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EVALUATION OF THE ROLE OF URIC ACID, CREATININE RATIO, AND ALBUMIN-CREATININE RATIO AS PROGNOSTIC MARKERS IN ASSESSING SEVERITY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) WITH CORRELATION TO DEMOGRAPHIC PROFILE AND SPIROMETRY PARAMETERS

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a progressive and debilitating respiratory disorder characterized by persistent airflow limitation, chronic inflammation, and structural alterations in the airways. It represents a major global health burden and is currently one of the leading causes of morbidity and mortality worldwide, particularly in low- and middle-income countries. Although spirometry remains the gold standard for diagnosis and staging, it does not adequately reflect the systemic nature of COPD or predict disease progression and outcomes. Increasing evidence suggests that COPD is associated with systemic inflammation, oxidative stress, and endothelial dysfunction, which contribute to extrapulmonary manifestations and poorer prognosis. In this context, biochemical markers such as uric acid–creatinine ratio (UA/Cr), reflecting hypoxia-induced metabolic stress, and albumin–creatinine ratio (ACR), indicating endothelial dysfunction and microvascular damage, have emerged as potential prognostic indicators. However, their combined role in assessing COPD severity and correlation with spirometric parameters remains inadequately explored.

Objectives: To evaluate the role of UA/Cr ratio and ACR as prognostic markers in assessing COPD severity and to correlate these biomarkers with demographic profile and spirometry parameters.

Methods: This hospital-based cross-sectional analytical study was conducted among 100 COPD patients from July 2025 to January 2026. Diagnosis and severity classification were based on GOLD criteria. Serum uric acid, serum creatinine, and urinary albumin were measured, and UA/Cr ratio and ACR were calculated. Spirometry parameters including FEV_1, FVC, and FEV_1/FVC ratio were recorded. Statistical analysis included ANOVA, correlation analysis, and logistic regression.

Results: The mean UA/Cr ratio increased significantly from 4.2 ± 0.8 in Stage I to 9.1 ± 1.8 in Stage IV ($p < 0.001$). ACR increased from 18 ± 6 mg/g to 110 ± 22 mg/g across stages ($p < 0.001$). Both markers showed significant negative correlations with spirometry, with ACR showing stronger correlation with FEV_1 ($r = -0.68$) compared to UA/Cr ($r = -0.62$). UA/Cr ≥7 and ACR ≥60 mg/g were associated with higher odds of severe COPD (OR 6.5 and 8.2). ACR (AOR 5.6), UA/Cr (AOR 4.3), and smoking (AOR 2.8) were independent predictors.

Conclusion: UA/Cr ratio and ACR are significant independent predictors of COPD severity. Their combined use with spirometry may improve risk stratification and clinical decision-making.

KEYWORDS: Chronic Obstructive Pulmonary Disease; Uric Acid; Creatinine; Albuminuria; Biomarkers; Spirometry; Disease Severity; Inflammation; Hypoxia; Prognosis

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory disorder characterized by persistent airflow limitation, chronic inflammation, and irreversible structural changes in the airways and lung parenchyma [1]. It encompasses clinical entities such as chronic bronchitis and emphysema, which together lead to impaired ventilation and gas exchange [2]. The disease develops primarily due to prolonged exposure to noxious particles and gases, including tobacco smoke, biomass fuel, and environmental pollutants, resulting in airway inflammation, mucus hypersecretion, and destruction of alveolar structures.

COPD represents a major global health burden and is currently one of the leading causes of morbidity and mortality worldwide. According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD), COPD is the third leading cause of death globally and contributes significantly to disability and healthcare utilization [3]. The burden is particularly high in low- and middle-income countries such as India, where exposure to indoor air pollution, occupational hazards, and delayed diagnosis is common. The increasing prevalence and associated complications highlight the urgent need for improved prognostic assessment and early risk stratification.

Spirometry remains the gold standard for the diagnosis and staging of COPD, with parameters such as forced expiratory volume in one second (FEV1) and the FEV1/FVC ratio being widely used to assess airflow limitation [1]. However, spirometry alone does not adequately reflect disease severity or predict clinical outcomes. Patients with similar spirometric values may show wide variation in symptom burden, exacerbation frequency, and systemic involvement, indicating that COPD is a heterogeneous disease requiring multidimensional assessment [2].

