Research Square

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Effect of aspirin and statins on pulmonary function and inflammation in patients with AECOPD

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Abstract

Background: The influence of coronary atherosclerosis and related treatment drugs on acute exacerbation of chronic obstructive pulmonary disease (AECOPD) development requires in-depth study. The study investigated the effect of coronary artery calcification (CAC) and drugs for the treatment of CAC on the development of AECOPD. Methods : This retrospective clinical study recruited subjects with AECOPD from Weifang People's Hospital from May 2017 to May 2019. All subjects were performed spirometry and coronary computed tomography (CT), and were divided into two groups according to whether coronary CT revealed coronary artery calcification: AECOPD group and AECOPD+CAC group. Then the AECOPD+CAC subjects were subdivided into two groups according to whether they had received oral aspirin and statins: AECOPD + CAC non-medication and AECOPD + CAC medication. T he t -test and nonparametric test were used for analyzed the lung function, arterial blood gas, routine blood and blood lipid between groups. Results : AECOPD subjects with CAC had significant increases in FEV 1 %pred, PaO 2 and Lym% (P <0.05), but WBC, Neu, and Neu% were lower (P <0.05) compared with the AECOPD group. There were no statistically significant differences in blood lipid levels between the two groups. Compared to the AECOPD group, the AECOPD+CAC medication group also had significantly higher PaO 2 and Lym% (P <0.05), and WBC, Neu, and Neu% in the AECOPD+CAC medication group were significantly lower (P <0.05) than in the AECOPD group. Conclusions : Aspirin and statins for the treatment of cardiovascular diseases can improve lung function, normalize blood gas levels, and reduce inflammation in patients with AECOPD and CAC.

Background

COPD is a common, preventable chronic airway inflammatory disease characterized by persistent respiratory symptoms and restricted airflow. Progressive airflow limitation is progressive, first affecting the airways followed by the lung tissue. It is associated with chronic inflammatory reactions such as harmful gases or particles such as cigarette smoke. COPD affects more than 170 million people worldwide and caused ~ 3.2 million deaths in 2015 [1], while increasing socio-economic and medical burdens. AECOPD is the main cause of death, and the most common cause of acute exacerbation is viral or bacterial infection. Recent studies have shown that it comorbid conditions can also induce or promote AECOPD, including diabetes, cardiovascular disease, or a systemic inflammatory response.

Atherosclerosis in the endometrium begins with intimal injury, followed by lipid accumulation, fibrous tissue hyperplasia and calcinosis, and progressive degeneration of the arterial layer. These events are followed by calcification, secondary plaque hemorrhage, plaque rupture, and local thrombosis. Coronary arteries are commonly affected vessels. When the diameter is sufficient narrowed by atherosclerosis, coronary heart disease, arrhythmia, and even sudden death may occur. Cigarette smoke is a risk factor for coronary atherosclerosis, and it can also cause COPD. Previous studies [2–4] demonstrated that COPD or airflow limitation can promote the development of coronary atherosclerosis. CAC can reflects coronary atherosclerosis and is a risk factor for adverse cardiovascular outcomes [5]. The influence of coronary atherosclerosis on COPD development requires in-depth study. Here we analyzed the clinical data of

patients with AECOPD and/or CAC to explore the effects of CAC and related drugs (aspirin and statins) on patients with AECOPD.

Methods

Protocol and registration

This retrospective clinical study was conducted in accordance with the Declaration of Helsinki and was approved by the Weifang Medical University Medical Ethics Committee. Institutional Review Board approval was obtained, but informed consent from patients was not required due to the retrospective nature of the study. However, written consent affirming that patients were informed of the risks associated with AECOPD and all treatment modalities were obtained from all patients upon their initial admission. Patient records and information were anonymized.

Study Selection

The study population was recruited from subjects undergoing spirometry and coronary CT in Weifang People's Hospital from May 2017 to May 2019. All subjects were diagnosed with AECOPD. The following criteria was used for subject selection: 1) clinical symptoms (chronic cough and/or exertional dyspnea) and a post bronchodilator forced expiratory volume in 1 second/forced vital capacity (FEV_1/FVC) ratio < 0.7; 2) acute changes in symptoms such as dyspnea, cough, and/or sputum; 3) use of systemic corticosteroids, antibiotics, and oxygen therapy, etc. Subjects were excluded for heart failure; infectious disease, acute inflammatory disease or conditions that may affect metabolic parameters (eg, thyroid dysfunction, anemia, and malignancy, renal and liver dysfunction based on medical history or laboratory tests); or episodes of previous pulmonary embolism, immunological disease, or history of venous thrombosis. All subjects were divided into two groups according to whether coronary CT revealed CAC: AECOPD (n = 18) and AECOPD + CAC (n = 37). The AECOPD + CAC group subjects were further subdivided into two groups according to whether they had received oral aspirin and statins: AECOPD + CAC non-medication (n = 22) and AECOPD + CAC medication (n = 15).

Outcome Measures

Lung function and arterial blood gas

Lung function were performed with Master Screen (CareFusion). Subjects had been lying down for at least 15 minutes, and arterial blood samples were taken from the radial artery after admission. The blood samples were immediately measured with GEM PREMIER 3500. All operations were carried out in accordance with manufacturer's protocols.

