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The role and clinical significance of myeloperoxidase (MPO) and TNF-α in prognostic evaluation of T-COPD

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Abstract

Purpose Chronic obstructive pulmonary disease (COPD) is a progressive inflammatory disorder that requires effective biomarkers for assessing disease activity and severity. This study aimed to compare clinical characteristics, inflammatory biomarker levels, and pulmonary function between stable COPD (S-COPD) and treated COPD (T-COPD) patients, with a focus on the prognostic value of inflammatory markers such as TNF-α, MPO, and IL-6.

Methods A total of 81 patients were enrolled in the study, including 39 with stable COPD (S-COPD) and 42 with treated COPD (T-COPD). Clinical characteristics, lung function (measured by FEV1%), and inflammatory biomarkers (IL-6, MMP-9, SAA, MPO, TNF-α, and others) were assessed. Inflammatory biomarkers were compared between the two groups, and their associations with pulmonary function were examined using correlation and regression analyses. Prognostic value was assessed using ROC curve analysis.

Results The T-COPD group exhibited significantly more severe disease, with higher rates of exacerbations, worse quality of life (CAT and mMRC scores), and reduced lung function (FEV1%, 6-minute walk distance). Inflammatory biomarker analysis revealed no significant differences for IL-6, MMP-9, SAA, RDW, LCN2, PLR, and NLR, but TNF-α and MPO were significantly higher in T-COPD patients ($P = 0.015$ and $P = 0.012$, respectively). Among these biomarkers, MPO and TNF-α showed strong negative correlations with FEV1% in T-COPD patients ($r = -0.521$ and $r = -0.459$, respectively). ROC curve analysis indicated that TNF-α (AUC = 0.821) was the most predictive biomarker, followed by MPO (AUC = 0.785) and IL-6 (AUC = 0.711). Combining TNF-α and MPO provided the best prognostic performance (AUC = 0.878).

Conclusion TNF-α, MPO, and IL-6 are significant biomarkers associated with disease severity and pulmonary function in T-COPD patients. The combination of TNF-α and MPO offers superior prognostic value, suggesting that these biomarkers may serve as useful tools for monitoring disease progression and guiding treatment decisions in treated COPD patients.

Keywords Chronic obstructive pulmonary disease, Inflammatory biomarkers, TNF-α, Myeloperoxidase, Pulmonary function, Prognostic value

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Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive inflammatory lung disease primarily caused by long-term exposure to noxious particles and gases, most commonly from cigarette smoke [1]. It is characterized by chronic airflow limitation, respiratory symptoms, and a decline in lung function. According to the World Health Organization (WHO), COPD is the third leading cause of death globally, accounting for approximately 3.23 million deaths annually, and it is projected to become the third leading cause of death worldwide by 2030 [2]. The global prevalence of COPD among adults aged 40 years and older is estimated to be approximately 11.7%, with significant variation by region [3]. While cigarette smoking remains the primary risk factor for COPD, accounting for up to 90% of cases in high-income countries, other factors—including environmental exposures, occupational hazards, and infections—also play important roles in the disease's development [4].

Smoking-Related COPD(S-COPD) refers to the phase of COPD in which patients exhibit chronic symptoms such as cough, sputum production, and dyspnea, but these symptoms remain relatively stable over time, with few exacerbations [5]. In S-COPD, the disease is often associated with long-term exposure to tobacco smoke, which leads to airway inflammation, oxidative stress, and progressive lung tissue damage. S-COPD is typically diagnosed in patients with a long smoking history, and the disease severity is assessed using pulmonary function tests, such as forced expiratory volume in 1 s (FEV1), and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification system [6, 7]. Although patients with stable COPD may experience relatively stable disease, the gradual decline in lung function and systemic inflammation contribute to the long-term disability associated with the disease.