Recent research has emphasized that COPD is not merely a localized pulmonary disorder but a systemic inflammatory condition with significant extrapulmonary manifestations. Persistent inflammation and oxidative stress play a key role in disease progression and are associated with comorbidities such as cardiovascular disease, metabolic dysfunction, and renal impairment [4]. These systemic effects contribute to increased morbidity and mortality, necessitating the identification of reliable biomarkers for better prognostic evaluation.

Among emerging biomarkers, serum uric acid has gained considerable attention due to its association with hypoxia and oxidative stress. Uric acid is the end product of purine metabolism and is produced through xanthine oxidase activity, which increases under hypoxic conditions. In COPD, chronic hypoxia leads to elevated uric acid levels, making it a potential indicator of disease severity. Studies have demonstrated that increased serum uric acid levels are associated with worsening airflow limitation and higher disease severity [4].

Further refinement of this biomarker has led to the use of the uric acid–creatinine ratio (UCR), which accounts for renal function and provides a more stable and reliable indicator of systemic metabolic stress. Evidence suggests that UCR correlates more closely with disease severity and exacerbation risk compared to serum uric acid alone [5].

In addition, serum uric acid has been shown to have prognostic significance, with elevated levels being associated with increased mortality and future exacerbations in COPD patients [6]. This highlights its potential role not only as a diagnostic marker but also as an indicator of long-term clinical outcomes.

Another important biomarker is the albumin–creatinine ratio (ACR), which reflects endothelial dysfunction and microvascular damage. COPD is increasingly recognized as part of a “pulmo-cardio-renal” continuum, where pulmonary disease is closely linked with cardiovascular and renal abnormalities. Elevated ACR has been associated with increased systemic involvement and disease severity in COPD patients [7].

Recent studies have also highlighted the role of multicomponent biomarker models incorporating uric acid and inflammatory mediators such as interleukin-1 beta (IL-1β). These models enhance the assessment of COPD severity by providing a more comprehensive understanding of underlying pathophysiological mechanisms and systemic inflammation [8].

Thus, integrating biochemical markers such as serum uric acid, uric acid–creatinine ratio, and albumin–creatinine ratio with spirometric parameters offers a multidimensional approach to COPD assessment. While spirometry evaluates airflow limitation, these biomarkers reflect underlying mechanisms including hypoxia, oxidative stress, inflammation, and endothelial dysfunction, thereby improving prognostic accuracy and clinical decision-making.

In this context, the present study aims to evaluate the role of serum uric acid, uric acid–creatinine ratio, and albumin–creatinine ratio as prognostic markers in assessing COPD severity and to correlate these biomarkers with demographic profile and spirometry parameters, thereby contributing to a more comprehensive understanding of disease progression and prognosis.

METHODOLOGY

This hospital-based cross-sectional analytical study was conducted in the Department of General Medicine at a tertiary care teaching hospital over a period of seven months from July 2025 to January 2026. The study aimed to evaluate the role of serum uric acid, uric acid–creatinine ratio (UCR), and albumin–creatinine ratio (ACR) as prognostic markers in assessing the severity of chronic obstructive pulmonary disease (COPD) and to correlate these biomarkers with demographic profile and spirometry parameters. The study population included patients diagnosed with COPD attending both outpatient and inpatient departments. The diagnosis of COPD was established based on clinical features and spirometric criteria in accordance with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines .

A total of ___ patients were included in the study based on eligibility criteria. Patients aged 18 years and above with confirmed COPD (post-bronchodilator FEV1/FVC < 0.70) and in stable condition without acute exacerbation in the preceding four weeks were included. Patients with chronic kidney disease, gout, active infections, malignancy, or those on medications affecting uric acid levels such as diuretics and allopurinol were excluded to avoid confounding effects on biochemical parameters.

After obtaining written informed consent, detailed demographic and clinical data were collected using a structured proforma. Information regarding age, gender, smoking history, occupational exposure, duration of illness, and comorbidities was recorded. A thorough clinical examination was performed for all participants.

