

The data thus obtained was processed and coded by manual sorting and put in Microsoft Excel sheet in a computer. An unpaired student's *t*-test was applied. The interpretation was made by comparing the result of eGFR and GOLD stages of COPD and with different severity indicators of COPD such as mMRC score, CAT score, and 6MWT, and their strength of association was evaluated. The research proposal was approved by the institutional ethics committee.

Results

In this study, the majority of the patients were from 41–60 years age group (66.3%). About 64.2% of the COPD patients were males. The mean age of COPD patients was 56 ± 8 years. Among them, 63.8% of the patients were smokers and 33.8% of the patients were exposed to biomass fuel, and 2.4% of the patients were exposed to both. About 78 (32.5%) patients were of dyspnea mMRC grade I, 81 (33.8%) patients were of grade II, 48 (20.0%) patients were of grade III, and 33 (13.8%) patients grade IV. In this study, 13.8% of the patients were of GOLD stage I, 40.0% of stage II, 40.0% of the patients of stage III, and 6.3% of stage IV. About 46.3% of the patients had reduced eGFR. Among them, 81 (73.0%) patients were from the G2 eGFR subgroup, and 30 (27.0%) patients were from the G3a eGFR subgroup.

The association of smoking with the eGFR group was statistically significant [Chi-square value: 48.1378; $p < 0.0001$; odds ratio: 0.1326 (0.0726, 0.2420)] as the reduction of eGFR was significantly higher among smokers. Among patients with reduced eGFR, 56.8% were GOLD stage II and 43.2% were stage III. The association of the GOLD stage with the eGFR group was statistically significant ($p < 0.0001$). Among patients with reduced eGFR, the mean mMRC score was 2.32 ± 1.17 and that was statistically significant ($p = 0.0145$) (Table 1). The mean CAT score of these patients was 19.38 ± 9.05. The distribution of the mean CAT score with a reduced eGFR group was statistically significant ($p < 0.0001$) (Table 2). Among patients with normal eGFR, the mean 6MWD was 324.98 ± 47.08. In reduced eGFR, the mean 6MWD of patients was 278.29 ± 75.97. The distribution of mean 6MWD with the eGFR group was statistically significant ($p < 0.0001$) (Table 3). There was a negative correlation between eGFR vs GOLD stage [Pearson correlation coefficient (*r*) was −0.014] (Table 4 and Fig. 1).

Table 1: Distribution of mean mMRC score and eGFR group

	Number	*Mean*	*SD*	*Minimum*	*Maximum*	*Median*	*p-value*
mMRC score							
Normal eGFR	129	2.00	0.87	1.00	3.00	2.00	0.0145
Reduced eGFR	111	2.32	1.17	1.00	4.00	2.00	

Table 2: Distribution of mean CAT score and eGFR group

	Number	*Mean*	*SD*	*Minimum*	*Maximum*	*Median*	*p-value*
CAT score							
Normal eGFR	129	14.23	6.09	7.00	25.00	13.00	<0.0001
Reduced eGFR	111	19.38	9.05	9.00	35.00	18.00	

Table 3: Distribution of mean 6MWD and eGFR group

	Number	*Mean*	*SD*	*Minimum*	*Maximum*	*Median*	*p-value*
6MWD							
Normal eGFR	129	324.98	47.08	260.00	390.00	344.00	<0.0001
Reduced eGFR	111	278.30	75.97	159.00	402.00	280.00	

Table 4: Correlation between eGFR and GOLD stage

	GOLD stage		*Remarks*
eGFR	Pearson correlation coefficient (*r*)	−0.014	Negative correlation
	Number	240	