Tuberculosis-Related COPD(T-COPD) refers to COPD that develops in patients with a history of tuberculosis (TB) infection [8]. In these patients, the lung damage resulting from TB infection leads to chronic inflammation and scarring, ultimately resulting in airflow limitation characteristic of COPD. T-COPD is common in regions with high TB prevalence, such as parts of Asia, Africa, and Eastern Europe, where TB is still a major public health issue [9]. The pathophysiology of T-COPD is unique in that it combines the effects of chronic inflammation and fibrosis caused by both the initial TB infection and subsequent inflammatory responses, which can further impair lung function. TB-related COPD tends to be more complex due to the prior history of lung infection and scarring, and patients often experience more frequent exacerbations and faster disease progression compared to those with S-COPD [10]. The presence of TB-related lung damage complicates both the diagnosis and management of COPD in these patients, making it essential to identify biomarkers that can help differentiate between smoking-related and TB-related COPD.

COPD is characterized by chronic inflammation in the lungs, and inflammatory biomarkers have been widely studied as potential indicators of disease activity, severity, and progression [11]. Several biomarkers, including TNF-α (tumor necrosis factor alpha), MPO (myeloperoxidase), and IL-6 (interleukin-6), are involved in the inflammatory pathways that drive the disease. In both smoking-related (S-COPD) and TB-related COPD (T-COPD), these biomarkers are elevated and reflect the ongoing inflammatory process [12]. TNF-α is a pro-inflammatory cytokine that plays a key role in the recruitment of inflammatory cells to the lungs and in tissue damage [13]. MPO, produced by neutrophils, contributes to oxidative stress and further damage to lung tissue, while IL-6 is involved in systemic inflammation and has been shown to correlate with disease severity and lung function decline [14].While these inflammatory markers have been studied in COPD patients, there is limited research comparing their levels between S-COPD and T-COPD patients, especially regarding their ability to reflect disease severity and progression in each group. Furthermore, the prognostic value of these biomarkers in predicting outcomes such as exacerbation frequency, lung function decline, and quality of life in T-COPD patients remains unclear [15].

Given the increasing prevalence of T-COPD in regions with high TB burdens, there is a need to better understand the role of inflammatory biomarkers in distinguishing between smoking-related and TB-related COPD. This study aims to compare clinical characteristics, inflammatory biomarker levels, and pulmonary function between stable COPD (S-COPD) and treated COPD (T-COPD) patients. Specifically, we will focus on biomarkers such as TNF-α, MPO, and IL-6, which have been implicated in COPD pathogenesis, to evaluate their association with lung function and disease severity. Additionally, we will assess the prognostic value of these biomarkers in predicting disease progression, exacerbation frequency, and overall clinical outcomes in T-COPD patients.By comparing the inflammatory profiles of S-COPD and T-COPD patients, this study aims to provide insights into the distinct mechanisms underlying these two forms of COPD and to identify biomarkers that could serve as useful tools for monitoring disease activity and guiding treatment strategies. Ultimately, the goal is to improve the management of COPD, particularly in populations affected by both smoking and TB, by offering more precise diagnostic and prognostic tools.

Method and material

Study samples

A total of 160 patients diagnosed with S-COPD and T-COPD at the Department of Respiratory and Critical Care Medicine, Chongqing Seventh People's Hospital, from January to December 2024 were enrolled (80 patients in each group). All participants provided written informed consent.

Inclusion criteria for the S-COPD group: (1) aged 18–80 years, regardless of sex; (2) smoking history; (3) diagnosis of COPD according to the 2023 Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, with a post-bronchodilator FEV1/FVC ratio < 0.70; (4) no respiratory infection symptoms in the past 6 weeks; (5) able to understand and cooperate with the study; (6) voluntary informed consent.

Inclusion criteria for the T-COPD group: (1) aged 18–80 years, regardless of sex; (2) no smoking history; (3) diagnosis of COPD; (4) history of tuberculosis with no significant changes on chest imaging in the past year; (5) chest imaging meeting the criteria for inactive tuberculosis (WS196-2017), including isolated or multiple calcified lesions, clear-bordered fibrotic lesions, consolidation, or pleural thickening with calcification; (6) no respiratory infection symptoms in the past 6 weeks; (7) able to understand and cooperate with the study; (8) voluntary informed consent.

Patients information collection

All patients had complete clinical data, including full pulmonary function tests and chest imaging confirming the diagnosis of S-COPD or T-COPD. Collected baseline information included age, sex, occupation, BMI, smoking history (including smoking amount), history of hypertension, diabetes, stroke, relevant family medical history, and the number of acute exacerbations in the past year (defined as worsening dyspnea and/or cough and sputum production requiring hospitalization within 14 days). Quality of life was assessed using the CAT score and the modified Medical Research Council (mMRC) dyspnea scale. Additional assessments included the 6-minute walk test (6MWT) and pulmonary function parameters (FEV1% predicted, FVC % predicted, and FEV1/FVC ratio).

