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ORIGINAL RESEARCH

Impact of the COVID-19 Pandemic on ACO Prevalence Among AECOPD Patients (2019-2023) and Clinical Characteristics by Blood Eosinophil Levels

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Purpose: This study aimed to evaluate changes in the prevalence of Asthma-COPD Overlap (ACO) among patients with Acute Exacerbations of COPD (AECOPD) from 2019 to 2023. It also compared the clinical characteristics of patients across EOS thresholds (50, 150, and 300 cells/μL) to identify disease severity markers and guide individualized treatment strategies.

Patients and Methods: Clinical data from AECOPD and ACO patients hospitalized at the Second Hospital of Hebei Medical University between January 2019 and December 2023 were analyzed. Patients were grouped by EOS levels (50, 150, and 300 cells/μL), and their clinical characteristics were compared.

Results: Among 408 AECOPD and 275 ACO patients, the prevalence of ACO during the late pandemic period in 2023 was significantly higher than in the pre-pandemic period in 2019. ACO patients during the late pandemic period showed increased EOS counts and FeNO levels compared to pre-pandemic patients ($P < 0.05$). In AECOPD patients, those with EOS <50 cells/μL had lower lymphocyte counts and higher NLR and FDP levels than other groups. Similarly, in ACO patients, the EOS <50 cells/μL group showed lower lymphocyte counts and higher NLR levels. Patients with EOS ≥300 cells/μL were younger and exhibited higher FeNO levels than the EOS <50 and 50–150 cells/μL groups ($P <0.05$).

Conclusion: The prevalence of ACO among AECOPD patients increased during the late pandemic period, possibly indicating a role for type 2 inflammation. EOS thresholds of 50, 150, and 300 cells/μL may serve as markers of disease severity and aid in tailoring individualized treatment strategies.

Keywords: type 2 inflammation, acute exacerbation of chronic obstructive pulmonary disease, asthma-COPD overlap, eosinophils, COVID-19 pandemic

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a persistent airflow obstruction due to airway abnormalities and/or alveolar abnormalities.[1] Asthma-COPD Overlap (ACO) has characteristics associated with asthma and COPD and has a higher burden of disease.[2] Coronavirus disease 2019 (COVID-19) is already exerting a significant adverse influence on global public health.[3] Since January 8, 2023, the National Health Commission of China has issued a notice[4] to treat SARS-CoV-2 infection as a Category B disease, signifying the transition into the post-COVID-19 era. Many patients who have recovered from the infection still experience persistent cough and respiratory difficulties. In the United States, the prevalence of adult asthma rises from 8.0% in 2019 to 8.7% in 2022.[5] A Korean population-based cohort study found that the prevalence of new-onset asthma after SARS-CoV-2 infection was 2.1 times higher than in uninfected individuals, and was particularly significant in older adults.[6] These patients with new-onset asthma had high blood eosinophil (EOS)

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counts or fractional exhaled nitric oxide (FeNO) levels, suggesting a key role for type 2 inflammation.[7] The current situation does not provide clarity regarding the potential increase in asthma incidence following the COVID-19 pandemic in China, the impact on ACO prevalence, and the role of Th2 inflammation. Emerging targeted therapies have increasingly proven to be effective treatments for type 2 inflammatory diseases in recent years.[8] GINA[9] defines type 2 inflammation and guides biologic therapy using the blood EOS threshold of 150 cells/μL. However, the results of biologic therapy for COPD and ACO patients with type 2 inflammation have been inconsistent in terms of clinical efficacy, and the blood EOS thresholds selected for each study varied, including 150, 220 and 300 cells/μL.[10] In contrast, blood EOS below 50 cells/μL in COPD patients was associated with a 2 to 3 fold increase in hospitalized deaths, defined as eosinopenia.[11] Given that blood EOS levels correlate with race and disease state,[12] there is a need to further explore the clinical characteristics of AECOPD and ACO patients with different blood EOS levels to guide precise treatment and reduce clinical burden.

Materials and Methods

Patient Selection

Patients with AECOPD and ACO, who were admitted to the Department of Respiratory and Critical Care Medicine at the Second Hospital of Hebei Medical University from January 2019 to December 2023, were included in the study. AECOPD meets the diagnostic criteria of GOLD (2023):[13] increased dyspnea and/or cough and sputum that worsens in < 14 days which may be accompanied by tachypnea and/or tachycardia; ACO: AECOPD meets the diagnostic criteria of GOLD (2023) and GINA (2023): ① history of typical variable respiratory symptoms (wheeze, shortness of breath, chest tightness and cough); ② confirmed variable expiratory airflow limitation (positive bronchodilator (BD) responsiveness (reversibility) test - increase in FEV_1 of >12% and >200 mL; positive bronchial challenge test - fall in FEV_1 from baseline of ≥20% with standard doses of methacholine, or ≥15% with standardized hyperventilation, hypertonic saline or mannitol challenge). Exclusions: (1) patients with allergic diseases, parasitic infections and autoimmune diseases; (2) patients with acute SARS-CoV-2 infection (nucleic acid or antigen-negative 48 hours prior to admission), active tuberculosis, bronchiectasis with infection, allergic bronchopulmonary aspergillosis, severe pneumonia, pulmonary embolism, interstitial lung diseases and other lung diseases with restrictive ventilation dysfunction; (3) patients in the acute phase of cardiovascular and cerebrovascular diseases, with hepatic/renal insufficiency, or diagnosed malignancies/hematologic disorders; (4) patients who received oral or intravenous glucocorticosteroids within 48 hours prior to the blood tests conducted on the morning following their admission and those who needed long-term application of systemic glucocorticosteroids due to other illnesses; (5) patients with incomplete clinical data; and (6) those who could not be cooperated with the psychiatric-related diseases (Figure 1). This study was reviewed and approved by the Medical Ethics Committee of the Second Hospital of Hebei Medical University (2019-R194). The informed consent was not obtained from the patients. The requirement for consent was waived by the Medical Ethics Committee of the Second Hospital of Hebei Medical University as this was a retrospective analysis of anonymized patient's record with no interventional treatment tested. The study complies with the Declaration of Helsinki.