Routine Blood Testing And Blood Lipid Measurement

Fasting venous blood was taken from the ulnar vein on the morning of admission, and was put into tubes with EDTA or with coagulant respectively. Peripheral blood cell counts were measured by an automatic blood cell counter (Sysmex). Blood lipids were measured with an automatic biochemical analyzer (Beckman).

Statistical analysis

An independent statistician blinded to participant allocation used SPSS 21 statistical software (IBM Corp., Armonk, NY, USA) to analyze data, and the results were presented as mean ± SD. We performed t-test for data with normal distributions and nonparametric test was used for those data without normal distributions between two groups, analysis of variance was used for data with normal distributions and Kruskal Wallis Test for those data without normal distributions between three groups. Chi-square test was used for gender. Values of $P < 0.05$ was considered statistically significant.

Results

Subject characteristics

Between May 2017 and May 2019, 55 subjects were recruited. They were aged 51–85 years; 45 were males and 10 were females. All subjects were divided into two groups: AECOPD (n = 18) and AECOPD + CAC (n = 37). There were no differences in age, sex, height, or weight between groups (Table 1).

Table 1
Baseline characteristics.

	AECOPD group	AECOPD + CAC group	P value
Age (years)	66.39 ± 9.23	69.32 ± 6.69	0.219
Female, n (%)	2 (11.1)	8 (21.62)	0.565
Height (cm)	161.72 ± 7.09	161.89 ± 7.50	0.936
Weight (kg)	63.50 ± 9.08	63.05 ± 13.21	0.898

Comparison of outcomes among the AECOPD, AECOPD+CAC non-medication, and AECOPD+CAC medication groups

AECOPD + CAC subjects had significant increases in FEV_1%pred, PaO_2 and Lym% ($P < 0.05$), but WBC, Neu, and Neu% were lower ($P < 0.05$) compared with the AECOPD group. There were no statistically

significant differences in blood lipid levels between the two groups ($P > 0.05$; Table 2).

Analysis of lung function tests at the time of admission showed no significant difference in FEV_1 or FEV_1/FVC between groups ($P > 0.05$; Fig. 1A, 1C). The FEV_1%pred of the AECOPD + CAC and AECOPD groups were 45.70 ± 17.90% and 37.42 ± 24.05%, respectively ($P = 0.024$; Fig. 1B).

The results for PaO_2 was shown in Fig. 2. PaO_2 in the AECOPD + CAC group was significantly higher than the AECOPD group (72.49 ± 14.20 mm Hg vs 65.33 ± 18.08 mm Hg, $P = 0.023$; Fig. 2A). The result suggested that subjects in AECOPD group had more severe hypoxia. There was no difference in $PaCO_2$ between the two groups ($P = 0.461$; Fig. 2B).

Routine blood testing showed that the Lym% values were of 22.55 ± 9.17% and 15.98 ± 5.04% in the AECOPD + CAC and AECOPD group, respectively ($P = 0.001$; Fig. 3A). There was no significant difference in Lym counts between the two groups ($1.62 \pm 0.55 \times 10^9$/L vs $1.51 \pm 0.59 \times 10^9$/L, $P = 0.502$; Fig. 3B). The WBC, Neu, and Neu% values of the AECOPD + CAC group were significantly lower than those of the AECOPD group ($P = 0.041$, $P = 0.016$, $P = 0.028$, respectively; Fig. 3C-E). The changes in WBC and Neu levels suggested a stronger systemic inflammatory response in the AECOPD group compared to the AECOPD + CAC group.

Table 2
Outcomes by group.

Outcomes	AECOPD group	AECOPD + CAC group
FVC (L)	1.69 ± 0.86	1.85 ± 0.72
FVC%pred (%)	55.10 ± 30.62	61.20 ± 19.59
FEV_1 (L)	0.88 ± 0.50	1.06 ± 0.47
FEV_1%pred (%)	37.42 ± 24.05	45.70 ± 17.90*
FEV_1/FVC (%)	53.75 ± 10.56	57.87 ± 10.02
PH	7.44 ± 0.04	7.44 ± 0.03
$PaCO_2$ (mm Hg)	41.28 ± 7.75	39.92 ± 6.15
PaO_2 (mm Hg)	65.33 ± 18.08	72.49 ± 14.20*
WBC (× 10^9/L)	9.60 ± 3.28	8.14 ± 3.60*
Lym (× 10^9/L)	1.51 ± 0.59	1.62 ± 0.55
Neu (× 10^9/L)	7.25 ± 2.72	5.69 ± 3.57*
Lym% (%)	15.98 ± 5.04	22.55 ± 9.17**
Neu% (%)	75.27 ± 7.55	68.75 ± 11.06*
RBC (× 10^{12}/L)	4.82 ± 0.64	4.74 ± 0.48
HB (g/L)	147.61 ± 19.31	144.84 ± 13.09
PLT (× 10^9/L)	257.50 ± 90.57	252.57 ± 90.03
Mon (× 10^9/L)	0.62 ± 0.30	0.54 ± 0.29
Eos (× 10^9/L)	0.17 ± 0.30	0.10 ± 0.09
Bas (× 10^9/L)	0.04 ± 0.04	0.03 ± 0.02
Cholesterol (mmol/L)	4.26 ± 1.10	4.61 ± 1.02
Triglyceride (mmol/L)	1.04 ± 0.46	1.26 ± 0.78
HDL-C (mmol/L)	1.35 ± 0.38	1.46 ± 0.38

*Statistically significant at $P < 0.05$.