ELISA

Morning fasting venous blood samples were collected from S-COPD and T-COPD patients, and serum or plasma was separated by centrifugation and stored at -80 °C until analysis. Levels of IL-6 (Beyotime, PI330), MMP-9 (Beyotime, PM738), SAA (Sangon, D711272-0048), RDW (Abcam, ab279415), TNF-α (YEASEN, 97072ES96), LCN2 (Abcam, ab119600), and MPO (Beyotime, PM574) were measured using enzyme-linked immunosorbent assay (ELISA). Briefly, 96-well ELISA plates were coated with the corresponding capture antibody solution and incubated at room temperature for 1–2 h or overnight at 4 °C. The plates were then blocked with a blocking solution at room temperature for 1 h to prevent non-specific binding. Serum samples were added to the wells and incubated at room temperature for 2 h. After incubation, the plates were washed 4 times with washing buffer to remove unbound material. Subsequently, biotinylated secondary antibodies specific to the target antigens were added and incubated at room temperature for 1 h, followed by another round of washing. Finally, substrate solution was added, and after a defined incubation period, color development was measured using a microplate reader at the appropriate wavelength. The concentrations of biomarkers were determined by comparing the optical density (OD) values with a standard curve.

Pulmonary function testing

Pulmonary function testing was performed within 24 h of admission. Pulmonary function was classified based on the percentage of FEV1 predicted. GOLD 1 (mild) was defined as FEV1 ≥ 80% of the predicted value; GOLD 2 (moderate) as 50% ≤ FEV1 < 80%; GOLD 3 (severe) as 30% ≤ FEV1 < 50%; and GOLD 4 (very severe) as FEV1 < 30% of the predicted value.

Statistical analysis

All data was performed using SPSS 27.0 software. Normally distributed continuous variables were expressed as mean ± standard deviation (x ± s) and compared between groups using independent t-tests. Non-normally distributed continuous variables were expressed as median (Q1, Q3) and compared using the Mann-Whitney U test. Categorical data were presented as n (%), with group comparisons made using the χ^2 test. Variables with statistically significant differences in univariate analysis were further analyzed using multivariate logistic regression to identify inflammatory biomarkers predictive of T-COPD severity. The prognostic value of biomarkers was assessed using receiver operating characteristic (ROC) curves. $P < 0.05$ was considered statistically significant.

Results

Comparison of clinical characteristics and lung function between S-COPD and T-COPD patients

The baseline comparison between the S-COPD (stable COPD, $n = 39$) and T-COPD (treated COPD, $n = 42$) groups reveals significant differences, suggesting that the T-COPD group has more severe disease. The average age and gender distribution were similar between the groups ($P = 0.125$ and $P = 0.890$, respectively), but the S-COPD group had a higher BMI (23.8 ± 3.1 vs. 22.4 ± 3.5,

$P = 0.045$). There were no significant differences in smoking history, hypertension, diabetes, or family history ($P > 0.05$ for all).

The T-COPD group had significantly more frequent acute exacerbations (2.3 ± 0.9 vs. 1.2 ± 0.7, $P < 0.001$), worse quality of life (CAT score: 21.7 ± 4.1 vs. 14.5 ± 3.2, $P < 0.001$), and more severe dyspnea (mMRC score: 2.5 ± 0.7 vs. 1.8 ± 0.6, $P < 0.001$). In functional assessments, the T-COPD group showed poorer performance in the 6-minute walk test (285.3 ± 35.1 vs. 360.4 ± 40.2 m, $P < 0.001$) and had worse pulmonary function (FEV1%, FVC%, and FEV1/FVC ratio; $P < 0.001$ for all).

