Journal of Cardiovascular Disease Research
ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 12, 2024

Relationship Of Microalbuminuria & COPD –Study On 101 Patients At A Tertiary Care Centre Of Gujarat.

Dr Parth Patel[1], Dr Chandra Shekhar Purohit[2], Dr Varun Patel[3], Dr Kalpesh Patel[4*]

[1](Mbbs, Md Respiratory Medicine) Assistant professor, Dept of respiratory medicine Gujarat Adani Institute of Medical Sciences, Bhuj Gujarat 370001, 918469952346, drparthpatel122@gmail.com
[2](Mbbs, Md Respiratory Medicine), Professor, Pacific Institute Of Medical Sciences, Udaipur Rajasthan. 919927077972, papurv1988@yahoo.co.uk
[3](Mbbs,DTCD,DNB Respiratory Medicine), Associate Professor, Gujarat Adani Institute of Medical Science, pulmonary medicine GAIMS, G K General Hospital, Bhuj, Gujarat, IN 370001 918980047631.
[4*](Mbbs, Md Respiratory Medicine), Professor, Gujarat Adani Institute of Medical Science, pulmonary medicine GAIMS, G K General Hospital, Bhuj, Gujarat, Gujarat, IN 370001 918980047631, drkalpeshpatel@hotmail.com

***Corresponding Author:** Dr Kalpesh Patel
*(Mbbs, Md Respiratory Medicine), Professor, Gujarat Adani Institute of Medical Science, pulmonary medicine GAIMS, G K General Hospital, Bhuj, Gujarat, Gujarat, IN 370001 918980047631, drkalpeshpatel@hotmail.com

Abstract

BACKGROUND: Microalbuminuria, marker of endothelial abnormality, is a predictor of mortality for any reason and of cardiovascular events. Recent research on the management of COPD has focused more on comorbidities, including cardiovascular events. The main objective of this study was to investigate microalbuminuria and its association with physiological and clinical characteristics in a subject group that was classified in line with the new version of the GOLD (Global Initiative for Chronic Obstructive Lung Disease) stages.

METHODS:101 stable patients with mild stage to very severe stage COPD were included. The urinary albumin/creatinine (UACR) ratio was calculated using an established formula. Microalbuminuria was accepted as UACR >20 in males and >30 in females as positive finding.

RESULTS: UACR was significantly higher in subjects grouped as having more symptoms. In addition, significant differences were observed when the subjects were grouped based on PaO2 (<65 mm Hg vs >65 mm Hg), PaCO2 (<41 mm Hg vs >41 mm Hg), arterial oxygen saturation (<92% vs >92%), and median. Pearson correlation analysis revealed that the UACR was significantly inversely correlated with percent of predicted FEV1 (r-0.56, p = .001), SaO2 (r-0.48, p = .001) and PaO2 (r -0.60, p= .001). Positive correlation was also found between UACR and CAT scores (r =0.53, p = .001).

CONCLUSIONS: We conclude that there is a strong relationship between microalbuminuria and cardiovascular incidents in patients with COPD, commonly in patients with higher symptoms and high future risk. *Key words: COPD; microalbuminuria; severity of illness; scoring system.*

Introduction-

COPD is an important cause of morbidity and mortality in the world. The mortality rate of COPD is increasing, and this disease is estimated to become the third significant cause of death in world by

2020.[1] The complexity of COPD makes a comprehensive evaluation necessary for its management. COPD is a heterogenic disease with both pulmonary and extrapulmonary symptoms characterized by long-term poor air flow. In particular, cardiovascular disease remains one of the leading causes of mortality and morbidity in patients with COPD, independent of the well-recognized risk factors, including age, sex, and smking status[2] Microalbuminuria is one of the precise indicators of cardiovascular risk[3,4] A consistent association has been shown between microalbuminuria and poor cardiovascular outcomes in subjects with hypertension and diabetes mellitus and, most importantly, in the general population[5,6] Studies conducted on the determinants of microalbuminuria have reported a close association between vascular disease and systemic endothelial abnormalities and have also suggested glomerular endothelial dysfunction in microalbuminuria[7] In one study, lower FEV1 and severity of emphysema have been shown to be correlated with endothelial dysfunction[8] It has been demonstrated that microalbuminuria increases in worsening periods of COPD, suggesting an association with increased glomerular filtration, resulting in protein leakage because of increased hypoxia during COPD event.[9] There have only been a limited number of studies in the literature reporting a high incidence of microalbuminuria in COPD patients compared with age-matched controls having a smoking pack-year value[10], with no comorbidities such as hypertension, diabetes mellitus, renal disease, cardiovascular disease, or malignancy in both groups.[9-11] However, till date, there is still single study investigating the association of microalbuminuria with COPD assessment test scores and the risk of exacerbation based on the new version of the COPD GOLD stages.[12] Therefore, in this study, we investigate the association between microalbuminuria and the new version of GOLD stages and the clinical features that may predict cardiovascular risk in COPD patients.