**Statistically significant at $P < 0.01$.

Outcomes	AECOPD group	AECOPD + CAC group
LDL-C (mmol/L)	2.44 ± 0.79	2.57 ± 0.93
*Statistically significant at P < 0.05.		
**Statistically significant at P < 0.01.		

Comparison of outcomes among the AECOPD, AECOPD + CAC non-medication, and AECOPD + CAC medication groups

Previous studies reported significantly higher WBC and Neu levels in patients with COPD and coronary heart disease, while FEV_1%pred was significantly lower compared to patients with only COPD [6]. The above results were contrary to our findings. Mroz et al [7] suggested that statins can reduce the number of neutrophils in the sputum of patients with COPD. To determine whether the discrepancies with the above-cited studies were associated with aspirin and statin, subjects in the AECOPD + CAC group were further divided into AECOPD + CAC non-medication (n = 22) and AECOPD + CAC medication (n = 15) groups. The results of lung function testing, arterial blood gas analyses, routine blood tests and blood lipid measurements were similar for both groups (Table 3). Compared with the AECOPD group, Lym% were significantly higher (P = 0.033) in both the AECOPD + CAC non-medication and the AECOPD + CAC medication. The AECOPD + CAC medication group also had significantly higher PaO_2 (P < 0.05). WBC, Neu, and Neu% in the AECOPD + CAC medication group were significantly lower (P < 0.05) compared to the AECOPD group.

There were no significant difference in FEV_1, FEV_1%pred or FEV_1/FVC among the three groups (P > 0.05; Fig. 4A-C). The PaO_2 was significantly higher in the AECOPD + CAC medication group. There were no significant difference between the AECOPD and AECOPD + CAC non-medication groups (Fig. 5A). $PaCO_2$ values were not significantly different among the three groups (P > 0.05; Fig. 5B).

The Lym% were 15.98 ± 5.04%, 21.61 ± 9.02%, and 23.95 ± 9.52% in the AECOPD, AECOPD + CAC non-medication, and AECOPD + CAC medication groups, respectively. Values were significantly higher for AECOPD + CAC non-medication and AECOPD + CAC medication groups compared with the AECOPD group (P = 0.033 and P = 0.007; Fig. 6A). There were no significant difference in lymphocyte numbers among the three groups (P > 0.05; Fig. 6B). The WBC, Neu and Neu% of the AECOPD + CAC medication group were significantly lower compared to AECOPD group. But those between the AECOPD + CAC non-medication and AECOPD + CAC medication groups were not significant, and there were no significant differences between the AECOPD and AECOPD + CAC non-medication groups (P > 0.05; Fig. 6C-E).

Table 3

Results of outcomes among three groups.

Outcomes	AECOPD group	AECOPD + CAC non-medication group	AECOPD + CAC medication group
FVC (L)	1.69 ± 0.86	1.83 ± 0.70	1.88 ± 0.76
FVC%pred (%)	55.10 ± 30.62	61.60 ± 19.93	60.60 ± 19.75
FEV_1 (L)	0.88 ± 0.50	1.00 ± 0.37	1.15 ± 0.59
FEV_1%pred (%)	37.42 ± 24.05	44.00 ± 14.75	48.20 ± 22.07
FEV_1/FVC (%)	53.75 ± 10.56	56.56 ± 9.22	59.79 ± 11.14
PH	7.44 ± 0.04	7.45 ± 0..03	7.44 ± 0.03
$PaCO_2$ (mm Hg)	41.28 ± 7.75	39.18 ± 5.32	41.00 ± 7.27
PaO_2 (mm Hg)	65.33 ± 18.08	70.32 ± 13.51	75.67 ± 15.07*
WBC (× 10^9/L)	9.60 ± 3.28	8.56 ± 3.85	7.53 ± 3.22*
Lym (× 10^9/L)	1.51 ± 0.59	1.63 ± 0.64	1.61 ± 0.40
Neu (× 10^9/L)	7.25 ± 2.72	6.02 ± 3.96	5.21 ± 2.96**
Lym% (%)	15.98 ± 5.04	21.61 ± 9.02*	23.95 ± 9.52**
Neu% (%)	75.27 ± 7.55	70.41 ± 11.19	66.31 ± 10.75*
RBC (× 10^{12}/L)	4.82 ± 0.64	4.79 ± 0.43	4.66 ± 0.56
HB (g/L)	147.61 ± 19.31	146.82 ± 12.51	141.93 ± 13.81
PLT (× 10^9/L)	257.50 ± 90.57	270.50 ± 99.58	226.27 ± 68.71
Mon (× 10^9/L)	0.62 ± 0.30	0.52 ± 0.27	0.56 ± 0.32
Eos (× 10^9/L)	0.17 ± 0.30	0.09 ± 0.09	0.12 ± 0.09
Bas (× 10^9/L)	0.04 ± 0.04	0.03 ± 0.02	0.03 ± 0.02

*Statistically significant at P < 0.05.

**Statistically significant at P < 0.01.

Outcomes	AECOPD group	AECOPD + CAC non-medication group	AECOPD + CAC medication group
Cholesterol (mmol/L)	4.26 ± 1.10	4.70 ± 1.07	4.49 ± 0.96
Triglyceride (mmol/L)	1.04 ± 0.46	1.33 ± 0.75	1.16 ± 0.85
HDL-C (mmol/L)	1.35 ± 0.38	1.44 ± 0.34	1.49 ± 0.45
LDL-C (mmol/L)	2.44 ± 0.79	2.58 ± 0.98	2.55 ± 0.90
*Statistically significant at $P < 0.05$.			
**Statistically significant at $P < 0.01$.			