Additionally, when considering general laboratory parameters, no significant differences were observed in white blood cell count (7.2 ± 1.3 vs. 7.5 ± 1.5, $P = 0.345$), red blood cell count (4.8 ± 0.5 vs. 4.7 ± 0.4, $P = 0.620$), or hemoglobin levels (13.5 ± 1.4 vs. 13.2 ± 1.3, $P = 0.312$). However, platelet count (230 ± 52 vs. 245 ± 60, $P = 0.196$) and erythrocyte sedimentation rate (ESR) (18.4 ± 9.2 vs. 19.1 ± 8.7, $P = 0.674$) did not show any significant differences between the two groups.

These findings indicate that T-COPD patients experience more severe symptoms, frequent exacerbations, and worse lung function. Despite no significant differences in basic laboratory parameters such as white blood cell count and hemoglobin levels, the T-COPD group's clinical presentation suggests a more advanced disease stage, which may underscore the importance of biomarkers like MPO and TNF-α in assessing prognosis in T-COPD (Table 1).

Comparison of inflammatory biomarkers between S-COPD and T-COPD patients

Chronic obstructive pulmonary disease (COPD) is a progressive inflammatory disease where monitoring inflammatory biomarkers can help assess disease severity and progression. Herein, we compared the levels of various inflammatory markers between stable COPD (S-COPD) and treated COPD (T-COPD) patients to explore their potential role in reflecting disease activity.

The comparison of inflammatory biomarkers revealed no significant differences between the two groups for IL-6, MMP-9, SAA, RDW, LCN2, PLR, and NLR, suggesting these markers may not be strongly associated with the clinical status of COPD. However, TNF-α and MPO levels were significantly higher in the T-COPD group (1.89 ± 0.30 vs. 1.64 ± 0.22, $P = 0.015$; 65.29 ± 9.45 vs. 58.13 ± 8.71, $P = 0.012$, respectively), indicating that these biomarkers may reflect exacerbation and disease severity in T-COPD(Table 2).

Association between inflammatory biomarkers and pulmonary function in T-COPD patients

Next we compared the pulmonary function of S-COPD and T-COPD patients based on the GOLD classification. T-COPD patients showed a significantly higher proportion in the severe (GOLD 3) and very severe (GOLD

Table 1 The comparison of general data between two groups

Baseline data	S-COPD ($n = 39$)	T-COPD ($n = 42$)	*P*
Age (years)	65.4 ± 8.2	68.1 ± 7.6	0.125
Gender (Male/Female)	28/11	30/12	0.890
BMI (kg/m^2)	23.8 ± 3.1	22.4 ± 3.5	0.045*
Smoking History	30/9	35/7	0.538
Smoking Pack-Years	45.7 ± 12.5	46.9 ± 11.8	0.250
Hypertension History(Yes/No)	18/21	25/17	0.218
Diabetes History(Yes/No)	8/31	12/30	0.400
Stroke History (Yes/No)	5/34	8/34	0.501
Family History (Yes/No)	12/27	14/28	0.749
Acute Exacerbation Frequency in the Last Year (times)	1.2 ± 0.7	2.3 ± 0.9	< 0.001*
Quality of Life Score (CAT Score)	14.5 ± 3.2	21.7 ± 4.1	< 0.001*
Modified MRC Dyspnea Scale Score (mMRC)	1.8 ± 0.6	2.5 ± 0.7	< 0.001*
6-Minute Walk Test (6MWT, meters)	360.4 ± 40.2	285.3 ± 35.1	< 0.001*
Pulmonary Function Parameters (FEV1%)	68.3 ± 12.5	51.7 ± 10.2	< 0.001*
Pulmonary Function Parameters (FVC%)	82.1 ± 10.3	72.4 ± 9.8	< 0.001*
Pulmonary Function Parameters(FEV1/FVC ratio)	61.4 ± 8.3	51.2 ± 6.7	< 0.001*
Hemoglobin Level (g/dL)	13.5 ± 1.4	13.2 ± 1.3	0.312
Platelet Count (×10^9/L)	230 ± 52	245 ± 60	0.196
White Blood Cell Count (×10^9/L)	7.2 ± 1.3	7.5 ± 1.5	0.345
Red Blood Cell Count (×10^12/L)	4.8 ± 0.5	4.7 ± 0.4	0.620
Erythrocyte Sedimentation Rate (ESR, mm/h)	18.4 ± 9.2	19.1 ± 8.7	0.674