Data Collection

Clinical data (age, gender, BMI, smoking status, smoking amount, clinical comorbidities), laboratory tests (PaO_2 /FiO_2, absolute EOS, absolute LY, HGB, NLR, hsCRP, ALB, TBIL, FDP, SCr, UA), pulmonary function tests (FEV1/FVC, FEV1%pred), FeNO and treatments (days of hospitalization, antibiotic and glucocorticoid use, total amount of glucocorticoids) were collected from patients. Data from peripheral blood tests were obtained on the morning following the patient's admission to the hospital, and pulmonary function assessments were conducted once the patient had reached a relatively stable condition. The total amount of glucocorticoids was converted based on the equivalent dose of nebulized inhaled budesonide: 40 mg of methylprednisolone sodium succinate = 8 mg of nebulized inhaled budesonide.[14]

Statistical Analysis

The data were analyzed using SPSS 25.0, while GraphPad was employed for the creation of graphs. Independent samples *t*-test was used for comparison between two groups, and one-way analysis of variance (ANOVA) was used for comparison

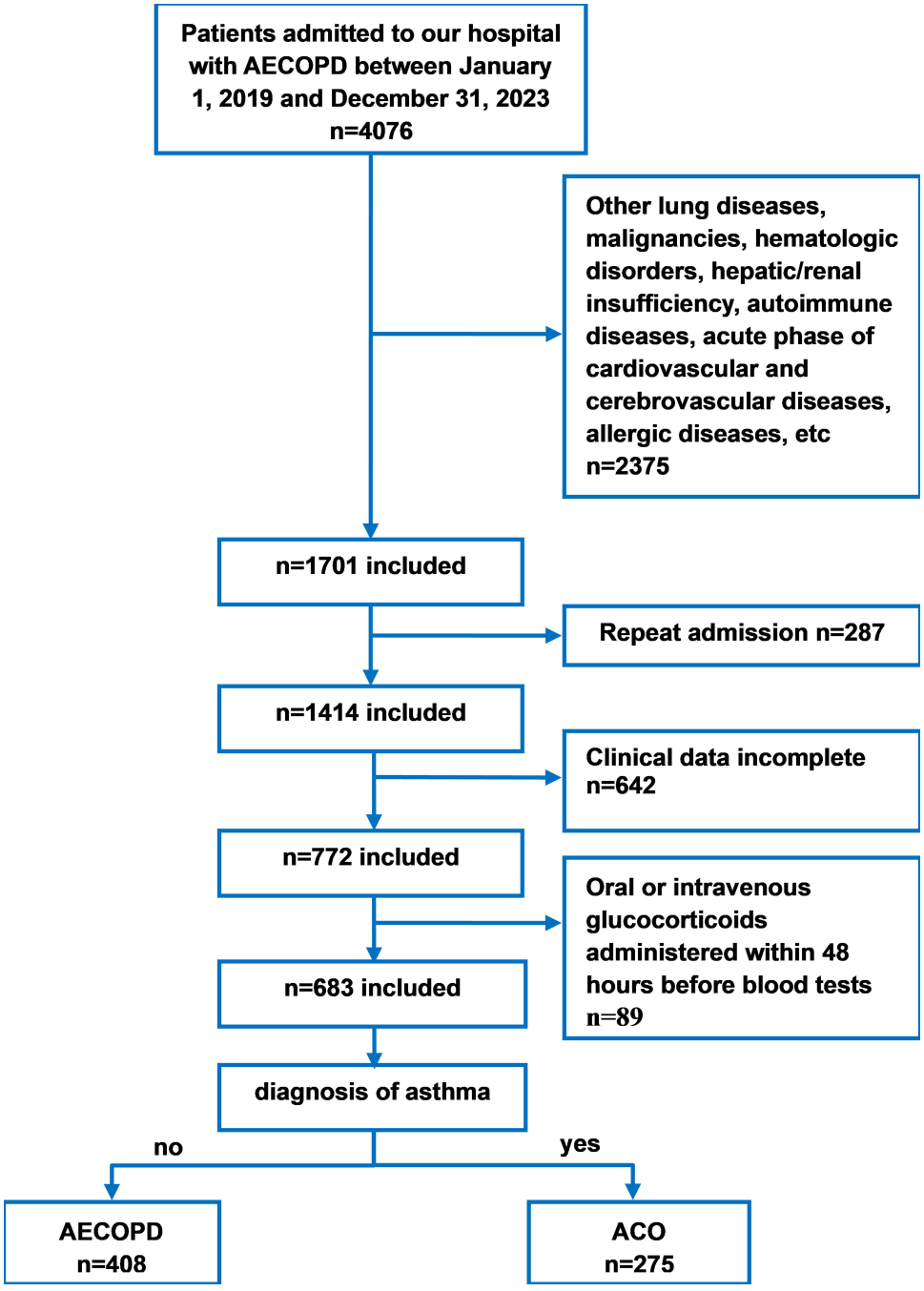

Figure 1 Flow chart of the study.