Discussion

COPD is a common respiratory disease with high morbidity and is becoming a growing social health problem. This chronic inflammation is mainly characterized by chronic inflammation of the airways, lung parenchyma, and pulmonary blood vessels. Cigarette smoking is the major risk factor for COPD. Fabbri et al [8] proposed that cigarette smoke induced airway and lung inflammation and at the same time caused systemic cellular and humoral inflammation, oxidative stress, altered endothelial function, and enhanced circulating concentrations of several procoagulant factors. Cigarette smoke can also cause other systemic diseases such as cardiovascular and metabolic diseases. Common comorbidities of COPD include skeletal muscle abnormalities, hypertension, diabetes, coronary artery disease, heart failure, lung infection, cancer, and pulmonary vascular disease [9]. Atherosclerosis is the most common complication of COPD.

This study showed that subjects with AECOPD + CAC had significantly higher FEV_1%pred and PaO_2 than the AECOPD group. Although increasing trends were observed for FVC, FVC%pred, FEV_1, and FEV_1/FVC, the differences were not statistically significant. Previous studies have shown that lung function in patients with COPD complicated with coronary heart disease was lower than that in COPD [6, 10–11]. Jia et al [12] found that low-dose aspirin can reduced blood viscosity, improved gas exchange in the lungs, and improved lung function and arterial blood gas levels. Yao et al [13] had shown that statins can promoted blood gas improvement and reduced hypoxemia in patients with COPD. Melo et al [14] used elastase to prepared a mouse model of emphysema and treated the animals with atorvastatin. Notably, the numbers of elastic and collagen fibers in the lungs of the treated group were significantly increased compared with the untreated group, demonstrating that statins could significantly repaired lung tissue in injured mice. To further analyze the effects of oral medications on AECOPD, we subdivided the AECOPD + CAC subjects into two subgroups according to whether oral aspirin and statins were administered. There were no significant differences in FVC, FEV_1, FVC%pred and FEV_1/FVC among the three groups, but levels were higher in the AECOPD + CAC medication group compared to the AECOPD and AECOPD + CAC non-

medication groups. The lack of significance was likely due to the small sample size, and a larger study is needed to verify our findings. PaO_2 in the AECOPD + CAC medication group was significantly improved compared with the AECOPD group, and the difference was statistically significant. Jia et al [12] found that aspirin can inhibited cyclooxygenase activity, thereby reducing arachidonic acid production of prostaglandins, leading to decreased production of its metabolite thromboxane A_2, which normally induces platelet aggregation and vasoconstriction. Aspirin can dilate blood vessels by reducing thromboxane A_2, improving gas exchange in the lungs, increase oxygen partial pressure, and improve lung function. Emphysema is a major pathological feature of COPD; it leads to different degrees of hypoxemia by reducing capillaries, increasing ineffective cavity volume, and producing an imbalance between ventilation and blood flow. Notably, some of the indicators in the AECOPD + CAC group were significantly improved compared with the AECOPD group, probably due to the effects of statins and aspirin.

The Lym% was significantly higher in AECOPD patients with CAC compared to the AECOPD group, and lymphocyte numbers showed an increasing (but nonsignificant) trend. COPD is a systemic inflammatory disease [15], and the most common exacerbating factor is infection. Atherosclerosis is also an inflammatory state [16]. The combination of AECOPD and CAC can cause lymphocyte and neutrophil numbers to rise. We found the WBC and Neu numbers were significantly lower in the AECOPD + CAC group than those of AECOPD group. Some previous studies [6, 10–11, 17] reported that patients with AECOPD and CAC have higher WBC and Neu than those with only AECOPD. Others have shown that oral aspirin and statins can reduce neutrophils in sputum and peripheral blood from patients with COPD. To further analyze the effects of oral drugs on AECOPD, the AECOPD + CAC group was subdivided into two groups according to oral aspirin/statin use. WBC and Neu were significantly lower in AECOPD + CAC who had taken these medications. Hamid [18] and colleagues selected healthy volunteers to receive placebo or aspirin for 7 days prior to lipopolysaccharide inhalation followed by bronchoalveolar lavage (BAL). They found that aspirin could reduce BAL neutrophilia and secretion of neutrophil-derived enzymes (matrix metalloproteinase-8, -9). Peripheral neutrophils were not significantly reduced by aspirin but exhibited a downward trend, possibly due to the short duration of action. Aspirin treatment did not significantly change the number of lymphocytes in BAL fluid. This indicated that aspirin does not effectively reduce the number of lymphocytes, which is consistent with our results. Statins inhibit 3-hydroxy-3methylglutaryl coenzyme A (HMG-CoA) reductase, which inhibits the intracellular hydroxyvalerate metabolic pathway by competitive inhibition of the enzyme, thereby reducing intracellular cholesterol synthesis. Therefore, the feedback stimulates the increase in the number and activity of low-density lipoprotein receptors on cell membrane surface, which increases serum cholesterol clearance and lowers its level. They are mainly prescribed for lowering cholesterol, which is very beneficial for preventing coronary heart disease. In addition to lipid-lowering effects, statins are also anti-inflammatory, immunosuppressive, and inhibit platelet aggregation. Some studies [19–21] have reported that statins reduced mortality and morbidity in patients with COPD. Potentially important actions of statins in this population include reducing neutrophil numbers, reducing T cell activation and differentiation, and increasing eosinophil apoptosis [22]. Mroz et al [7] found that statins use was

associated with reduced neutrophils in sputum from patients with COPD, and the authors also performed genetic testing. They found decreased expression of genes that regulated immune response and leukocyte activation in statin-treated subjects and speculated that statins reduced neutrophils and reduced inflammation by altering gene expression. However, the relationship between gene and protein levels has not been elucidated. The collective evidence suggested administration of aspirin and statins in patients with AECOPD + CAC can reduced the numbers of neutrophils but not lymphocytes.