*P<0.05

Table 2 Comparison of inflammatory markers in patients with S-COPD and T-COPD

Items	S-COPD ($n=39$)	T-COPD ($n=42$)	*P*
IL-6(ug/mL)	0.39 ± 0.08	0.41 ± 0.07	0.153
MMP-9(ng/mL)	222.18 ± 30.11	230.45 ± 35.67	0.210
SAA(mg/L)	25.31 ± 5.12	26.87 ± 6.03	0.132
RDW	12.9 (12.5, 13.4)	13.0 (12.6, 13.5)	0.234
TNF-α(ug/mL)	1.64 ± 0.22	1.89 ± 0.30	0.015*
LCN2	175.51 ± 19.45	182.34 ± 21.23	0.168
PLR	113.29 (91.02, 132.33)	115.45 (92.78, 135.24)	0.089
NLR	4.23 (1.89, 7.56)	4.87 (2.13, 7.98)	0.074
MPO(mmol/mL)	58.13 ± 8.71	65.29 ± 9.45	0.012*

*$P<0.05$

Table 3 Comparison of pulmonary function based on GOLD classification between S-COPD and T-COPD patients

GOLD Classification	Severity	S-COPD ($n=39$)	T-COPD ($n=42$)	*P*
GOLD 1	Mild	10 (25.6%)	2 (4.8%)	0.015*
GOLD 2	Moderate	18 (46.2%)	10 (23.8%)	0.039*
GOLD 3	Severe	8 (20.5%)	20 (47.6%)	0.011*
GOLD 4	Very Severe	3 (7.7%)	10 (23.8%)	0.048*

*$P<0.05$

Table 4 Correlation analysis between inflammatory biomarkers and pulmonary function parameters (FEV1%) in T-COPD patients

Indicator	Correlation Coefficient (*r*)	*P*
IL-6 (μg/mL)	-0.322	0.048*
MMP-9 (ng/mL)	-0.279	0.062
SAA (mg/L)	-0.165	0.208
TNF-α (μg/mL)	-0.459	0.003**
LCN2 (ng/mL)	-0.243	0.089
MPO (mmol/mL)	-0.521	< 0.001**
VEGF (ng/mL)	-0.318	0.052
NLR	-0.189	0.167
PLR	-0.203	0.134

*$P<0.05$;**$P<0.01$

4) stages, with 47.6% of T-COPD patients classified as GOLD 3 and 23.8% as GOLD 4, compared to only 20.5% and 7.7%, respectively, in the S-COPD group. This suggests that T-COPD patients have more advanced disease and poorer lung function overall(Table 3).

Then, we examined the correlation between inflammatory biomarkers and pulmonary function parameters, specifically FEV1% predicted, in T-COPD patients. Among the biomarkers assessed, MPO and TNF-α exhibited the strongest negative correlations with FEV1%, with correlation coefficients of -0.521 ($P<0.001$) and −0.459 ($P=0.003$), respectively. This indicates that higher levels of these markers are associated with worse lung function. IL-6 also showed a moderate negative correlation (r = -0.322, $P=0.048$). Other markers, such as MMP-9 and SAA, showed weaker or non-significant correlations with FEV1%(Table 4).

Table 5 Predictive model for disease severity in T-COPD patients based on multiple linear regression analysis

Variable	Regression Coefficient (β)	Standard Error (SE)	t	*P*
TNF-α (μg/mL)	-0.183	0.058	-3.155	0.002**
MPO (mmol/mL)	-0.225	0.063	-3.571	0.001**
IL-6 (μg/mL)	-0.097	0.048	-2.021	0.048*
Intercept	85.632	5.284	16.208	< 0.001**

*$P<0.05$;**$P<0.01$

Table 6 The ROC curve and cutoff values of inflammatory biomarkers in T-COPD patients

Inflammatory Biomarker	AUC	Cutoff value	Sensitivity (%)	Specificity (%)	*P*
TNF-α (μg/mL)	0.821	1.78	75.2	83.1	< 0.001**
MPO (mmol/mL)	0.785	63.4	70.5	80.9	< 0.001**
IL-6 (μg/mL)	0.711	0.43	68.9	74.6	0.003**

**$P<0.01$

Furthermore, multiple linear regression analysis identified MPO, TNF-α, and IL-6 as significant predictors of disease severity in T-COPD patients. These biomarkers were found to be negatively associated with the severity of COPD, with higher levels correlating with more severe disease. MPO, in particular, was the strongest predictor, followed by TNF-α and IL-6(Table 5).

