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ORIGINAL RESEARCH

IL-6 and $CD4^+/CD8^+$ are Important Indicators for Predicting Prognosis in Elderly AECOPD Patients: A Retrospective Study

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Purpose: Evaluating the role of IL-6 and $CD4^+/CD8^+$ in predicting the prognosis of elderly patients with acute exacerbations of chronic obstructive pulmonary disease (AECOPD).

Patients and Methods: This study retrospectively enrolled 413 elderly patients who were hospitalized for AECOPD between January 2019 and December 2021. Patients were divided into event and non-event groups based on whether they were readmitted or died due to AECOPD during 18 months of follow-up. The associations between IL-6 and $CD4^+/CD8^+$ with adverse events were assessed using Cox proportional hazards regression models, Kaplan–Meier survival analysis, and restricted cubic spline (RCS) models. Additionally, subgroup analyses were conducted to evaluate the stability of these associations, and ROC curves were used to assess the predictive ability of IL-6 combined with $CD4^+/CD8^+$ for adverse events.

Results: A total of 413 patients were included in the study, with 218 experiencing adverse events. Patients with high levels of IL-6 and low levels of $CD4^+/CD8^+$ had a higher risk of adverse events. There was a non-linear relationship between IL-6 and $CD4^+/CD8^+$ with adverse events ($p<0.05$). Subgroup analyses further confirmed the robustness of this association. ROC curve analysis indicated that combining IL-6 with $CD4^+/CD8^+$ significantly improved the predictive value for adverse events.

Conclusion: There is a non-linear relationship between IL-6 and $CD4^+/CD8^+$ and adverse events in elderly patients with AECOPD. Combining IL-6 with $CD4^+/CD8^+$ ratios significantly enhances the predictive value for adverse events.

Keywords: elderly, acute exacerbation of chronic obstructive pulmonary disease, IL-6, $CD4^+/CD8^+$, prognosis

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is one of the global priority diseases, and repeated acute exacerbations are the main causes of hospitalization and death.[1,2] According to the 2017 GBD data study, the fatality rate of COPD accounted for 4.72% of all-cause deaths, showing an exponential increase pattern with age.[2,3] Age-related changes in T lymphocyte subpopulations impact their presence and function, leading to reduced resistance to infections and atypical inflammatory responses. Traditional inflammatory markers often show only slight elevations, making them inadequate for assessing patient prognosis.[4–7] Therefore, there is an urgent need to find assessment indicators to predict poor prognosis in elderly acute exacerbations of chronic obstructive pulmonary disease (AECOPD) patients.

As a phase-specific cytokine, IL-6 is more sensitive to inflammatory responses and is activated earlier than acute inflammatory markers (such as CRP and procalcitonin), which plays an anti-inflammatory role and has significant value in predicting the prognosis of patients with AECOPD.[8,9] It predicts the frequency of two or more exacerbations in a year, increasing the risk of death.[10] However, Yongtao Wei et al revealed that IL-6 showed high sensitivity but low specificity in predicting outcomes for AECOPD patients (sensitivity 88.24% vs specificity 49.02%),[11] predicting prognosis in elderly patients alone is flawed. Considering the age-related immune dysfunction in the elderly,[12] patients over 60 years of age are

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twice as likely to have low $CD4^+/CD8^+$ as those under 60 years of age.[13,14] Low levels of $CD4^+/CD8^+$ also play a role in the exacerbation of COPD patients by impairing the immune system's ability to mount an effective response, leading to worsened health outcomes and an elevated risk of mortality.[15,16] However, studies have shown that $CD4^+/CD8^+$ has high specificity but low sensitivity for predicting respiratory failure in AECOPD patients (specificity 75.0% vs Sensitivity 47.9%).[17] Therefore, we propose that IL-6 and $CD4^+/CD8^+$, which, respectively, reflect inflammatory status and immune regulation, complement each other's deficiencies when used together for prognosis prediction, offering a potential advantage for elderly AECOPD patients. Studies have demonstrated an association between IL-6 or $CD4^+/CD8^+$ and the prognosis of patients with AECOPD, but no further analysis of the dose–response relationship between the two has been conducted, and these studies have rarely been studied in the elderly population, nor have the two been combined to explore the risk of readmission or death. Therefore, this study combined IL-6 and $CD4^+/CD8^+$ to evaluate the prognosis of elderly patients with AECOPD has significant value.