Conclusions

CAC can aggravate COPD, but aspirin and statins can improve lung function, normalize blood gas levels, and reduce inflammation in patients with AECOPD.

Abbreviations

AECOPD: Acute exacerbation of chronic obstructive pulmonary disease; CAC: Coronary artery calcification; CT: Computed tomography; FEV_1: Forced expiratory volume in 1 second; FEV_1/FVC: FEV_1/forced vital capacity; PaO_2: Partial arterial oxygen pressure; $PaCO_2$: Partial arterial carbon dioxide tension; Lym%: Peripheral blood lymphocytes percentage; Lym: Peripheral blood lymphocytes count;WBC: Peripheral blood white blood cell count; Neu: Peripheral blood neutrophil count; Neu%: Peripheral blood neutrophil percentage

Declarations

Authors' contributors

NNY, WT, XSL, LJC, GFG, and GQD had full access to all data in the study, and take responsibility for integrity and accuracy of all data and data analyses. GQD, KXL, SYS, WT and NT contributed substantially to the study design, data analysis and interpretation, and writing of the manuscript.

All authors read and approved the final manuscript.

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Availability of data and materials

All data are provided in the manuscript.

Ethics approval and consent to participate

The protocol was approved by the Committee on the Ethics of Weifang Medical University.

Consent for publication

All list authors consent to the submission and all data are used with the consent of the person generating the data.

Competing interests

The authors declare that they have no competing interests.

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Figures

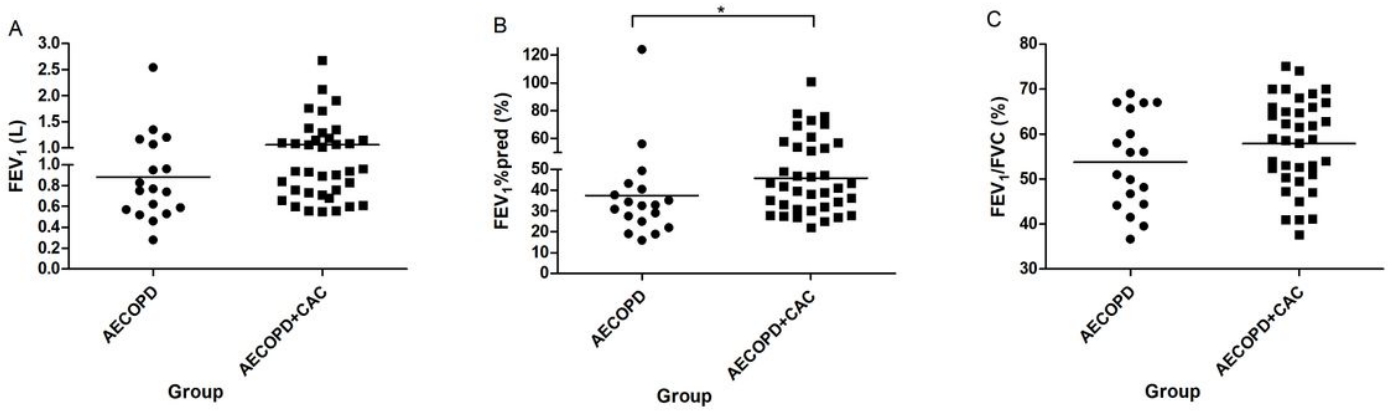

Figure 2

Analysis of lung function test results of subjects in the AECOPD and AECOPD+CAC groups. Scatter plot of (A) forced expiratory volume in 1 second (FEV1), (B) FEV1% predicted, (C) forced expiratory volume in 1 second/forced vital capacity (FEV1/FVC) *Statistically significant at P<0.05. **Statistically significant at P<0.01.