Overall, these findings suggest that inflammatory biomarkers, particularly MPO, TNF-α, and IL-6, are closely associated with pulmonary function and disease severity in T-COPD patients, and may serve as useful indicators for monitoring disease progression and guiding treatment decisions.

Prognostic value of inflammatory biomarkers in T-COPD

Building on the previous findings, we assessed the prognostic value of inflammatory biomarkers in T-COPD patients using ROC curve analysis. The results in Table 6 show that TNF-α had the highest AUC of 0.821 ($P<0.001$), with an optimal cutoff of 1.78 μg/mL, yielding 75.2% sensitivity and 83.1% specificity. MPO (AUC = 0.785, $P<0.001$) and IL-6 (AUC = 0.711, $P=0.003$) also showed significant predictive value, with MPO having a cutoff of 63.4 mmol/mL and IL-6 at 0.43 μg/mL(Table 6; Fig. 1).

In Table 7, combining TNF-α and MPO provided the best predictive performance (AUC = 0.878, $P<0.001$), followed by TNF-α + IL-6 (AUC = 0.788, $P=0.001$) and MPO + IL-6 (AUC = 0.764, $P=0.004$). These results suggest that the combination of these biomarkers, especially TNF-α and MPO, offers superior prognostic value compared to individual markers.

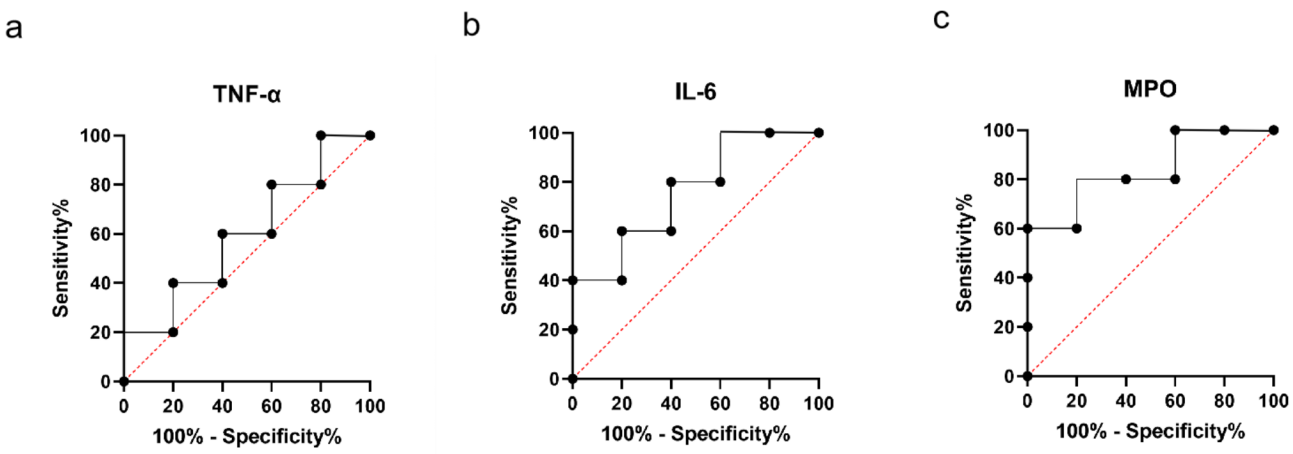

Fig. 1 The ROC curve of inflammatory biomarkers in T-COPD patients. a. TNF-α. b. IL-6. c. MPO

Table 7 Comparison of the combined predictive ability of different inflammatory biomarkers for prognosis in T-COPD patients using ROC curve analysis

Combination Biomarker	AUC	*P*
TNF-α + MPO	0.878	< 0.001**
TNF-α + IL-6	0.788	0.001**
MPO + IL-6	0.764	0.004**