between multiple groups. The Mann–Whitney *U*-test, a nonparametric method, was employed for the comparison between two groups. Additionally, the Kruskal–Wallis *H*-test was utilized for the analysis of multiple independent samples to facilitate comparisons among several groups, and the Bonferroni correction is utilized to adjust the significance level for each group. The comparison of qualitative data between groups was conducted using the chi-square test. Considering the previous studies,[15] blood EOS counts were found to be non-normally distributed. The 75th percentile was established as the threshold for elevated blood EOS levels. Binary logistic regression analysis was employed to identify factors associated with high blood EOS in patients with AECOPD and ACO. A p-value of <0.05 was considered significant.

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Results

Changes in ACO Prevalence Among AECOPD Patients Before and After the Pandemic

There were fewer hospitalizations from 2020 to 2022 than in 2019 and 2023 (Figure 2). The prevalence of ACO in AECOPD patients in 2023 (late pandemic) was higher (47.88%) than in 2019 (pre-pandemic) (32.22%) (P <0.05) (Figure 3). Blood EOS and FeNO were higher in ACO patients in the late pandemic than in the pre-pandemic period (P <0.05) (Figure 4).

Comparison of Clinical Characteristics of Different Blood EOS Levels

AECOPD patients with EOS ≥150 cells/μL had a higher proportion of ex-smokers, higher absolute value of LY, ALB, and lower NLR than those in the <150 cells/μL group (P <0.05) (Supplemental Table 1). They were further divided into four groups: the absolute value of LY was lower in EOS <50 cells/μL group while NLR and FDP were higher than other three groups, D-dimer and total glucocorticoids were higher than EOS 50–150 cells/μL group, and the application of systemic glucocorticoids was higher than EOS 50–150 and 150–300 cells/μL groups, hsCRP was higher than EOS 50–150 and ≥300 cells/μL groups. The proportion of ex-smokers in the EOS 150–300 cells/μL group was higher than that in the <50 and 50–150 cells/μL groups (P <0.05) (Table 1).

ACO patients with blood EOS ≥150 cells/μL group were younger and had lower NLR and higher FeNO, the absolute value of LY and SCr than <150 cells/μL group (P <0.05) (Supplemental Table 2). They were further categorized into four groups: the absolute value of LY in EOS <50 cells/μL group was lower while NLR was higher than other three groups.

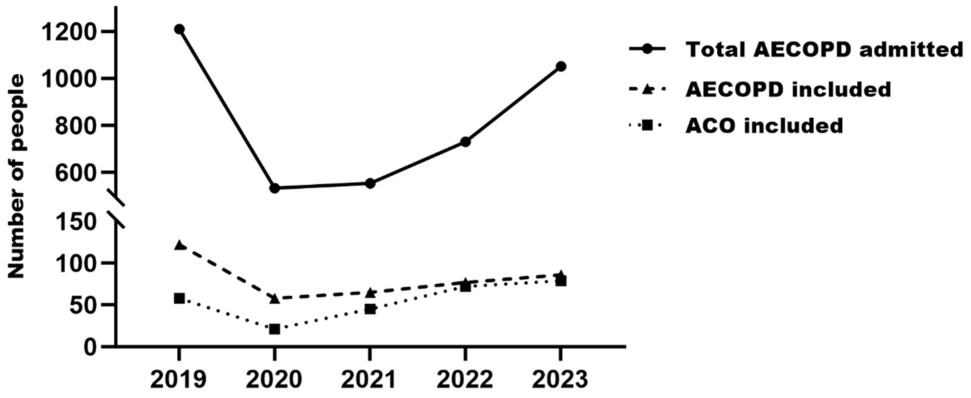

Figure 2 Change in the number of AECOPD patients and ACO patients hospitalized in 2019 to 2023.

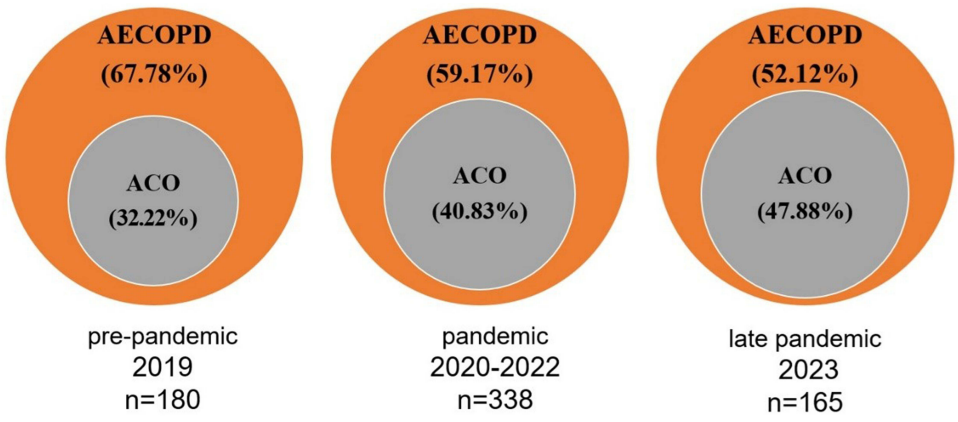

Figure 3 Prevalence of ACO among AECOPD patients included before and after the pandemic.