MATERIALS AND METHODS

Study Population and Study Design

The study was conducted in the Department of Pulmonary Medicine, Gujarat Adani Institute of Medical Sciences (GAIMS), Bhuj, Gujarat. After approval from institutional ethics committee after taking written inform consent of patients included in study.The study included 101 subjects with COPD in the stable period between 30 and 74 y old who had no previous diagnosis of cerebrovascular disease, ischemic heart disease, or peripheral arterial-venous disease and no clinical symptoms of these diseases and had not been treated for these diseases; nor was there a diagnosis of known renal or liver diseases or malignancies. Subjects with a history of the presence of macroalbuminuria (urinary albumin/creatinine ratio >300 mg/g) or previously diagnosed with diabetes mellitus; myocardial infarction; severe congestive cardiac failure; angina pectoris; electrocardiographic ST-T alterations suggesting ischemic heart disease; left bundle branch block and arrhythmias; other pulmonary diseases, including obstructive sleep apnea, asthma, and interstitial lung disease; acute infections; and comorbidities, such as severe hepatic failure and malignancy were excluded from the study

The diagnosis of COPD was confirmed with the GOLD 2016 guidelines. The disease was classified in line with the GOLD staging (classes A–D)[12] GOLD guidelines recommend the CAT (COPD assessment test) or MMRC (Modified Medical Research Council) dyspnea scale in evaluation of the symptoms[13] The CAT comprises 8 items scored from 0 to 5 points, including the severity of Sputum, phlegm, chest heaviness, shortness of breath, capacity for activities and exercise, confidence, sleep quality, and energy levels[14] whereas the MMRC dyspnea scale is a quantitative tool that evaluates only breathlessness.

In this study, the CAT was applied through face-to-face interviews by a pulmonary specialist. The subjects with COPD were classified as A, B, C, and D using a combination of the CAT symptom evaluation test and the risk for exacerbation, which was determined by the exacerbation history within the last year and the spirometric classification of air-flow limitation by the GOLD grade, which is categorized by percent-of-predicted FEV1. Category A included subjects a with low risk

and fewer symptoms; B included those with low risk and more symptoms; C included those with high risk and fewer symptoms; and D included those with high risk and more symptoms.
Smoking history was determined by pack-years, which were calculated by multiplying the number of cigarettes packs smoked per day by the number of years the person had smoked. The questionnaire was administered through a personal interview with a specific enquiry about the history of smoking, current smoking status, and pack-years of smoking. All subjects were current or ex-smokers with a history of smoking of 10 or more pack-years. A medical history and findings on physical examination were recorded for each subject. Weight and height were measured, the BMI (body mass index) value was calculated, and spirometry was carried out in line with international guidelines (American Thoracic Society/European Respiratory Society).[15] Arterial blood gases were measured in the samples collected by direct arterial puncture, in the morning after sitting at rest for 15 min and breathing room air for >45 min.

OBSERVATION AND RESULTS

The study included a total of 101 subjects who met the selection criteria. Of these subjects, 31(30.7) were in the Category GOLD A,26 (25.7) in GOLD B, 16(15.8) in GOLD C, and 28(27.7) in GOLD D. The characteristics of the subjects are given in Table 1.
The mean age was 62.25 y, and 75 (74.3) of the subjects were male. The severity of air-flow limitation varied from mild to very severe.

Discussion

This study aimed to examine the association of microalbuminuria and COPD with the new version of GOLD staging.The results of the study showed that UACR was much higher in the subjects classified in the group with more symptoms and high risk compared with the group with fewer symptoms and low risk. The UACR was determined to be statistically significantly different between the groups when classified based on FEV1, history of exacerbations and COPD assessment test scores. Although very few studies in the literature evaluate about microalbuminuria in COPD patients, there have been some that have reported the prevalence of microalbuminuria in such subjects[7,10,16] In one of these previous studies, the microalbuminuria level was measured in 25 subjects during exacerbations. Of these subjects, 56% had microalbuminuria at the time of admission and 28% at discharge, whereas this rate was only 4% in the control group. In the same study, microalbuminuria was correlated with hypoxemia but not with the FEV1[7] In another similar study that evaluated subjects during exacerbations, the authors reported that microalbuminuria was associated with the presence of respiratory failure. However, no spirometric measurements were performed in that study[10] in another study of 33 subjects with stable COPD, 26 subjects with exacerbation, and 16 healthy controls, the microalbuminuria level was significantly increased only in the exacerbation group. However, the microalbuminuria level in the COPD group was twice that of the control subjects.[16] These results show that microalbuminuria is common in COPD and seems to increase during exacerbations. However, in one publication, Casanova et al[17] showed that the microalbuminuria was high in subjects with COPD and was associated with hypoxemia independently of the other cardiac risk factors. Bulcun et al,[18] demostrated that there was also association between microalbuminuria with disease severity. Likewise, in the study, microalbuminuria was present in 56 (55.4%) of the patients.
Subjects with COPD in all GOLD categories were included in the current study, and the UACR values were found to be higher in groups C and D than in groups A and B. BMI decreases in patients with severe COPD. Morbidity and mortality increase as the body mass index value decreases, particularly in elderly and hypoxic subjects[19] Although a limited number of studies have found an association between urinary albumin excretion rate and obesity, other studies have found no significant correlation[17,20-22] Similarly, in the present study, no such relation was seen between the study groups. Smoking decreases renal blood flow, glomerular filtration rate, and filtration fraction in healthy persons, all of which increase renovascular resistance, resulting in thickening of