***P*<0.01

Discussion

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide, characterized by progressive airflow limitation and persistent respiratory symptoms [16–18]. While cigarette smoking remains the primary risk factor for COPD, other causes, such as tuberculosis (TB), are increasingly recognized, particularly in regions with high TB prevalence. The development of treated COPD (T-COPD) in patients with a history of TB is a growing concern, as TB-induced lung damage can contribute to chronic inflammation and accelerate the decline in lung function, leading to a more severe disease course. Thus, identifying reliable biomarkers to assess disease activity and severity in T-COPD is crucial for early intervention and personalized treatment. This study compared the clinical characteristics, inflammatory biomarkers, and pulmonary function between stable COPD (S-COPD) and T-COPD patients, highlighting the role of biomarkers like TNF-α and MPO in disease assessment.

Our findings indicate that T-COPD patients exhibit more severe disease compared to S-COPD patients, as evidenced by higher rates of acute exacerbations, worse quality of life scores (CAT and mMRC), and significantly reduced lung function (FEV1%, 6-minute walk test, and FVC%). These results align with previous studies that suggest T-COPD patients experience a more progressive decline in pulmonary function due to the residual effects of TB-induced lung damage, compounded by chronic inflammation [19]. This study also reinforces the growing recognition of T-COPD as a distinct phenotype, with unique challenges in terms of management and prognosis.

Inflammatory biomarkers in T-COPD and S-COPD

Our analysis of inflammatory biomarkers revealed significantly higher levels of TNF-α and MPO in T-COPD patients compared to S-COPD patients. TNF-α, a key pro-inflammatory cytokine, plays a central role in the pathogenesis of COPD by promoting airway inflammation and tissue remodeling [20]. Previous studies have shown that elevated TNF-α levels are associated with increased exacerbation frequency, worsened lung function, and poorer outcomes in COPD patients [21]. The present study supports these findings and further highlights TNF-α as a potential marker for monitoring disease severity and exacerbation risk in T-COPD.

In healthy individuals, TNF-α and MPO are typically present at low levels. TNF-α is a pro-inflammatory cytokine involved in immune responses and tissue repair, and its baseline levels are usually low in the absence of infection or injury [22]. Similarly, MPO is a marker of neutrophil activation, and its expression is typically minimal under normal conditions. However, both TNF-α and MPO can be rapidly upregulated in response to acute inflammatory stimuli, such as infection or trauma. These observations align with the role of these biomarkers in the pathogenesis of diseases like COPD, where chronic inflammation leads to sustained elevation of these markers [23].

MPO, an enzyme released by neutrophils during inflammation, was also significantly higher in T-COPD patients. MPO is a marker of neutrophil activation and has been linked to airway damage and oxidative stress in COPD [24]. Studies have demonstrated that elevated

MPO levels correlate with more severe disease and worse prognosis in COPD patients [25]. The present findings further underscore MPO as a promising biomarker for assessing disease severity, particularly in T-COPD, where ongoing inflammation and tissue damage are prominent.

In other lung diseases, such as idiopathic pulmonary fibrosis (IPF), TNF-α and MPO also play critical roles but with distinct regulatory patterns. In IPF, TNF-α is known to contribute to fibrosis by promoting fibroblast activation and extracellular matrix deposition, processes that are central to the disease [26]. MPO, on the other hand, has been shown to correlate with neutrophilic inflammation in IPF, which exacerbates tissue damage and fibrosis progression [27]. Similarly, in asthma and acute hypersensitivity reactions (AHR), both TNF-α and MPO are upregulated, albeit through different mechanisms. In asthma, TNF-α is involved in the recruitment and activation of various immune cells, including eosinophils and neutrophils, while MPO levels increase as a result of neutrophilic inflammation in the airways [28]. AHR, characterized by airway hyperresponsiveness and inflammation, also shows elevated levels of both TNF-α and MPO, linking these biomarkers to the inflammatory milieu associated with allergic responses [29].

Interestingly, other biomarkers, such as IL-6, MMP-9, SAA, and RDW, did not show significant differences between S-COPD and T-COPD patients in this study. This suggests that while these markers may reflect general inflammation in COPD, they might not be as closely associated with the severity or progression of disease in T-COPD, which could be more influenced by specific inflammatory pathways related to TB-induced lung damage. Our results are consistent with prior research that found IL-6 to be a less reliable biomarker in distinguishing between stable and exacerbated COPD states, although it remains useful for overall inflammation monitoring.