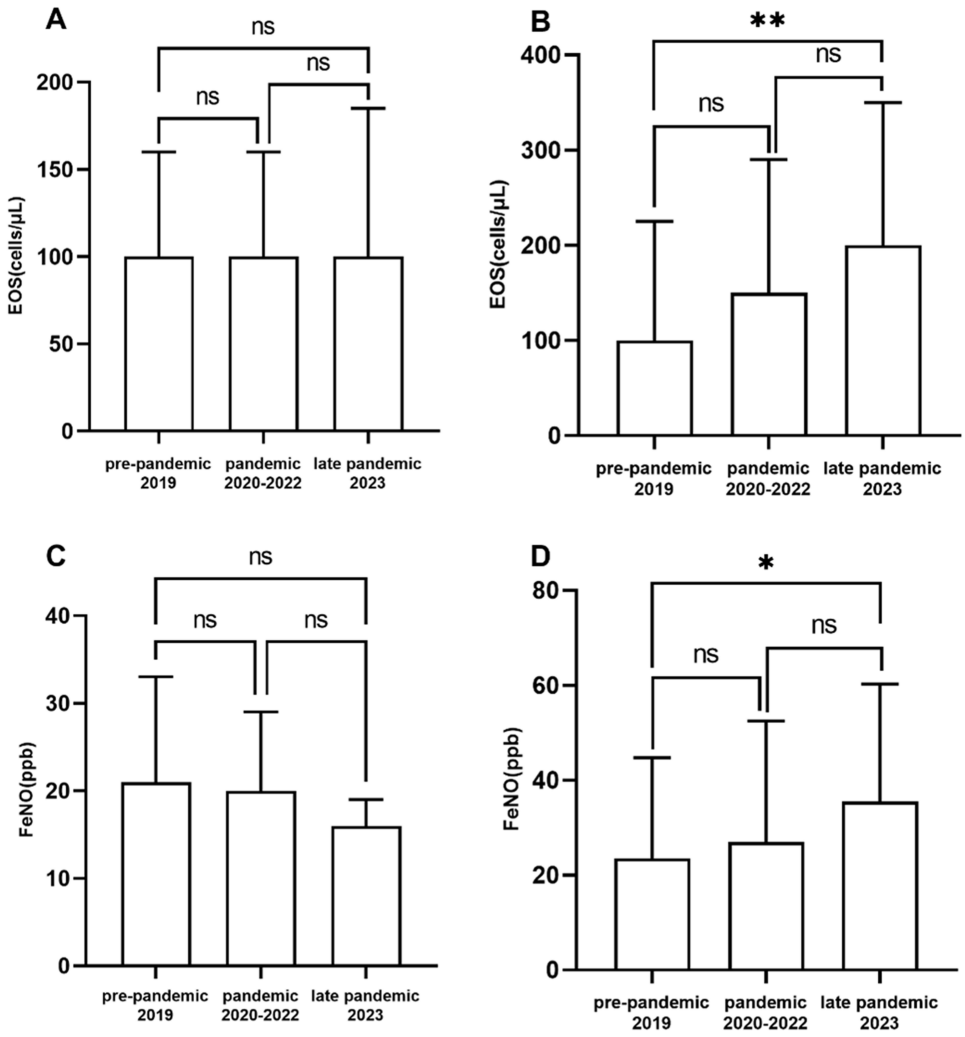

Figure 4 Blood EOS and FeNO levels in AECOPD (**A** and **C**) and ACO patients (**B** and **D**) before and after the pandemic.
Notes: *P <0.05, **P <0.01.

The total amount of glucocorticoids in EOS <50 cells/μL group was higher than in EOS 50–150 and 150–300 cells/μL groups. EOS ≥300 cells/μL group exhibited a younger age distribution than other three groups, along with higher FeNO than EOS <50 and 50–150 cells/μL groups. The application of systemic glucocorticoids in EOS <50 and ≥300 cells/μL groups is higher than 150–300 cells/μL group (P <0.05) (Table 2).

Distribution of Blood EOS Counts and Factors Associated with High EOS

Frequency distributions of blood EOS counts in AECOPD and ACO patients are shown in Figure 5. Binary logistic regression analyses were conducted for indicators that demonstrated statistically significant differences in the univariate analyses: High blood EOS (≥170 cells/μL) was associated with reduced risk of NLR but increased risk of being an ex-smoker in patients with AECOPD. While in patients with ACO, high blood EOS (≥300 cells/μL) was associated with increased risk of being younger and high levels of LY, SCr, FeNO (Figure 6).