the renal arterioles and causing renal blood flow to be functionally disrupted. Consequently, the filtration rate is decreased in persons with a normal glomerular filtration rate. However, small repeated transient renal hypoperfusion episodes may damage glomeruli and eventually lead to structural changes, such as hyperfiltration and hypertrophy in remnant glomeruli, causing increased glomerular filtration rate and albumin excretion[23] It has been argued that increased hypoxic stimulation in endothelial cells could cause endothelial dysfunction, resulting in higher microalbuminuria in smokers[20] Although some studies have found a positive correlation between microalbuminuria and smoking history in patients with COPD, others have observed no such association[9,22,24] In our study, no correlation was determined between microalbuminuria and smoking history.

Increased sympathetic activity due to hypoxemia can also play a role in capillary endothelial permeability, causing proteinuria through increased capillary permeability. This is not influenced by altered renal tubular function, increased blood pressure, and renal filtration rate[25] A study performed on 102 subjects with similar serum protein levels demonstrated a significant correlation between decreased PaO2 level and high urinary protein excretion[11.]Vasoconstriction resulting from hypoxemia and respiratory acidosis-induced glomerular albumin filtration are increased in patients with cor pulmonale with sleep apnea syndrome. This mechanism may be responsible for the short-term proteinuria seen in subjects with COPD[26]. Casanova et al[17] showed that significant COPD patients with microalbuminuria were found to have hypoxemia, with the highest values (>50 mg/g) of microalbuminuria observed in subjects with a PaO2 level of <70 mm Hg. Likewise, in our study, the UACR values of subjects were found to be much higher when the subjects were grouped based on median split PaO2 levels (<65 mm Hg vs >65 mm Hg). Nevertheless, some subjects with hypoxemia may not show microalbuminuria, suggesting that other factors, including genetic susceptibility to oxidative stress, may also be implicated[27] Again in another study, COPD patients with microalbuminuria were found to be statistically significantly more hypoxic and more hypercapnic compared with COPD subjects without microalbuminuria. As a result of that study, PaO2, which showed a negative correlation with microalbuminuria, was determined to be the most important predictive factor[28]. Ko¨mu¨rcuog˘lu et al[10] established a negative relationship was determined between microalbuminuria identified in COPD patients and levels of PaO2 and arterial oxygen saturation, although no significant association between microalbuminuria with levels of pH and PaCO2 was observed. The study suggested that microalbuminuria developed due to increased glomerular filtration due to increase hypoxemia, eventually developing protein leakage[10] In our study, a significant inverse correlation was determined between UACR and PaO_2 , and a positive correlation was found between UACR and $PaCO_2$.

Celli et al[29] showed that most COPD patients with GOLD stage III and IV showed microalbuminuria, whereas GOLD stage I and II had no microalbuminuria; the difference was statistically significant. This could possibly be explained by impaired lung function, including COPD, which has been associated with increased systemic arterial stiffness. Given the relationship between abnormal lung function and arterial stiffness, an increase in arterial stiffness should lead to increased kinetic energy transmission to the distal microcirculation, thus resulting in microvascular damage[29] Emerging evidence demonstrates that the degree of air-flow limitation is poorly predictive of dyspnea and quality of life[30] Therefore, the classification of severity groups, as described by the GOLD committee, has moved away from a linear approach based only on degree of airway limitation to a 2-dimensional evaluation that includes both the risk and symptom assessment[12] In the present study, subjects with COPD patients were classified in A, B, C and D groups, combining symptom assessment by CAT scores, air-flow limitation, and risk of exacerbation. The urinary albumin/creatinine ratio values were found to be higher in groups C and D than in groups A and B. Celli et al[29]showed that the MMRC scores of 3 and 4 in COPD patients with microalbuminuria, the scores were 1 and 2 in COPD subjects without microalbuminuria. This was considered to be due to

the increased endothelial damage caused by hypoxia in subjects with grade III and IV dyspnea leading to microalbuminuria.

In the current study, symptoms were assessed with COPD assessment test scores, and the urinary albumin/ creatinine ratio levels were found to be much higher when the subjects were grouped based on median split COPD assessment test (<10 vs >10). However, when GOLD C and D subjects with a FEV1 value <50% were evaluated according to the symptoms, no significant correlation was found.