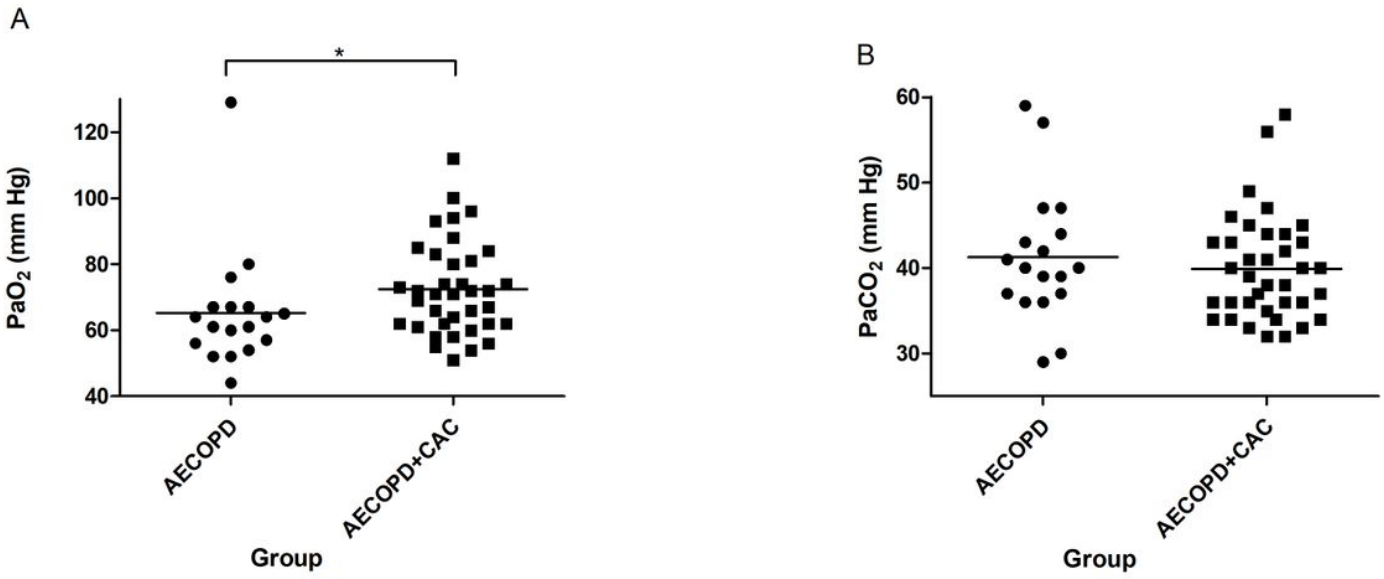

Figure 4

Analysis of blood gas results of subjects in the AECOPD and AECOPD+CAC groups. Scatter plot of (A) partial arterial oxygen pressure (PaO2), (B) partial arterial carbon dioxide tension (PaCO2) *Statistically significant at P<0.05. **Statistically significant at P<0.01.