Thus, while TNF-α and MPO are elevated in both T-COPD and other inflammatory lung diseases, their roles may vary based on the underlying pathophysiological processes. In T-COPD, the persistent lung damage induced by TB, in combination with chronic inflammation, likely contributes to the sustained elevation of these biomarkers, differentiating T-COPD from other forms of COPD or lung diseases. In comparison to S-COPD, where inflammatory markers like IL-6 and MMP-9 might reflect general inflammation, TNF-α and MPO appear to be more directly linked to the severity and progression of T-COPD, reflecting the unique inflammatory pathways associated with TB-induced lung damage.

Association between inflammatory biomarkers and pulmonary function

A key finding in this study is the strong negative correlation between MPO and TNF-α levels and pulmonary function (FEV1%) in T-COPD patients. The inverse relationship between these biomarkers and lung function highlights their potential role in predicting disease progression. Specifically, higher levels of MPO and TNF-α were associated with worse lung function, a finding that is consistent with other studies linking increased inflammation to the deterioration of respiratory parameters in COPD [30]. The moderate negative correlation observed with IL-6 also suggests that this cytokine may have a role, although it appears to be less predictive than MPO and TNF-α in the context of T-COPD.

Our regression analysis further supports the hypothesis that MPO and TNF-α, along with IL-6, are significant predictors of disease severity in T-COPD patients. Importantly, MPO emerged as the strongest predictor of disease severity, which may be explained by its direct role in neutrophilic inflammation and its ability to reflect ongoing airway damage and remodeling.

Prognostic value of inflammatory biomarkers in T-COPD

Finally, we assessed the prognostic value of inflammatory biomarkers in T-COPD patients using receiver operating characteristic (ROC) curve analysis. Our results indicate that TNF-α had the highest AUC (0.821), followed by MPO (0.785) and IL-6 (0.711), suggesting that these biomarkers have strong predictive value for T-COPD prognosis. The combination of TNF-α and MPO further improved prognostic performance (AUC = 0.878), indicating that a multi-biomarker approach may offer superior predictive accuracy [31].

Study limitations and future perspectives

While our study provides valuable insights into the role of inflammatory biomarkers in T-COPD, several limitations should be acknowledged. First, this study did not analyze the specific treatments that patients received for COPD or their comorbidities. The lack of detailed treatment data may limit the ability to assess the impact of therapeutic interventions on the observed biomarker levels and clinical outcomes. Future studies should incorporate treatment data to better understand how different therapeutic strategies influence biomarker profiles and disease progression in T-COPD.Moreover, the cross-sectional nature of this study prevents us from drawing conclusions about causality or long-term disease progression. Longitudinal studies are needed to track the changes in biomarkers over time and their relationship to disease progression and exacerbations. Additionally, while we identified specific biomarkers such as TNF-α and MPO as potential markers for T-COPD, further

research is needed to explore their exact role in disease pathogenesis and their utility in clinical practice, including their potential use as monitoring tools in the management of T-COPD.

Conclusion

In conclusion, this study reinforces the importance of inflammatory biomarkers, particularly TNF-α and MPO, in assessing disease severity and prognosis in T-COPD patients. Our findings suggest that these biomarkers, in combination with clinical assessments and lung function tests, could serve as valuable tools for monitoring disease progression and guiding treatment decisions in T-COPD. Further research, particularly large-scale longitudinal studies, is needed to validate these biomarkers in clinical practice and explore their potential for guiding therapeutic interventions in this increasingly recognized COPD phenotype.

Author contributions

Wen Li led the design of the study, and E Jiang was responsible for the data collection and article writing. Yingya Fu, Yalin Wang, Li Ying are responsible for the proofreading of the article data.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was ethically reviewed and supervised by The Seventh People's Hospital of Chongqing. (Approval Number: (2024) -0109).All subjects signed informed consent forms in writing. This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained, and all participants provided written informed consent before participating in the study. The study adhered to all relevant ethical guidelines and regulations, ensuring the protection of participants' rights, privacy, and confidentiality.

Consent for publication

Not Applicable.

Conflict of interest

We declare that there is no interests in this work.

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