Discussion

The COVID-19 pandemic has posed a great challenge to the management of chronic respiratory diseases. This study revealed that significantly fewer patients with AECOPD and ACO visited our hospital during the pandemic period. This decline can be attributed to the fact that most acute exacerbations of COPD are triggered by respiratory viral infections,

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Table 1 Comparison of Clinical Characteristics and Treatment of AECOPD Patients with Different EOS Levels

	<50 cells/μL n=115	50–150 cells/μL n=173	150–300 cells/μL n=72	≥300 cells/μL n=48	*P*
Age, years, mean±SD	70.40±10.37	68.89±10.04	68.90±8.37	68.60±11.12	0.576
Male, (n, %)	88 (76.5)	124 (71.7)	63 (87.5)	38 (79.2)	0.063
BMI (kg/m^2), mean±SD	22.23±4.19	23.35±4.45	22.61±3.53	23.83±4.48	0.062
Smoking status (n, %)					0.027*
Current smoker	50 (43.5)	62 (35.8)	24 (33.3)	17 (35.4)	
Ex-smoker	29 (25.2)[b]	48 (27.7)[b]	34 (47.2)	16 (33.3)	
None	36 (31.3)	63 (36.4)	14 (19.4)	15 (31.3)	
Smoking Index (packs years), median (IQR)	40 (30, 60)	40 (25, 50)	40 (30, 52.5)	40 (20, 40)	0.217
PO_2/FiO_2, mean±SD	341.56±98.90	346.46±74.86	347.58±79.68	357.52±98.04	0.758
FEV_1/FVC, median (IQR)	50.97 (43.31, 59.95)	56.62 (42.80, 63.54)	49.88 (41.20, 61.50)	56.54 (44.23, 64.24)	0.179
FEV_1%pred, median (IQR)	44.55 (33.22, 60.93)	54.00 (35.70, 66.73)	40.25 (30.48, 62.35)	48.50 (32.78, 63.88)	0.089
FeNO (ppb), median (IQR)	24.5 (10.0, 38.3)	17.0 (13.0, 22.0)	17.0 (14.0, 29.0)	23.0 (14.5, 44.5)	0.316
Pulmonary hypertension (n, %)	52 (45.2)	61 (35.3)	18 (25.0)[a]	16 (33.3)	0.042*
Pulmonary artery pressure (mmHg), median (IQR)	36.0 (27.5, 47.0)	32.0 (25.0, 45.0)	31.0 (25.0, 37.5)	30.0 (24.0, 37.5)	0.078
CHD (n, %)	44 (38.3)	65 (37.6)	26 (36.1)	15 (31.3)	0.849
Diabetes (n, %)	20 (17.4)	14 (8.1)	13 (18.1)	7 (14.6)	0.064
Hypertension (n, %)	63 (54.8)	72 (41.6)	33 (45.8)	21 (43.8)	0.173
HGB (g/L), mean±SD	132.11±19.08	132.55±16.47	131.88±14.43	132.98±15.36	0.975
LY (*10^9/L), median (IQR)	1.03 (0.62, 1.36)	1.30 (1.00, 1.70)[a]	1.30 (0.92, 1.80)[a]	1.58 (1.15, 1.87)[a]	<0.001*
NLR, median (IQR)	5.46 (3.32, 9.74)	2.92 (1.86, 4.47)[a]	3.01 (2.30, 4.68)[a]	2.49 (1.90, 4.59)[a]	<0.001*
hsCRP (mg/L), median (IQR)	12.50 (3.23, 72.13)	4.95 (1.00, 19.18)[a]	6.50 (3.18, 37.75)	4.00 (1.80, 11.40)[a]	<0.001*
FDP (mg/L), median (IQR)	1.49 (0.93, 2.67)	0.90 (0.60, 1.50)[a]	1.10 (0.60, 1.98)[a]	0.80 (0.59, 1.30)[a]	<0.001*
D-Dimer (μg/mL), median (IQR)	0.20 (0.12, 0.39)	0.15 (0.09, 0.27)[a]	0.15 (0.09, 0.35)	0.14 (0.11, 0.29)	0.046*
ALB (g/L), mean±SD	36.73±4.94	37.65±4.59	38.05±4.44	39.44±4.35[a]	0.007*
TBIL (μmol/L), median (IQR)	9.76 (6.87, 14.40)	9.60 (6.90, 13.03)	8.75 (6.83, 13.08)	9.10 (6.70, 10.59)	0.462
SCr (μmol/L), mean±SD	68.31±18.88	68.04±17.34	68.59±16.16	73.45±18.05	0.292
UA (μmol/L), median (IQR)	228.5 (163.3, 294.0)	253.0 (203.5, 318.0)	236.0 (178.8, 330.5)	280.0 (235.9, 359.3)[a]	0.001*
Systemic glucocorticoid application (n, %)	52 (45.2)	40 (23.1)[a]	14 (19.4)[a]	19 (39.6)	<0.001*
Combination of antibiotics (n, %)	66 (57.4)	92 (53.2)	36 (50.7)	22 (45.8)	0.566
Total glucocorticoid, median (IQR)	27.0 (15.0, 51.0)	20.0 (5.5, 36.0)[a]	19.5 (10.5, 29.0)	27.5 (14.3, 44.5)	0.003*
Length of stay, median (IQR)	10.0 (7.0, 12.0)	10.0 (7.0, 12.0)	9.0 (7.0, 12.5)	9.0 (7.3, 12.0)	0.986

Notes: [a]*P*<0.05 compared with <50 cells/μL group, [b]*P*<0.05 compared with 150–300 cells/μL group, and * notes *P*<0.05. PaO_2/FiO_2, oxygenation index.