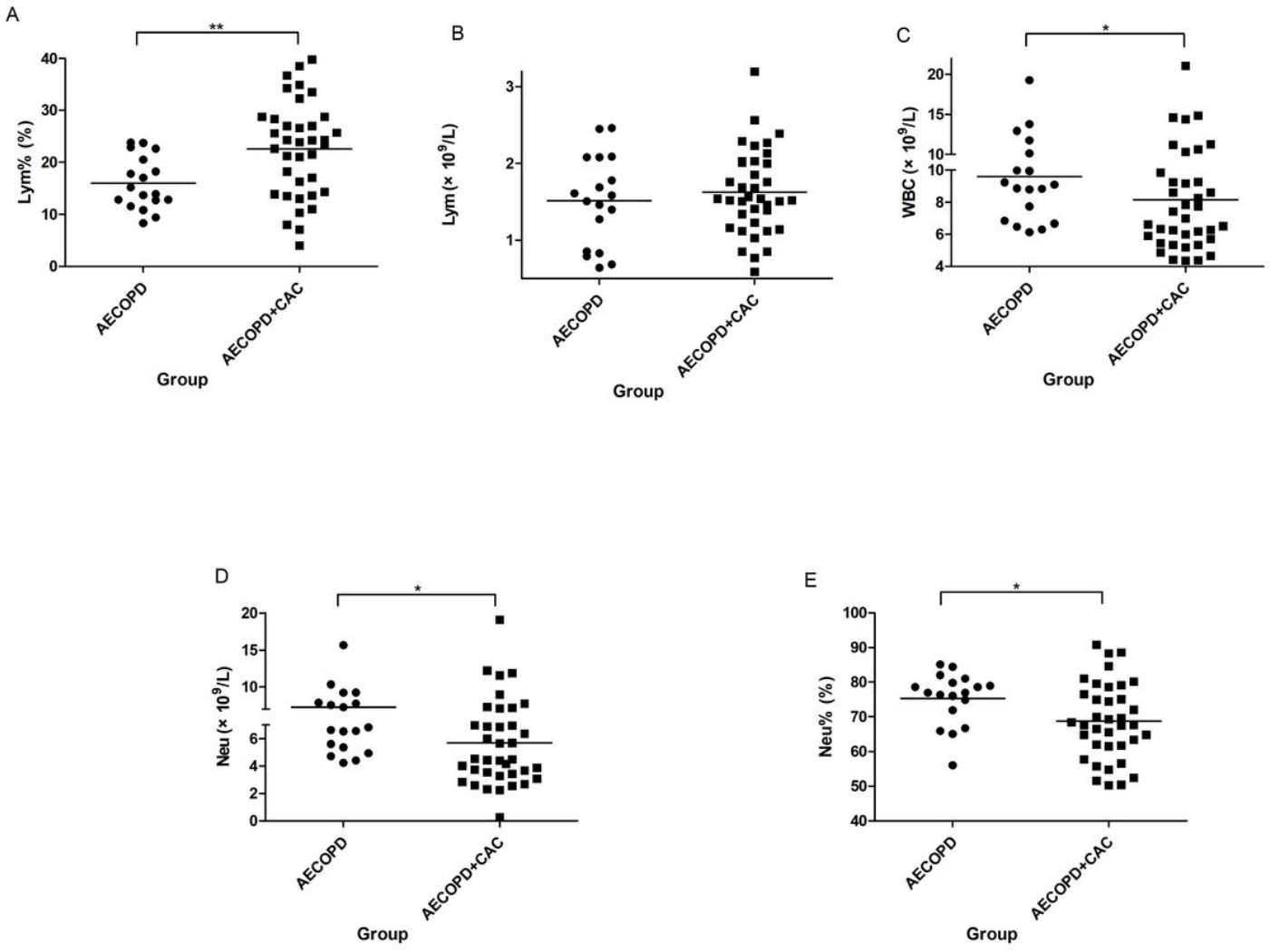

Figure 6

Analysis of routine blood test results of subjects in the AECOPD and AECOPD+CAC groups. Scatter plot of (A) peripheral blood lymphocytes percentage (Lym%), (B) peripheral blood lymphocytes count (Lym), (C) peripheral blood white blood cell count (WBC), (D) peripheral blood neutrophil count (Neu), (E) peripheral blood neutrophil percentage (Neu%) *Statistically significant at $P<0.05$. **Statistically significant at $P<0.01$.

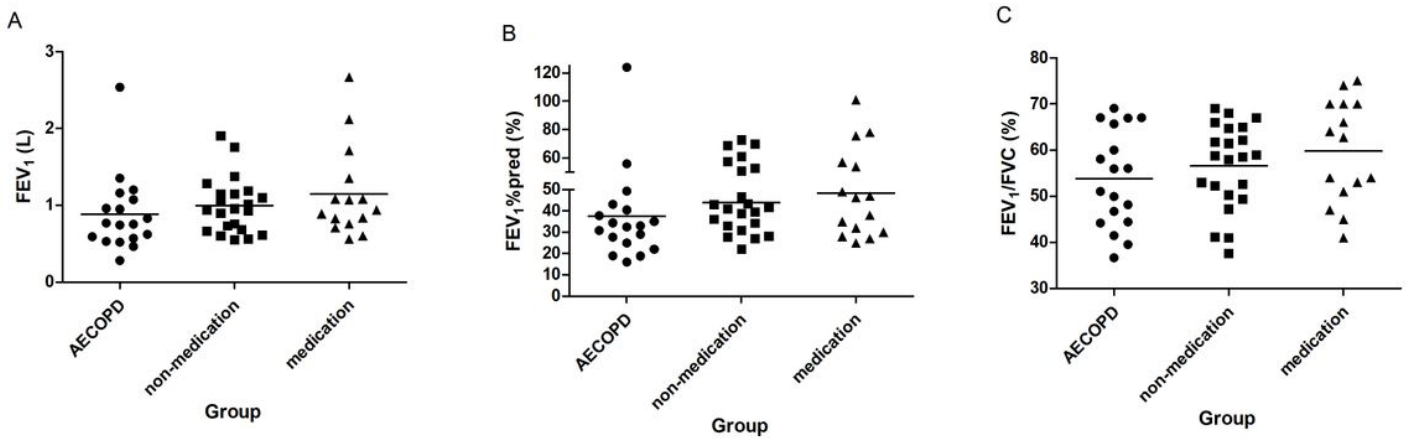

Figure 8

Analysis of lung function test results of subjects in the AECOPD, AECOPD+CAC non-medication, and AECOPD+CAC medication groups. Scatter plot of (A) forced expiratory volume in 1 second (FEV1), (B) FEV1% predicted, (C) forced expiratory volume in 1 second/forced vital capacity (FEV1/FVC) *Statistically significant at P<0.05. **Statistically significant at P<0.01.