CONCLUSIONS

The results of our study conclude a firm correlation between microalbuminuria and COPD according to the new version of GOLD stages. Microalbuminuria is evaluated as a risk for cardio-vascular diseases. Because the diagnosis of microalbuminuria is simple, inexpensive, and noninvasive, it can be evaluated routinely in COPD cases, especially those with many symptoms who are at high risk, in terms of cardiovascular morbidity and mortality. Further studies are warranted to determine the association between microalbuminuria and severity of disease, including successful treatment and longitudinal subject processes, and COPD.

The present study has several limitations. First, the narrow sample size of the study may not be representative for subjects with COPD. Moreover, all subjects were in a stable period, and therefore comparisons could not be made of UACR in both the exacerbation and stable periods. In addition, since the main aim of our study was to determine the microalbuminuria relationship in COPD subgroups, no control group was included. There is a need for further studies with larger sample sizes to confirm these findings. Furthermore, the cross-sectional structure of the data did not allow causal links to be established. Another limitation was that, because the number of female subjects was limited, possible sex differences in microalbuminuria could not be evaluated

Conflict of interests- The author reports no conflicts of interests.

References

1. Mannino DM, Buist AS. Global burden of COPD: risk factors, prevalence, and future trends. Lancet 2007;370(9589):765-773 DOI:https://doi.org/10.1016/S0140-6736(07)61380-4 **CrossRef PubMed Google Scholar**
2. Ghoorah K, De Soyza A, Kunadian V. Increased cardiovascular risk in patients with chronic obstructive pulmonary disease and the potential mechanisms linking the two conditions: a review. Cardiol Rev 2013;21(4):196-202. DOI http://dx.doi.org/10.1136/bmjopen-2017-020713 **CrossRef PubMed Google Scholar**
3. Diercks GF, van Boven AJ, Hillege JL, de Jong PE, Rouleau JL, van Gilst WH et al. The importance of microalbuminuria as a cardiovascular risk indicator: Areview. Can J Cardiol 2002;18(5):525-535. DOI: 10.2215/CJN.05530610 **PubMed Google Scholar**
4. Weir MR. Microalbuminuria and cardiovascular disease. Clin J Am Soc Nephrol 2007;2(3):581-590. DOI: 10.2215/CJN.03190906 **Abstract/FREE Full TextGoogle Scholar**
5. Papaioannou GI, Seip RL, Grey NJ, Katten D, Taylor A, Inzucchi SE, et al. Brachial artery reactivity in asymptomatic patients with type 2 diabetes mellitus and microalbuminuria. Am J Cardiol 2004; 94(3):294-299. https://doi.org/10.1016/j.amjcard.2004.04.022 **CrossRef PubMed Google Scholar**
6. Mule` G, Cottone S, Vadala` A, Volpe V, Mezzatesta G, Mongiovì R, et al. Relationship between albumin excretion rate and aortic stiffness in untreated essential hypertensive patients. J Intern Med 2004; 256(1):22-29. https://doi.org/10.1038/ajh.2009.132 **CrossRef PubMed Google Scholar**