Methods

Study Population

This was a single-center, retrospective and observational study of elderly patients with AECOPD who were hospitalized at Shanghai Fifth People's Hospital, Fudan University from January 2019 to December 2021. Inclusion Criteria: 1) First diagnosis of AECOPD on admission; 2) AECOPD meets the diagnostic criteria of the 2019 GOLD guideline;[1] 3) The condition should be stable for at least 6 months prior to admission; 4) Age≥65 years old. Exclusion Criteria: 1) Other respiratory diseases, such as bronchiectasis, lung cancer and pneumonia; 2) Serological specimens or nasal/throat swabs confirming viral infection; 3) Other diseases in the acute stage: Such as heart failure, acute stroke, atrial fibrillation, acute coronary syndrome, pulmonary thromboembolism, venous thrombosis of the lower limbs and other diseases; 4) Active infection in other parts: Such as heart failure, acute stroke, atrial fibrillation, acute coronary syndrome, pulmonary embolism, and deep vein thrombosis; 5) Those who have used antibiotics and systemic hormones for acute exacerbation in the past 1 month; 6) Combined thyroid disease, immune system, hematologic system, malignant tumor or chronic wasting disease; 7) Those with incomplete data, lack of sufficient data or those who did not follow the original plan for treatment and examination or those who were lost to follow-up. The research process is illustrated in Figure 1. The study was conducted with the approval of the Ethics Committee of Shanghai Fifth People's Hospital, Fudan University, Ethics Approval NO.2024–198.

Data Collection and Processing

Collect the patient's hospitalization data from the electronic medical record system, basic data: Gender, age, smoking history, blood pressure, time of readmission (second admission within the follow-up time), time of death; Comorbidities include type 2 diabetes, hypertension, cerebral infarction, and coronary atherosclerotic heart disease; Hematological indicators were measured by the clinical laboratory of our hospital, including blood routine within 24 hours of admission, IL-6, $CD4^+/CD8^+$, C-reactive protein, procalcitonin, thyroid function, coagulation function, arterial blood gas analysis.; Serum IL-6 was detected by chemiluminescence assay using cytokine kit (Riscal, Qingdao, China), with normal values ranging from 0 to 5.4pg/mL; The CD4+/CD8+ ratio was measured by flow cytometry using Multitest 6-Color TBNK reagent (instrument: BD CANTO) to measure the number of $CD4^+$ T lymphocytes and $CD8^+$ T lymphocytes in peripheral blood, and then the ratio of the two was calculated, and the normal values ranged from 0.9 to 3.6.

Statistical Analysis

Data were processed using SPSS 25.0, MedCalc 15.0, and R 4.2.1. Normal test was used for continuous variables, and mean standard deviation was used for data conforming to normal distribution, and median (interquartile distance) was used for data disconforming to normal distribution. The categorical variables are represented by the number of cases (percentage) and the *t*-test or the non-parametric rank sum test are used to compare the differences between continuous variables. The Chi-square test or Fisher test was used to compare the differences between groups of categorical variables, and univariate and multivariate analyses were performed using the COX proportional risk model. Kaplan–Meier plots with log-rank statistics were used to assess differences in outcome across quartiles of IL-6 or $CD4^+/CD8^+$. The association between IL-6 or $CD4^+/CD8^+$ and adverse events was evaluated using restricted cubic spline plots, and age-sex smoking combined with history of stroke combined with