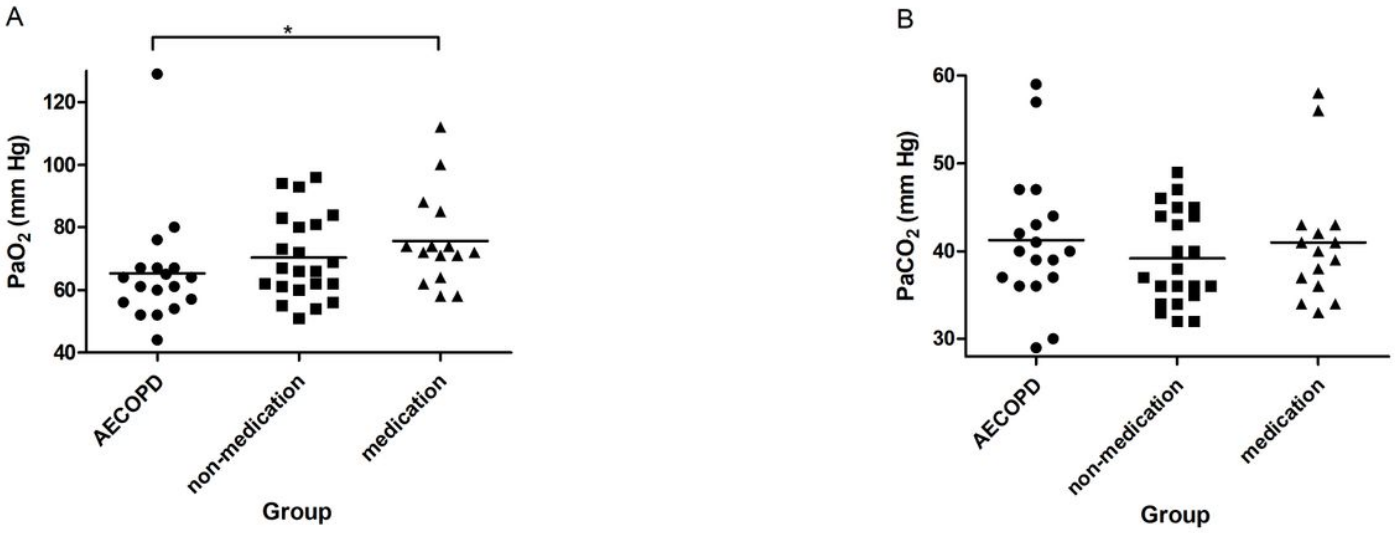

Figure 10

Analysis of blood gas results of subjects in the AECOPD, AECOPD+CAC non-medication, and AECOPD+CAC medication groups. Scatter plot of (A)partial arterial oxygen pressure (PaO2), (B) partial arterial carbon dioxide tension (PaCO2) *Statistically significant at P<0.05. **Statistically significant at P<0.01.

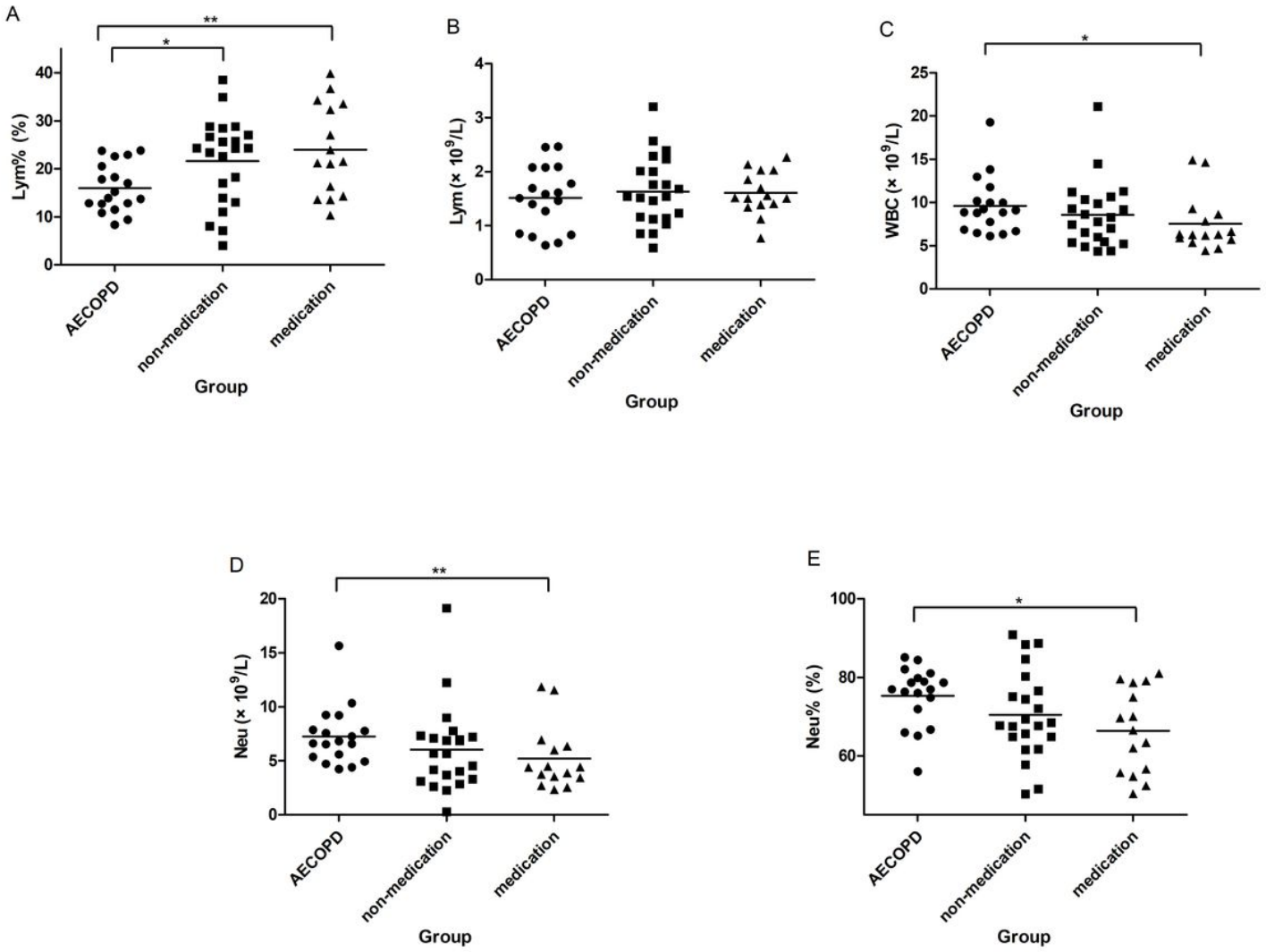

Figure 12

Analysis of blood routine test results of subjects in the AECOPD, AECOPD+CAC non-medication, and AECOPD+CAC medication groups. Scatter plot of (A) peripheral blood lymphocytes percentage (Lym%), (B) peripheral blood lymphocytes count (Lym), (C) peripheral blood white blood cell count (WBC), (D) peripheral blood neutrophil count (Neu), (E) peripheral blood neutrophil percentage (Neu%) *Statistically significant at P<0.05. **Statistically significant at P<0.01.