7. Ibsen H, Olsen MH, Wachtell K, Borch-Johnsen K, Lindholm LH, Mogensen CE, et al. Reduction in albuminuria translates to reduction in cardiovascular events in hypertensive patients: losartan intervention for end point reduction in hypertension study. Hypertension 2005;45(2):198-202. DOI: 10.1161/01.HYP.0000154082.72286.2a **CrossRef PubMed Google Scholar**
8. Barr RG, Mesia-Vela S, Austin JH, Basner RC, Keller BM, Reeves AP, et al. Impaired flow mediated dilation is associated with low pulmonary function and emphysema in ex-smokers: the Emphysema and Cancer Action Project (EMCAP) Study. Am J Respir Crit Care Med 2007;176(12):1200-1207. DOI: 10.1164/rccm.200707-980oc**CrossRef PubMed Google Scholar**
9. Polatli M, Cakir A, Cildag O, Bolaman AZ, Yenisey C, Yenicerioglu Y et al Microalbuminuria, von Willebrand factor and fibrinogen levels as markers of the severity in COPD exacerbation. J Thromb Thrombolysis 2008;26(2):97-102 DOI: 10.1007/s11239-007-0073-1 **CrossRef PubMed Google Scholar**
10. Kalenci S, Kalenci D, Ko¨mu¨rcu¨og˘lu B, Tibet G et al. Microalbuminuria in chronic obstructive pulmonary disease. Monaldi Arch Chest Dis 2003;59(4):269-272. https://doi.org/10.1164/rccm.201003-0360OC **PubMed Google Scholar**
11. Gogo A, Ciaccia A, Legorini C, Grimaldi A, Milani Get al Proteinuria in COPD patients with and without respiratory failure. Chest 2003; 123(2):652-653; DOI:10.1164/rccm.201003-0360OC . **CrossRef PubMed Google Scholar**
12. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. 2016. http://goldcopd.org/globalstrategy- diagnosis-management-prevention-copd-2016. DOI:http:// ow.ly/XxfD308BDfc **Google Scholar**
13. Bestall JC, Paul EA, Garrod R, Garnham R, Jones PW, Wedzicha JA et al. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. Thorax 1999;54(7):581-586. DOI: 10.1136/thx.54.7.581 **Abstract/FREE Full TextGoogle Scholar**
14. Jones PW, Harding G, Berry P, Wiklund I, Chen WH, Kline Leidy N et al. Development and first validation of the COPD Assessment Test. Eur Respir J 2009;34(3):648-654. DOI**:** 10.1183/09031936.00102509 **Abstract/FREE Full TextGoogle Scholar**
15. Brusasco V, Crapo R, Viegi G, American Thoracic Society, European Respiratory Society. Coming together: the ATS/ERS consensus on clinical pulmonary function testing. Eur Respir J. 2005;26(1):1-2 **DOI:** 10.1183/09031936.05.00034205 **FREE Full TextGoogle Scholar**
16. Wachtell K, Ibsen H, Olsen MH, Borch-Johnsen K, Lindholm LH, Mogensen CE, et al. Albuminuria and cardiovascular risk in hypertensive patients with left ventricular hypertrophy: the LIFE Study. Ann Intern Med 2003;139(11):901-906. doi: 10.7326/0003-4819-139-11-200312020-00008.**CrossRef PubMed Google Scholar**
17. Casanova C, de Torres JP, Navarro J, Aguirre-Jaíme A, Toledo P, Cordoba E, et al. Microalbuminuria and hypoxia in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2010;182(8):1004-1010. DOI: 10.4103/0970-2113.201299 **CrossRefPubMedGoogle Scholar**
18. Bulcun E, Ekici M, Ekici A, Kisa U et al. Microalbuminuria in chronic obstructive pulmonary disease. COPD 2013;10(2):186-192. DOI: 10.3109/15412555.2012.735292 **CrossRef Google Scholar**
19. Phelps DT, Ferro TJ, Higgins PJ, Shankar R, Parker DM, Johnson A et al. TNF-_ induces peroxynitrite-mediated depletion of lung endothelial glutathione via protein kinase C. Am J Physiol 1995;269(4 Pt 1): L551–L559. https://doi.org/10.1161/01.CIR.101.1.33 Circulation. 2000;101:33–39 **Google Scholar**
20. Stuveling EM, Bakker SJ, Hillege HL, Burgerhof JG, de Jong PE, Gans RO, et al. C reactive protein modifies the relationship between blood pressure and microalbuminuria. Hypertension

2004;43(4):791- 796. https://doi.org/10.1161/01.HYP.0000178188.29446.48 **CrossRef Google Scholar**

21. Thoenes M, Reil JC, Khan BV, Bramlage P, Volpe M, Kirch W, Bo¨hm M et al. Abdominal obesity is associated with microalbuminuria and an elevated cardiovascular risk profile in patients with hypertension. Vasc Health Risk Manag 2009;5(4):577-585. https://doi.org/10.1093/eurheartj/suv016 **PubMed Google Scholar**
22. Kaysoydu E, Arslan S, Yıldız G, Candan F et al. Factors related to microalbuminuria in patients with chronic obstructive pulmonary disease.Adv Clin Exp Med 2014;23(5):749-755. DOI: https://doi.org/10.4187/respcare.05168 **PubMed Google Scholar**
23. Pinto-Sietsma SJ, Mulder J, Janssen WM, Hillege HL, de Zeeuw D, de Jong PE et al. Smoking is related to albuminuria and abnormal renal function in nondiabetic persons. Ann Intern Med 2000;133(8):585-591. DOI:https://doi.org/10.1053/ajkd.2002.36563 **CrossRef PubMed Google Scholar**
24. Metoki H, Ohkubo T, Kikuya M, Asayama K, Obara T, Hashimoto J, et al. Prognostic significance for stroke of a morning pressor surge and a nocturnal blood pressure decline: the Ohasama study. Hypertension 2006;47(2):149-154. https://doi.org/10.1038/ajh.2009.160 **CrossRef Google Scholar**
25. Hansen JM, Olsen NV, Feldt-Rasmussen B, Kanstrup IL, De´chaux M, Dubray C, Richalet JP et al. Albuminuria and over all capillary permeability of albumin in acute altitude hypoxia. J Appl Physiol 1994; 76(5):1922-1927. https://doi.org/10.1113/JP281028. **Abstract/FREE Full TextGoogle Scholar**
26. Sklar AH, Chaudhary BA. Reversible proteinuria in obstructive sleep apnea syndrome. Arch Intern Med 1988;148(1):87-89 doi:10.1001/archinte.1988.00380010091009 **CrossRef PubMed Google Scholar**
27. Shin KK, Jang Y, Koh SJ, Chae JS, Kim OY, Park S, et al. Influence of the IL-6-572C_G polymorphism on inflammatory markers according to cigarette smoking in Korean healthy men. Cytokine 2007; 39(2):116-122. DOI: 10.1089/jir.2012.0033 **CrossRef PubMed Google Scholar**
28. Mehmood K, Sofi FA. Microalbuminuria and hypoxemia in patients with COPD. J Pulm Respir Med 2015; 5:280. doi: 10.4172/2161- 105X.1000280. doi: 10.4172/2161-105X.1000280. **Google Scholar**
29. Celli BR, Cote CG, Marin JM, Casanova C, Montes de Oca M, Mendez RA, et al. The body mass index, airflow obstruction, dyspnea, exercise performance (BODE) index in chronic obstructive pulmonary disease. N Engl J Med 2004;350(10):1005-1012. DOI: 10.1056/NEJMoa021322, **CrossRef PubMed Google Scholar**
30. Garcia-Aymerich J, Serra Pons I, Mannino DM, Maas AK, Miller DP, Davis KJ et al. Lung function impairment, COPD hospitalizations and subsequent mortality Thorax 2011;66(7):585-590. DOI https://doi.org/10.2147/COPD.S234942. **Abstract/FREE Full Text Google Scholar**