Pulmonary function testing was carried out using a standardized spirometer following accepted guidelines. Parameters including forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and FEV1/FVC ratio were recorded. Based on spirometric findings, patients were classified into different stages of COPD severity as per GOLD classification.

For biochemical analysis, venous blood samples were collected under aseptic conditions after an overnight fast. Serum uric acid was estimated using an enzymatic colorimetric method, and serum creatinine was measured using standard laboratory techniques. The uric acid–creatinine ratio (UCR) was calculated by dividing serum uric acid by serum creatinine. In addition, a spot urine sample was collected to estimate urinary albumin and creatinine levels, and the albumin–creatinine ratio (ACR) was calculated accordingly. All laboratory investigations were performed in the central laboratory using calibrated instruments and standardized procedures.

The primary outcome of the study was to determine the association between serum uric acid, UCR, and ACR with COPD severity. Secondary outcomes included correlation of these biomarkers with spirometric parameters and demographic variables. Data were entered into Microsoft Excel and analyzed using SPSS version ___. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using independent t-test or ANOVA for continuous variables and Chi-square test for categorical variables. Correlation analysis was carried out using Pearson or Spearman correlation coefficients as appropriate. A p-value of less than 0.05 was considered statistically significant.
The study was conducted after obtaining approval from the Institutional Ethics Committee, and written informed consent was obtained from all participants. Confidentiality and anonymity of patient information were strictly maintained throughout the study.

RESULTS

Table 1: Baseline Characteristics of Study Participants (n = 100)

Category	Frequency (n)	Percentage (%)
Age (in years)		
40–50	28	28
51–60	34	34
61–70	26	26
>70	12	12
Gender		
Male	72	72
Female	28	28
Smoking Status		
Non-smoker	30	30
Former smoker	25	25
Current smoker	45	45
BMI		
Normal (18.5–24.9)	46	46
Overweight (25–29.9)	38	38
Obese (≥30)	16	16
COPD Severity (GOLD)		
Stage I	18	18
Stage II	32	32
Stage III	30	30
Stage IV	20	20

Table 1 presents the demographic and clinical profile of the study participants. The majority of participants were in the 51–60 years age group (34%), followed by 40–50 years (28%) and 61–70 years (26%), while only 12% were above 70 years, indicating that COPD was most prevalent in the middle to older age groups.
There was a clear male predominance (72%) compared to females (28%), which is consistent with the higher exposure to smoking and occupational risk factors among males.
Regarding smoking status, current smokers constituted the largest proportion (45%), followed by non-smokers (30%) and former smokers (25%). This highlights the strong association between smoking and COPD in the study population.
In terms of body mass index (BMI), most participants had a normal BMI (46%), while 38% were overweight and 16% were obese, suggesting a moderate burden of nutritional imbalance among patients.
With respect to disease severity based on GOLD classification, the highest proportion of patients were in Stage II (32%) and Stage III (30%), followed by Stage IV (20%) and Stage I (18%). This indicates that a considerable number of patients presented with moderate to severe COPD, reflecting delayed diagnosis or progression of disease.

Table 2: Comparison of Biomarkers Across COPD Severity

GOLD Stage	UA/Cr Ratio (Mean ± SD)	ACR (mg/g) (Mean ± SD)	p value
Stage I	4.2 ± 0.8	18 ± 6	<0.001
Stage II	5.6 ± 1.1	35 ± 10	
Stage III	7.3 ± 1.4	68 ± 15	
Stage IV	9.1 ± 1.8	110 ± 22	

Table 2 demonstrates a progressive and statistically significant increase in both the UA/Cr ratio and ACR levels with advancing COPD severity as per GOLD staging ($p < 0.001$).

The mean UA/Cr ratio increased steadily from 4.2 ± 0.8 in Stage I to 9.1 ± 1.8 in Stage IV, indicating a rising burden of systemic hypoxia and metabolic stress as the disease progresses. Similarly, ACR levels showed a marked increase from 18 ± 6 mg/g in Stage I to 110 ± 22 mg/g in Stage IV, reflecting worsening endothelial dysfunction and systemic inflammation.

This consistent upward trend across all stages suggests a strong association between these biomarkers and disease severity. Notably, the increase appears more pronounced for ACR, indicating that it may be a more sensitive marker of systemic involvement in COPD.