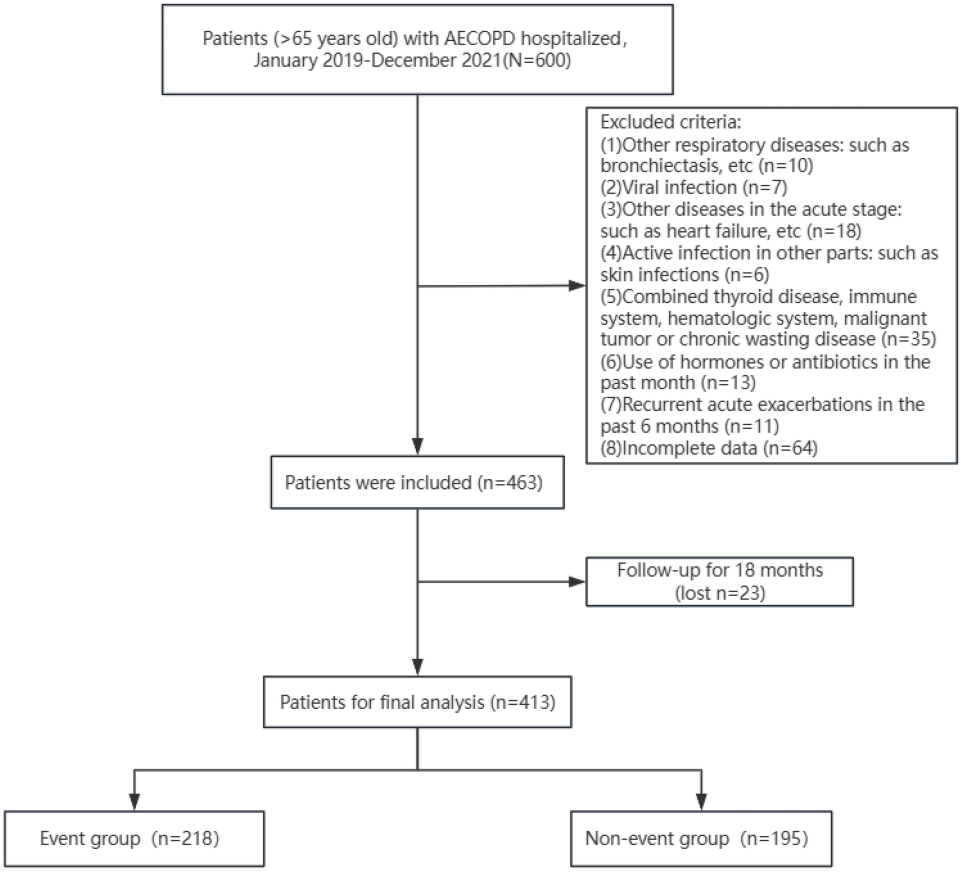

Figure 1 Flowchart of patients enrolled in the study.

history of hypertension combined with history of diabetes were subgroup analyzed. The area under the ROC curve (AUC) was used to compare the predictive value of the combination of IL-6 and $CD4^+/CD8^+$ for adverse clinical outcomes.

Results

Clinical Characteristics

Table 1 details the baseline characteristics of the study cohort. A total of 413 elderly patients with AECOPD were included in this retrospective study, and 218 adverse outcome events occurred during the follow-up (event group), including 180 readmissions and 38 deaths due to AECOPD. There were no adverse outcome events in 195 cases (non-event group). The average age of the 413 patients was 77 years (69–85 years), of which 329 (79.7%) were male, 84 (20.3%) were female, and 198 (47.9%) had a history of smoking. 222 (53.8%) patients had hypertension, 102 (24.7%) patients had coronary atherosclerotic heart disease, 73 (17.7%) patients had type 2 diabetes mellitus, and 30 (7.3%) patients had a personal history of cerebral infarction.

The IL-6 level in the event group was higher than that in the non-event group, the difference was statistically significant (9.95pgmL vs 2.97pg/mL, $p<0.001$), and the average IL-6 level in the event group was higher than the normal value. The $CD4^+/CD8^+$ level in the event group was lower than that in the non-event group (1.2 vs 1.6, $p<0.001$), as shown in Table 1.