Characteristics		Values (UACR)
Sex, n (%)	Male	75(74.3)
	Female	26(25.7)
Age, mean SD y		62.25±10.89
Smoking, mean SD packs/y		27.62±9.42
BMI, mean SD kg/m2		22.26±3.99
GOLD subgroups, n (%):	A	31(30.7)
	B	26(25.7)
	C	16(15.8)
	D	28(27.7)
% predicted FEV1, n (%):	≥80%	8(7.9)
	50–80%	50(49.5)
	50–30%	35(34.7)
	<30%	8(7.9)
Mean CAT score, n (%):	<10	25(24.8)
	≥10	76(75.2)
Exacerbations (total), n (%):	0	30(29.7)
	1	52(51.5)
	2	17(16.8)
	3	2(2)
PaO2, mean SD mm Hg		75.98±17.33
PaCO2, mean SD mm Hg		49.10±9.96
UACR, mean SD		28.46±14.91
Presence of MAB, n (%)		56(55.4)

TABLE 1

There was a significant difference between the categories in terms of UACR based on GOLD staging (A–D class) (Fig. 1) (*P* =.001). A significant differences in UACR between the subjects in categories A and B (*P* = .001), A and C (*P* = .001), A and D (*P* = .001), B and C (*P* =.001), and B and D (*P*= .001) but not between C and D (*P* _ .31)

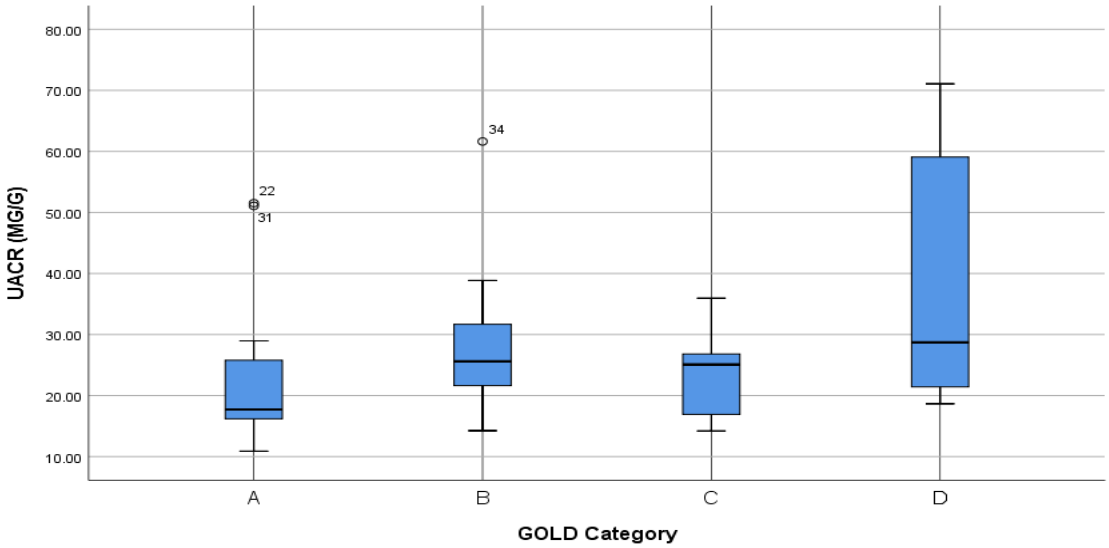

Figure 1. UACR of subjects grouped according GOLD categories. Upper & lower borders of boxes represent the third and first quartiles, centre lines denote the median, and whiskers show the 5th and 95th percentiles.