Abbreviations: FEV_1/FVC, Forced Expiratory Volume in the first second/Forced Vital Capacity; FEV1%pred, Forced Expiratory Volume in 1 second, percent predicted; FeNO, Fractional exhaled Nitric Oxide; CHD, Coronary heart disease; HGB, hemoglobin; LY, lymphocyte; NLR, neutrophil/lymphocyte ratio; hsCRP, hypersensitive C-reactive protein; FDP, fibrinogen degradation product; ALB, albumin; TBIL, total bilirubin; SCr, serum creatinine; UA, uric acid.

Table 2 Comparison of Clinical Characteristics and Treatment of ACO Patients with Different EOS Levels

	<50 cells/Ml n = 53	50–150 cells/μL n = 87	150–300 cells/μL n = 60	≥300 cells/μL n = 75	*P*
Age, years, mean±SD	65.87±12.49[c]	65.95±10.21[c]	65.58±9.17[c]	61.09±11.60	0.017*
Male, (n, %)	36 (67.9)	63 (72.4)	50 (83.3)	55 (73.3)	0.275
BMI (kg/m^2), mean±SD	23.78±4.19	30.27±9.84	24.20±4.15	25.24±6.05	0.317
Smoking status (n, %)					0.133
Current smoker	20 (37.7)	30 (34.5)	32 (53.3)	23 (30.7)	
Ex-smoker	12 (22.6)	26 (29.9)	11 (18.3)	18 (24.0)	
None	21 (39.6)	31 (35.6)	17 (28.3)	34 (43.3)	
Smoking Index (packs years), median (IQR)	40 (20, 50)	40 (20, 40)	30 (25, 50)	30 (15, 40)	0.632
PO_2/FiO_2, mean±SD	337.73±70.87	352.87±71.93	360.88±86.20	350.91±71.38	0.432
FEV_1/FVC, median (IQR)	57.70 (47.94, 63.89)	57.66 (44.29, 63.58)	51.81 (42.80, 59.24)	54.57 (46.33, 63.97)	0.146
FEV_1%pred, median (IQR)	51.00 (45.15, 70.70)	48.00 (33.90, 69.60)	43.90 (30.78, 64.20)	53.70 (42.90, 65.00)	0.067
FeNO (ppb), median (IQR)	21.0 (16.0, 32.5)[c]	24.0 (18.0, 45.5)[c]	27.0 (17.0, 41.0)	44.0 (26.5, 72.0)	0.002*

(*Continued*)

Table 2 (Continued).

	<50 cells/Ml n = 53	50–150 cells/μL n = 87	150–300 cells/μL n = 60	≥300 cells/μL n = 75	*P*
Pulmonary hypertension (n, %)	10 (18.9)	15 (17.2)	10 (16.7)	6 (8.0)	0.262
Pulmonary artery pressure (mmHg), median (IQR)	29.0 (22.5, 39.0)	29.5 (23.8, 34.3)	31.0 (23.0, 39.0)	26.0 (22.0, 33.0)	0.247
CHD (n, %)	18 (34.0)[c]	29 (33.3)[c]	10 (16.7)	10 (13.3)	0.004*
Diabetes (n, %)	8 (15.1)	14 (16.1)	5 (8.3)	12 (16.0)	0.535
Hypertension (n, %)	30 (56.6)	33 (37.9)	25 (41.7)	28 (37.3)	0.117
HGB (g/L), mean±SD	136.70±17.14	133.29±15.93	136.18±19.95	138.85±14.30	0.209
LY (*10^9/L), median (IQR)	1.00 (0.73, 1.64)	1.58 (1.10, 1.95)[a]	1.40 (1.20, 1.74)[a, c]	1.70 (1.30, 2.10)[a]	<0.001*
NLR, median (IQR)	3.56 (2.37, 7.58)	2.80 (1.87, 4.05)[a]	2.79 (2.17, 3.74)[a, c]	2.27 (1.56, 3.08)[a]	<0.001*
hsCRP (mg/L), median (IQR)	9.60 (2.00, 31.10)	3.79 (1.68, 17.03)	3.70 (2.20, 9.60)	3.45 (1.51, 9.60)	0.074
FDP (mg/L), median (IQR)	1.07 (0.67, 2.67)	0.70 (0.48, 1.28)[a]	0.73 (0.42, 1.45)	0.65 (0.44, 1.00)[a]	0.010*
D-Dimer (μg/mL), median (IQR)	0.21 (0.09, 0.51)	0.12 (0.06, 0.27)	0.12 (0.07, 0.40)	0.11 (0.06, 0.18)[a]	0.023*
ALB (g/L), mean±SD	38.98±4.42	38.65±4.46	39.47±4.46	40.04±4.06	0.216
TBIL (μmol/L), median (IQR)	8.19 (6.44, 11.50)	9.70 (6.57, 14.60)	8.85 (7.13, 11.19)	9.70 (6.50, 12.50)	0.365
SCr (μmol/L), mean±SD	64.09±14.10	67.27±13.72	72.47±24.64	72.85±18.16[a]	0.016*
UA (μmol/L), median (IQR)	245.0 (195.0, 322.5)	275.0 (232.0, 339.0)	284.4 (239.0, 350.0)	288.0 (237.0, 354.0)	0.077
Systemic glucocorticoid application (n, %)	31 (58.5)	32 (36.8)	17 (28.3)[a, c]	39 (52.0)	0.003*
Combination of antibiotics (n, %)	29 (54.7)	37 (42.5)	25 (43.1)	38 (50.7)	0.438
Total glucocorticoid, median (IQR)	44.0 (23.0, 69.5)	22.0 (13.0, 37.0)[a]	20.5 (12.4, 41.3)[a]	32.0 (15.0, 52.0)	<0.001*
Length of stay, median (IQR)	11.0 (8.0, 14.5)	9.0 (7.0, 12.0)	8.0 (7.0, 11.8)[a]	9.0 (7.0, 13.0)	0.029*