Cox Regression Analysis of IL-6 or $CD4^+/CD8^+$ with Adverse Outcomes in Elderly Patients with AECOPD

The univariable and multivariable adjusted associations between IL-6 or $CD4^+/CD8^+$ and adverse outcomes are presented in Table 2. As the quartiles of IL-6 and $CD4^+/CD8^+$ increased, both the incidences of adverse outcomes in patients increased. After adjustment for potential confounders, patients in the highest quartile of IL-6 showed higher risk (Q4 HR: 3.488, 95% CI:

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Table 1 Baseline Characteristics of Patients with or Without Event

	Total (n=413)	Event Group (n=218)	Non-Event Group (n=195)	P Value
General characteristics				
Age, years	77(69–85)	79(71–86)	76(68–83)	0.001
Male, %	329(79.7%)	184(84.4%)	145(74.4%)	0.011
Course of diseases (<10 years)	142(34.4%)	57(26.1%)	85(43.6%)	<0.001
≥10 years	241(58.4%)	134(61.5%)	107(54.9%)	
NA	30(7.2%)	27(12.4%)	3(1.5%)	
Smoking history, %	198(47.9%)	109(55.1%)	89(44.9%)	0.277
SBP (mmHg)	130(120–140)	130(120–140)	130(120–140)	0.647
DBP (mmHg)	75(70–80)	73(68–80)	78(70–80)	0.018
Comorbidities				
Hypertension, n (%)	222(53.8%)	116(53.2%)	106(54.4%)	0.815
Coronary heart disease, n (%)	102(24.7%)	59(27.1%)	43(22.1%)	0.238
Diabetes, n (%)	73(17.7%)	40(18.3%)	33(16.9%)	0.705
Stroke, n (%)	30(7.3%)	16(7.3%)	14(7.2%)	0.950
Laboratory results				
White blood cell (10^9/L)	7.65(5.96–10.7)	7.74(6.15–11.12)	7.57(5.51–10.19)	0.110
Neutrophils (10^9/L)	5.83(4.08–8.72)	6.14(4.49–9.28)	5.58(3.78–8.34)	0.055
Lymphocytes (10^9/L)	0.97(0.64–1.38)	0.87(0.60–1.32)	1.05(0.75–1.50)	0.013
Eosinophils (10^9/L)	0.01(0.00–0.13)	0.01(0.00–0.12)	0.02(0.00–0.14)	0.956
Platelet (10^9/L)	180 (142–222)	190(144–249)	213(169–264)	0.010
IL-6 (pg/mL)	4.74(1.50–16.53)	9.95(2.24–28.19)	2.97(1.50–6.28)	<0.001
PCT (ng/mL)	0.05(0.03–0.13)	0.07(0.04–0.34)	0.04(0.02–0.08)	<0.001
CRP (mg/L)	8.00(1.00–39.50)	16.00 (2.00–51.25)	5.00(1.00–25.00)	<0.001
$CD4^+/CD8^+$	1.40(0.90–2.10)	1.20(0.70–1.80)	1.60(1.10–2.20)	<0.001
T3 (nmol/L)	1.12(0.88–1.40)	1.06(0.82–1.28)	1.18(0.94–1.44)	0.004
T4 (nmol/L)	91.28(77.23–103.35)	88.78(72.13–101.25)	93.4(81.71–104.6)	0.001
TSH (mIU /L)	0.84(0.42–1.64)	0.97(0.45–1.67)	0.69(0.41–1.62)	0.150
Albumin (g/L)	38(34–41)	36(32–40)	39(36–42)	<0.001
D-dimer (mg/L)	0.60(0.33–1.29)	0.77(0.37–1.93)	0.47(0.27–0.93)	<0.001
Fibrinogen (g/L)	3.50(2.70–4.75)	3.70(2.70–4.90)	3.40(2.60–4.60)	0.095
PH	7.38(7.36–7.43)	7.36(7.33–7.41)	7.41(7.37–7.43)	0.121
SaO2 (%)	95.9(93.7–97.5)	94.7(92.3–97.5)	96.0(94.3–97.80)	0.074

Notes: Data was presented as mean ± SD, median (25th, 75th percentiles), or percentage.
Abbreviations: SBP, systolic blood pressure; DBP, Diastolic blood pressure; CRP, C-reactive protein; PCT, Procalcitonin; T3, triiodothyronine; T4, thyroxine; TSH, thyroid stimulating hormone.