COPD patients' subgroups were also compared in terms of UACR based on FEV1 GOLD stages, FEV1 (median split, <60% vs >60%), CAT (<10 vs >10), and exacerbations episode (0–1 vs 2 or more). UACR showed a significant difference, depending on the categories of each COPD parameter (Table 2). Significant differences were also observed when subjects were grouped according to median PaO2 (<65 mm Hg vs >65 mm Hg), PaCO2 (<41 mm Hg vs >41 mm Hg), and oxygen saturation (arterial)(<92% vs >92%) (Table 2).

Table 2 UACR of COPD patients Subgroups

Variables		n	Mean	*p* value
FEV_1(GOLD Stages)	1(≥80%)	8	18.14±4.53	0.01
	2(50%-80%)	50	25.20±9.74	
	3(50%-30%)	35	31.72±17.92	
	4(<30%)	8	44.84±19.30	
FEV_1(Median split)	<52.900	51	33.82±17.75	0.01
	≥52.900	50	22.98±8.45	
CAT	<10	25	21.16±5.94	0.01
	≥10	76	30.86±16.17	
Exacerbations	0	30	21.99±10.68	0.01
	1	52	28.83±11.84	
	2	17	33.70±20.02	
	3	2	70.98±0.00	
BMI	≥30	10	22.95±7.40	0.34
	<30	91	29.06±15.41	
PaO_2	≤65	33	38.09±18.99	0.01
	>65	68	23.77±9.56	
$PaCo_2$	≤41	23	23.86±7.38	0.30
	>41	78	29.81±16.27	

*(*p* value <0.01 is significant)

Table 3: Results of Pearson Correlation Analysis on all patients of the Study.

Variables	Urinary Albumin/Creatine Ratio	
	r	*p* value
BMI	-0.078	0.22
Age(y)	-0.109	0.14
P_aO_2	-0.423	0.01
P_aCO_2	0.245	0.01
CAT	0.275	0.01
Exacerbation	0.413	0.01
FEV_1	-0.453	0.01

*(*p* value <0.01 is significant)

Fig.2: Correlation of UACR and FEV1 in COPD pateints grouped according to GOLD categories (P <.01).

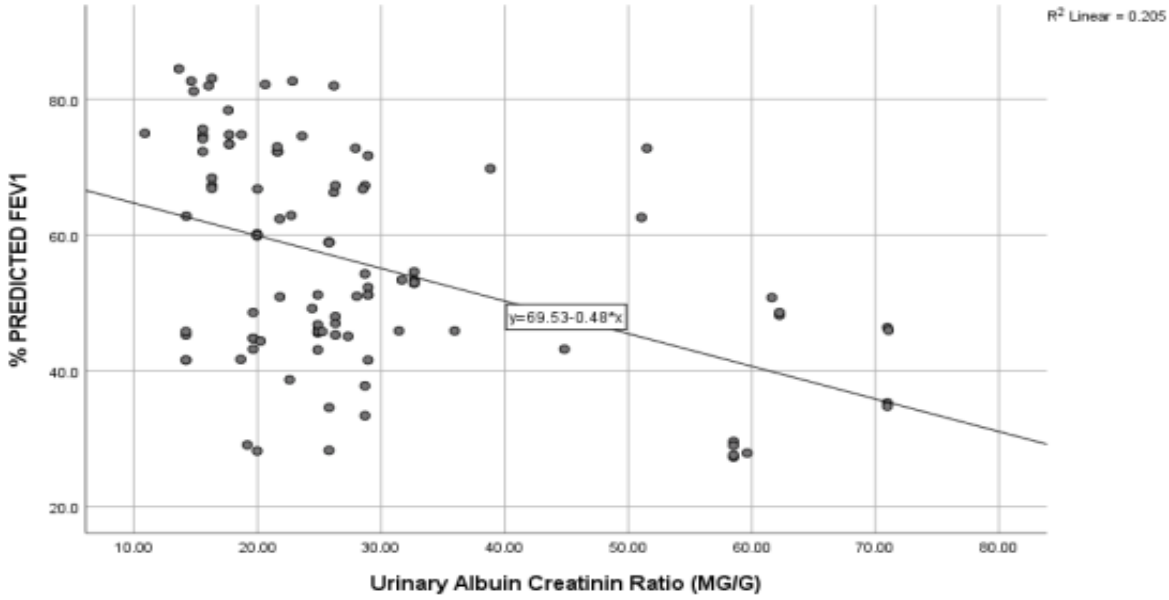

Fig. 3. Correlation of UACR and CAT in subjects with COPD grouped according to GOLD categories (P <.01).