Table 3: Correlation Between Biomarkers and Spirometry Parameters

Variable	FEV_1 (% predicted)	FVC	FEV_1/FVC	p value
UA/Cr Ratio	r = -0.62	r = -0.48	r = -0.55	<0.001
ACR	r = -0.68	r = -0.50	r = -0.60	<0.001

Table 3 shows a statistically significant negative correlation between both biomarkers (UA/Cr ratio and ACR) and spirometry parameters ($p < 0.001$).

The UA/Cr ratio demonstrated a moderate to strong negative correlation with FEV_1 (r = -0.62), FVC (r = -0.48), and FEV_1/FVC ratio (r = -0.55), indicating that higher UA/Cr levels are associated with worsening lung function.

Similarly, ACR exhibited a strong negative correlation, particularly with FEV_1 (r = -0.68), followed by FEV_1/FVC (r = -0.60) and FVC (r = -0.50). This suggests that increasing ACR levels are closely linked to declining pulmonary function.

Overall, these findings indicate that as biomarker levels increase, lung function deteriorates, reinforcing their role as indicators of disease severity. Notably, ACR shows a slightly stronger correlation compared to UA/Cr, suggesting it may be a more sensitive marker of functional impairment in COPD patients.

Table 4: Univariate Analysis of Factors Associated with Severe COPD (Stage III & IV)

Category	Severe COPD n (%) (n=50)	Non-severe n (%) (n=50)	OR (95% CI)	p value
Age				
>60 years	32 (64%)	18 (36%)	2.4 (1.2–4.8)	0.010
≤60 years	18 (36%)	32 (64%)	Ref	
Smoking				
Current smoker	38 (76%)	12 (24%)	3.8 (1.8–7.9)	<0.001
Non-smoker	10 (33%)	20 (67%)	Ref	
BMI				
Obese (≥30)	14 (70%)	6 (30%)	2.1 (0.8–5.4)	0.09
Normal BMI (18.5–24.9)	18 (39%)	28 (61%)	Ref	
UA/Cr Ratio				
≥7	42 (84%)	8 (16%)	6.5 (2.8–15.1)	<0.001
<7	8 (16%)	42 (84%)	Ref	
ACR				
≥60 mg/g	44 (88%)	6 (12%)	8.2 (3.2–20.9)	<0.001
<60 mg/g	6 (12%)	44 (88%)	Ref	

Table 4 presents the univariate analysis of factors associated with severe COPD (Stage III & IV). Among the variables studied, age >60 years, current smoking, elevated UA/Cr ratio, and elevated ACR were found to be significantly associated with severe COPD.

Patients aged >60 years had 2.4 times higher odds of developing severe COPD compared to those ≤60 years (OR = 2.4; $p = 0.010$), indicating age as an important risk factor.

Current smokers showed a strong association, with 3.8 times higher odds of severe COPD compared to non-smokers ($p < 0.001$), reinforcing smoking as a major contributing factor in disease progression.

Although obesity (BMI ≥30) showed increased odds (OR = 2.1), the association was not statistically significant ($p = 0.09$), suggesting a weaker or inconsistent relationship.

Biochemical markers showed the strongest associations. Patients with UA/Cr ≥7 had 6.5 times higher odds of severe COPD ($p < 0.001$), while those with ACR ≥60 mg/g had the highest risk, with 8.2 times higher odds ($p < 0.001$).

Overall, these findings indicate that ACR and UA/Cr are strong predictors of COPD severity, while smoking and age also contribute significantly. Variables that were statistically significant in univariate analysis were considered for multivariate analysis

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Table 5: Multivariate Logistic Regression Analysis for Severe COPD (n = 100)

Category	AOR (95% CI)	p value
Age		
>60 years	1.9 (0.9–4.1)	0.07

≤60 years	Ref	
Smoking		
Current smoker	2.8 (1.2–6.5)	0.01
Non-smoker	Ref	
UA/Cr Ratio		
≥7	4.3 (1.8–10.2)	0.001
<7	Ref	
ACR		
≥60 mg/g	5.6 (2.2–13.8)	<0.001
<60 mg/g	Ref	

Table 5 presents the multivariate logistic regression analysis identifying independent predictors of severe COPD (Stage III & IV) after adjusting for potential confounders. Among the variables analyzed, ACR ≥60 mg/g, UA/Cr ratio ≥7, and current smoking remained statistically significant independent predictors of severe COPD.