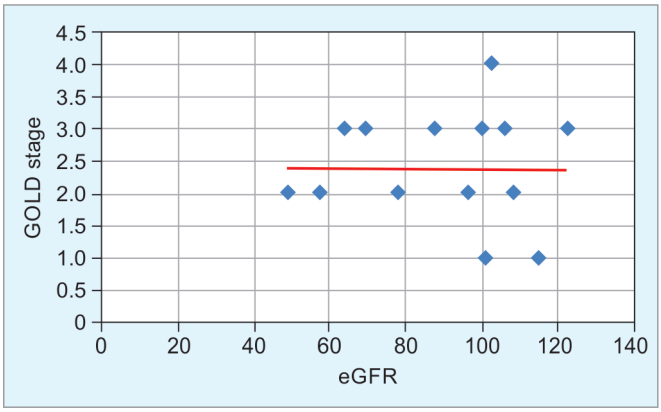

Fig. 1: Negative correlation between eGFR and GOLD stage

Discussion

Patients with COPD are at increased risk of renal dysfunction directly due to hypoxia or indirectly due to vascular disease and smoking.

There was suspicion that renal injury and COPD may be linked but no clinical evidence-based data published before to explain the relationship between albuminuria, renal dysfunction, smoking, and COPD.

Hypoxemia and hypercapnia of COPD often lead to renal tubular and interstitial injury, and sodium retention which play an important role in renal impairment in COPD patients.[4–6] Reduced glomerular filtration secondary to arterial stiffness also adds to the pathogenesis. Endothelins are frequently found as mediators in the pathophysiology of renal failure and COPD. Sofia et al. found a correlation between variations in endothelins and variations in $PaCO_2$ and PaO_2. In comparison to controls, COPD patients exhibited a considerably greater 24-hour urine excretion of endothelin, thus indicating the association of endothelin in the evolution of CKD in COPD.[7]

Inflammatory mediators, such as C-reactive protein (CRP), interleukin 6 (IL-6), IL-1β, tumor necrosis factor-alpha (TNF-α), toxic materials of cigarette smoke (nicotine and heavy metal); oxidative stress, neurohormonal activation, and abnormal immune cell signaling all contribute to renal damage of COPD patients.[8]

Elmahallawy and Qora studied the frequency of underdiagnosed renal failure in 300 COPD patients.[9] They found normal renal function, concealed and overt CKD in 54, 26, and 20% of the patients with COPD, respectively; in the control group, the values were 78, 10, and 12%, respectively. They concluded chronic renal failure (CRF) was an important comorbidity and estimated GFR was needed for screening.[9] A high prevalence of CKD among patients with COPD was seen in other studies also.[10–13] There was also a significant worsening of renal function over time. The higher incidence of CKD was also evident among patients with obstructive airway disease irrespective of diagnosis of COPD.[14,15]

In a study by Shihong et al., renal improvement was found in 30.59% of the group-D COPD but this was less than 15% in other groups. This study showed COPD patients having renal impairment had worse lung function and clinical symptoms compared with those with normal renal function. Among the lung function, FEV_1 % predicted, FEV_1/FVC was significantly affected.[16]

In this present study, patients with reduced eGFR had statistically significant higher mean mMRC scores, lower 6MWD, and higher CAT score. A negative correlation was found between eGFR vs GOLD stage; Pearson correlation coefficient (*r*) was −0.014. So, the findings of this study were similar to the study by Shihong et al.[16] We could not find any study showing a co-relation of renal impairment with mMRC score, CAT score, and 6MWD.

However, there were some limitations of our study. First, this was an observational study done in a tertiary care hospital in eastern India, so this study may not be representative of the general population at large. The sample size was relatively small. We did not evaluate other parameters of COPD such as QoL and frequency of acute exacerbations in patients with renal impairment in COPD. Proteinuria which is another marker of CKD was not evaluated in our study. The use of serum creatinine as a marker of renal impairment also has limitations. Also, COPD patients with renal impairment can have normal serum creatinine due to undernutrition and lean muscle mass; so, the eGFR formula may be ineffective in those cases.

In conclusion, it is advocated that renal function should be evaluated in all patients of COPD at the initial visit and also in subsequent visits for assessment of progression of renal impairment.

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