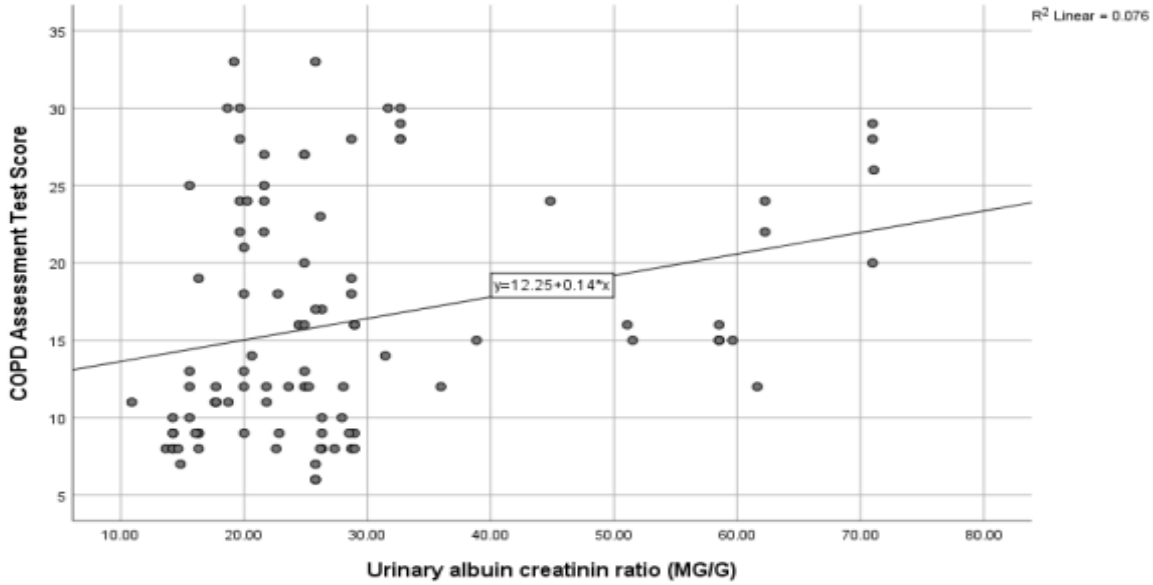

Fig. 4. Correlation of UACR and PaO2 in COPD patrients grouped according to GOLD categories .(P<.01).

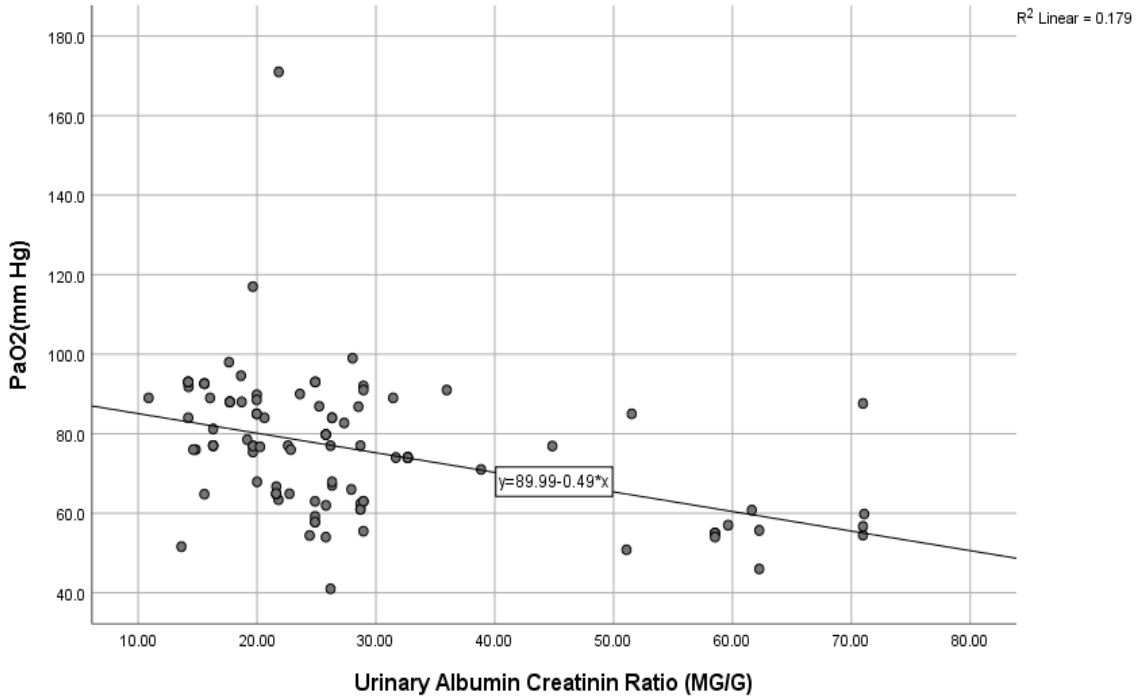

Table 4. Risk Factors for Cardiovascular Diseases in COPD patients : Multivariate Analysis

Risk Factors	Odds Ratio	95% CI	*p* value*
Age(y)	0.953	0.905-1.003	0.06
Male sex	0.057	0.013-0.243	0.01
BMI (kg/m^2)	0.900	0.793-1.021	0.10
FEV_1	0.953	0.916-0.990	0.01
Exacerbation	1.283	0.565-2.914	0.55
Smoking history	1.029	0.970-1.092	0.35

*(*p* value <0.01 is significant)