Note: [a]*P*<0.05 compared with <50 cells/μL group, [c]*P*<0.05 compared with≥300 cells/μL group, and **P*<0.05. PaO_2 /FiO_2, oxygenation index.
Abbreviations: FEV_1/FVC, Forced Expiratory Volume in the first second/Forced Vital Capacity; FEV1%pred, Forced Expiratory Volume in 1 second, percent predicted; FeNO, Fractional exhaled Nitric Oxide; CHD, Coronary heart disease; HGB, hemoglobin; LY, lymphocyte; NLR, neutrophil/lymphocyte ratio; hsCRP, hypersensitive C-reactive protein; FDP, fibrinogen degradation product; ALB, albumin; TBIL, total bilirubin; SCr, serum creatinine; UA, uric acid.

and physical interventions have been shown to mitigate the risk of respiratory viral transmission within the general population.[16] This reduction may also reflect a decrease in hospital visits, but a German study showed that the large decline in hospitalizations for AECOPD was more pronounced than the decline in hospitalizations for myocardial infarction.[17] The present study excluded COVID-19 patients with acute infections and still observed an increased prevalence of ACO and elevated EOS and FeNO levels in patients with AECOPD, suggesting a key role for type 2 inflammation. There may be a greater future demand for biological agents. There is still a need for a larger multicenter statistical analysis of the prevalence of ACO in the general population and the collection of patients' previous history of SARS-CoV-2 infections, to explore the relationship between COVID-19, type 2 inflammation, and the prevalence of ACO, and to provide ideas for the clinical differential diagnosis and selection of treatment options.

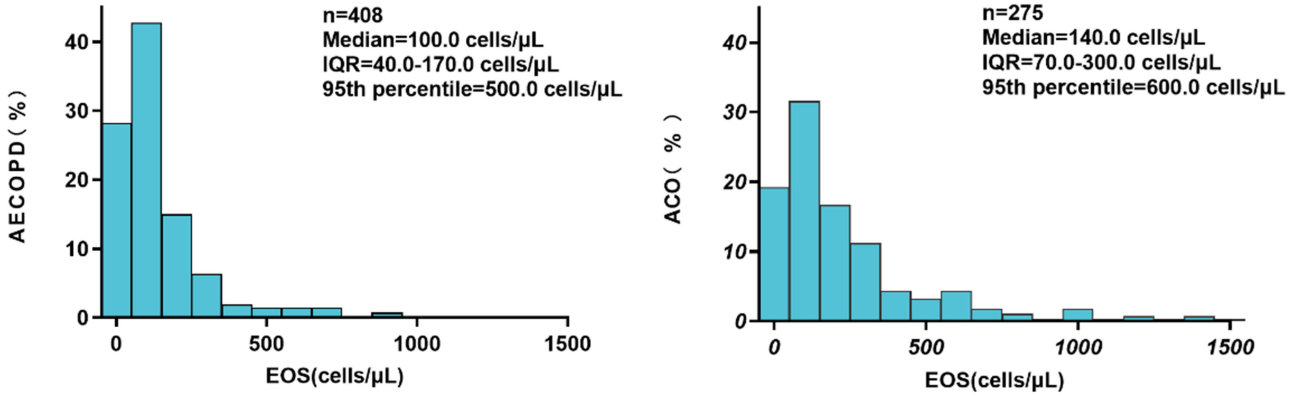

Figure 5 Frequency distribution of blood EOS counts in AECOPD and ACO patients.

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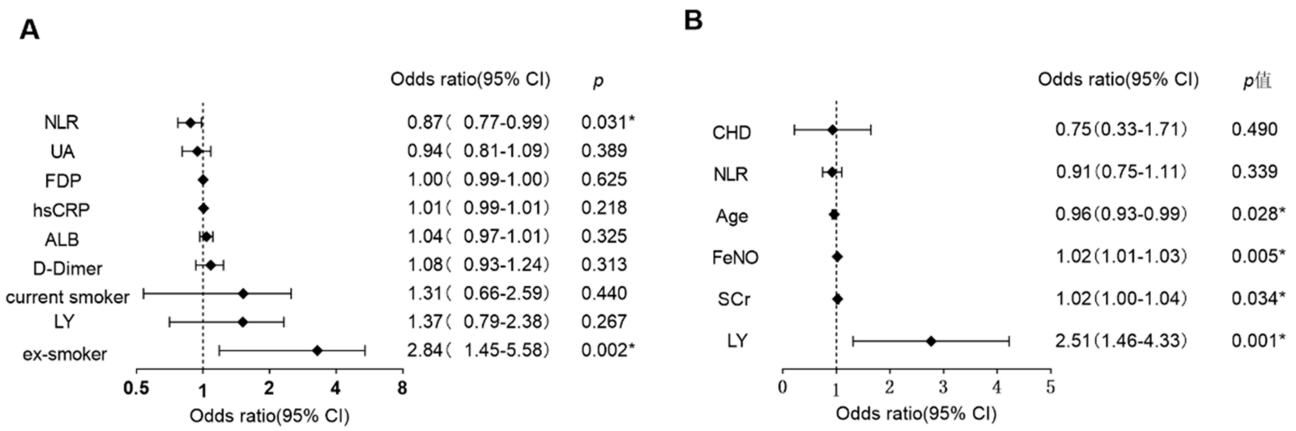