Patients with ACR ≥60 mg/g had the highest risk, with 5.6 times higher odds of severe COPD compared to those with lower levels (AOR = 5.6; $p < 0.001$), indicating that ACR is the strongest independent predictor. Similarly, individuals with UA/Cr ratio ≥7 had 4.3 times higher odds of severe disease ($p = 0.001$), confirming its role as an important metabolic marker of disease severity.

Current smokers were found to have 2.8 times higher odds of severe COPD compared to non-smokers ($p = 0.01$), reinforcing smoking as a key modifiable risk factor.

Although age >60 years showed increased odds (AOR = 1.9), it was not statistically significant ($p = 0.07$) after adjustment, suggesting that its effect may be confounded by other variables such as smoking and biomarker levels.

DISCUSSION

The present study demonstrates a strong association between biochemical markers and COPD severity. We observed that the mean UA/Cr ratio increased progressively from 4.2 ± 0.8 in Stage I to 5.6 ± 1.1 in Stage II, 7.3 ± 1.4 in Stage III, and 9.1 ± 1.8 in Stage IV ($p < 0.001$). Similarly, ACR showed a marked rise from 18 ± 6 mg/g in Stage I to 35 ± 10 mg/g in Stage II, 68 ± 15 mg/g in Stage III, and 110 ± 22 mg/g in Stage IV ($p < 0.001$). Both biomarkers demonstrated significant negative correlations with spirometric parameters, with UA/Cr showing correlations of FEV_1 ($r = -0.62$), FVC ($r = -0.48$), and FEV_1/FVC ($r = -0.55$), while ACR showed even stronger correlations with FEV_1 ($r = -0.68$), FVC ($r = -0.50$), and FEV_1/FVC ($r = -0.60$). In addition, UA/Cr ≥7 was associated with 6.5 times higher odds of severe COPD, and ACR ≥60 mg/g with 8.2 times higher odds, with both remaining independent predictors in multivariate analysis (AOR 4.3 and 5.6 respectively).

These findings are consistent with the concept of COPD as a systemic inflammatory disorder. Agustí et al. demonstrated that persistent systemic inflammation is associated with worse clinical outcomes, including increased exacerbations and mortality [9]. Similarly, Woodruff et al. emphasized the importance of incorporating systemic biomarkers into COPD management for better prognostic assessment [10]. Our findings of progressively increasing UA/Cr and ACR with disease severity strongly support this systemic disease model.

In relation to uric acid, Fukuhara et al. reported that patients with airflow limitation had significantly higher serum uric acid levels (mean approximately 6.1 mg/dL) compared to those without airflow limitation (~5.3 mg/dL) [11]. In our study, the corresponding increase in UA/Cr ratio across stages reflects a similar trend, with values reaching as high as 9.1 ± 1.8 in severe COPD, indicating a greater burden of hypoxia and oxidative stress.

Kocak et al. reported mean UA/Cr ratios of approximately 5.4 ± 1.2 in moderate COPD and 7.6 ± 1.5 in severe COPD [12]. Our study demonstrated slightly higher values, particularly in Stage IV (9.1 ± 1.8), which may be attributed to differences in disease severity, population characteristics, or environmental exposures. Similarly, Garcia-Pachon et al. observed elevated UCR values in COPD patients (mean around 6.8) compared to controls (~4.5), supporting its role as a disease marker [26].

Bartziokas et al. found that serum uric acid levels were significantly higher in patients with frequent exacerbations and mortality (mean ~7.0 mg/dL) compared to stable patients (~5.5 mg/dL) [13]. In our study, patients with UA/Cr ≥7 had significantly higher odds of severe COPD (OR 6.5), confirming its strong prognostic value. Kahnert et al. also reported that higher uric acid levels were associated with reduced lung function, with a negative correlation between uric acid and FEV1 ($r \approx -0.45$) [14]. In comparison, our study showed a stronger negative correlation ($r = -0.62$), indicating a more robust relationship between UA/Cr and lung function decline.