Figure 6 Analysis of factors associated with high blood EOS in patients with AECOPD (**A**) and ACO (**B**).
Notes: **P* <0.05, ***P* <0.01.

In this study, high blood EOS was found to be associated with ex-smokers among AECOPD patients. Smoking has been shown to increase systemic inflammation and elevate leukocyte and EOS counts in peripheral blood.[18] One study[19] found that patients with eosinophilic airway disease are usually former smokers and have high pack-years of smoking. In patients with severe asthma, a history of at least 10 pack-years of ex-smokers has been associated with increased airway eosinophilia, and smoking may induce activation and degranulation of EOS, which are relatively insensitive to hormonal therapy, and in turn induce increased airway autoimmunity and disease activity.[20] Another study[21] found a significant difference between ex-smokers and current smokers, with ex-smokers showing the higher exacerbation rate in patients with elevated blood EOS. They suggest that ex-smokers with stable COPD and elevated blood EOS may constitute a target population for more specific treatment of eosinophilic inflammation, because the increased risk was more pronounced in patients receiving ICS and this treatment does not appear to lower the blood eosinophil count. Together with our study, it is indicated that ex-smokers in COPD patients may be associated with high EOS and poor response to ICS treatment. Further investigation into the underlying mechanisms and effective treatment strategies for this subset of patients is necessary.

Induced sputum cell counts represent the most reliable method for identifying eosinophilic inflammation of the airways. However, induced sputum test could not be widely applicable due to its time-consuming and labor-intensive processes. FeNO is a convenient, easy-to-obtain, and non-invasive method for assessing active, mainly Th2-driven, airway inflammation, which is sensitive to treatment with standard anti-inflammatory therapy.[22,23] In patients with COPD, FeNO levels are elevated in high disease severity and acute exacerbations, and high FeNO suggests eosinophilic inflammation, the presence of asthmatic features, and an increased response to ICS.[24] Consistent with our observation that FeNO values were higher in the high EOS group. Blood EOS counts and FeNO levels are now recognized as type 2 inflammatory markers in the context of asthma and COPD-related biologics. The combination of these two biomarkers facilitates the identification of patients who are likely to benefit therapeutically from targeted drug therapies.[25,26]

Meta-analysis showed[27] that blood EOS counts were 2.5% (IQR 1.7–3.6%) in the general population, 220 cells/μL (IQR 70.0–300.0 cells/μL) in patients with asthma, 2.6% (IQR 1.8–4.0%) in patients with COPD, and 160 cells/μL (IQR 110–240 cells/μL) in patients with non-asthma. However, the number of studies that included Asian countries is insufficient to adequately address ethnic differences. A national cross-sectional study in China showed[15] that blood EOS was 110 cells/μL (IQR 67.2–192.9 cells/μL) in the general population, with 133.4 cells/μL (IQR 79.3–228.4 cells/μL) in smokers and 140.7 cells/μL (IQR 79.6–218.2 cells/μL) in asthmatics, 141.5 cells/μL (IQR 82.6–230.1 cells/μL) in those with post-bronchodilator airflow limitation (FEV_1%pred <0.7), which was lower than the blood EOS counts in foreign studies, and most of these large studies were from the community or outpatients. But our statistics of inpatients showed that blood EOS counts of patients with AECOPD 100 cells/μL (IQR 40–170 cells/μL) and ACO 140 cells/μL (IQR 70–300 cells/μL) were lower than the above studies, suggesting that if blood EOS levels are used to guide individualized medication, it is necessary

to consider the potential modulation of EOS by different diseases and states, and to find the threshold of blood EOS counts suitable for different type of populations. The present study further subdivided the blood EOS by 50 and 300 cells/μL and observed that the differences in clinical characteristics among the four groups were more pronounced than those between the two groups. This indicates that additional refinement of the group is necessary to effectively guide clinical treatment.

Conclusion

The results of this study showed that the prevalence of ACO in AECOPD patients was higher in the late pandemic than in the pre-pandemic period, and blood EOS counts and FeNO were elevated in patients with ACO, suggesting a key role of type 2 inflammation. Systemic inflammation was more severe and glucocorticoid application was more frequent in AECOPD and ACO patients with EOS <50 cells/μL. While eosinophilic airway inflammation was more severe in ACO patients with EOS ≥300 cells/μL, suggesting that in addition to comparing the recognized threshold of 150 cells/μL for blood EOS, a further breakdown by 50 cells/μL, 300 cells/μL may be indicative of disease severity and guide the development of individualized and precise treatment.

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Disclosure

All authors report no conflicts of interest in this work.

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