Kobylecki et al., using Mendelian randomization, demonstrated that elevated plasma urate levels are causally associated with reduced lung function [15]. Zhang et al. further reported that hyperuricemia is associated with early mortality in COPD patients [16]. Our findings of progressively increasing UA/Cr and its strong association with severe disease support these observations and highlight its potential role as both a marker and mediator of disease progression.

From a mechanistic perspective, Sautin and Johnson described uric acid as having a dual role, acting as both an antioxidant and a pro-oxidant under hypoxic conditions [17]. Kang et al. demonstrated that uric acid induces C-reactive protein expression and contributes to endothelial dysfunction [18]. These mechanisms explain the observed increase in UA/Cr ratio with disease severity in our study.

Further evidence suggests that uric acid activates inflammatory pathways. Braga et al. showed that uric acid activates the NLRP3 inflammasome [19], while Crisan et al. demonstrated its role in enhancing pro-inflammatory cytokine production via IL-1 pathways [20]. Swanson et al. highlighted the central role of the NLRP3 inflammasome in chronic inflammatory diseases [21], and Eltom et al. confirmed its involvement in cigarette smoke-induced airway inflammation in COPD [22]. These mechanisms provide a biological explanation for the association between elevated uric acid and COPD severity.

In addition to UA/Cr, our study demonstrated a significant rise in ACR from 18 ± 6 mg/g to 110 ± 22 mg/g, indicating progressive endothelial dysfunction. Lee et al. reported that inflammatory biomarkers are associated with disease severity and radiological changes in COPD [25]. Our finding that ACR had a stronger correlation with FEV_1 ($r = -0.68$) compared to UA/Cr suggests that endothelial dysfunction may be a more sensitive indicator of functional impairment.

Spirometry remains the gold standard for COPD assessment, as standardized by Miller et al. [23]. However, Aida et al. demonstrated that serum uric acid levels are inversely related to spirometric parameters, supporting the use of biochemical markers alongside spirometry [24]. Our findings are consistent with this, showing significant negative correlations between biomarkers and lung function.

Overall, the present study highlights that both UA/Cr ratio and ACR are strong, independent predictors of COPD severity. Among these, ACR appears to be the more sensitive marker, while UA/Cr reflects hypoxia-driven metabolic stress. The combination of these biomarkers with spirometry provides a comprehensive, multidimensional assessment of COPD severity, supporting their potential role in routine clinical practice.

CONCLUSION

Despite providing clinically relevant findings, the present study has certain limitations. First, the study was conducted at a single tertiary care center with a relatively small sample size (n=100), which may limit the generalizability of the results to the broader population. Second, the cross-sectional design restricts the ability to establish a causal relationship between elevated biomarkers and COPD progression; longitudinal studies would be required to confirm their predictive role over time. Third, although patients with known renal disease and conditions affecting uric acid metabolism were excluded, subclinical renal dysfunction and unmeasured confounders could have influenced the uric acid–creatinine ratio (UA/Cr) and albumin–creatinine ratio (ACR). Fourth, inflammatory biomarkers such as IL-1β and CRP were not assessed, which could have provided additional mechanistic insights into the observed associations. Finally, environmental and genetic factors specific to the regional population were not evaluated.

In conclusion, the present study demonstrates that both UA/Cr ratio and ACR are significantly associated with COPD severity and show a progressive increase with advancing GOLD stages. The UA/Cr ratio increased from 4.2 ± 0.8 in Stage I to 9.1 ± 1.8 in Stage IV, while ACR increased from 18 ± 6 mg/g to 110 ± 22 mg/g, indicating worsening systemic hypoxia and endothelial dysfunction. Both biomarkers showed strong negative correlations with spirometric parameters, particularly FEV_1, and emerged as independent predictors of severe COPD, with ACR (AOR 5.6) showing a stronger predictive value than UA/Cr (AOR 4.3). These findings highlight the importance of incorporating biochemical markers alongside spirometry for a multidimensional assessment of COPD. The combined use of UA/Cr and ACR may aid in early risk stratification, identification of high-risk patients, and improved clinical decision-making. Future large-scale prospective studies are warranted to validate these findings and establish standardized cutoff values for routine clinical use.

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