2.221–5.479, p<0.001) compared with those in the lowest quartile of IL-6, patients in the highest quartile of $CD4^+/CD8^+$ showed lower risk of adverse outcomes (Q4 HR: 0.407, 95% CI: 0.273–0.605, p<0.001) compared with those in the lowest quartile of $CD4^+/CD8^+$. Similar results were also observed in Kaplan–Meier survival curves analysis and sensitivity analysis (Figure 2). Furthermore, we observed a dose–response relationship of IL-6 or $CD4^+/CD8^+$ with the risk of adverse outcomes (P for trend p<0.001), which was further supported by the restricted cubic spline regression analysis (Figure 3).

Dose–Response Relationship of IL-6 and $CD4^+/CD8^+$ with Adverse Outcomes

IL-6 and $CD4^+/CD8^+$ were analysed as continuous variables in the limiting cubic spline plot to explore their relationship with adverse outcomes (Figure 3). There was a nonlinear correlation between IL-6 levels (P for non-linear<0.05) or $CD4^+/CD8^+$ (P for non-linear<0.05) and adverse outcomes across the cohort. When IL-6≥8pg/mL, IL-6 had a monotonically increasing relationship with poor prognosis in elderly patients with AECOPD (Figure 3A). When $CD4^+/CD8^+ \leq 1.4$, $CD4^+/CD8^+$ was linearly negatively correlated with poor prognosis in elderly patients with AECOPD (Figure 3B).

Table 2 Cox Regression of IL-6, $CD4^+/CD8^+$ Quartiles with Adverse Events

		Univariate Cox Regression (Model 1)		Multivariate Cox Regression (Model 2)	
	n (%)	HR (95% CI)	P Value	HR (95% CI)	P Value
IL-6					
Q1(<1.5)	68(16.46)	Reference (1.0)		Reference (1.0)	
Q2(1.5–4.74)	139(33.66)	1.077(0.668–1.736)	0.761	0.981(0.556–1.517)	0.739
Q3(4.74–16.27)	103(24.94)	2.337(1.611–3.392)	<0.001	2.765(1.841–4.153)	<0.001
Q4(≥16.27)	103(24.94)	3.485(2.428–5.001)	<0.001	3.488(2.221–5.479)	<0.001
p for trend			<0.001		<0.001
$CD4^+/CD8^+$					
Q1(<0.9)	96(23.24)	Reference (1.0)		Reference (1.0)	
Q2(0.9–1.4)	110(26.63)	0.496(0.349–0.704)	<0.001	0.458(0.318–0.661)	<0.001
Q3(1.4–2.1)	100(24.21)	0.465(0.324–0.667)	<0.001	0.419(0.288–0.609)	<0.001
Q4(≥2.1)	107(25.91)	0.393(0.268–0.578)	<0.001	0.407(0.273–0.605)	<0.001
p for trend			<0.001		<0.001

Notes: Multivariate Cox regression analysis (Model 2) was adjusted for positive variables in the univariate Cox model (Model 1), including age, sex, Diastolic blood pressure, Platelet, PCT, CRP, T3, T4, D-dimer.
Abbreviations: PCT, procalcitonin; CRP, C-reactive protein; T3, triiodothyronine; T4, thyroxine.

Subgroup Analysis

Results of stratified analysis suggested that the association between the IL-6 or $CD4^+/CD8^+$ and adverse outcomes was stable in various stratifications, which were divided by the covariates such as sex, course of disease, smoking, cerebral infarction (presence or no), diabetes mellitus (presence or no), coronary heart disease (presence or no), and history of hypertension (presence or no) (Figure 4 and 5). The results of subgroup analysis showed that in the gender, course of disease, smoking, diabetes, coronary heart disease, and hypertension groups, patients in the high IL-6 group (IL-6≥8pg/mL) were at higher risk of adverse outcomes than those in the low IL-6 group (IL-6<8pg/mL) ($p<0.05$), but there was no interaction between the groups ($p>0.05$). Similarly, in the gender, course of disease, smoking, and hypertension groups, patients in the low $CD4^+/CD8^+$ group ($CD4^+/CD8^+<1.4$) were at higher risk of adverse outcomes than those in the high $CD4^+/CD8^+$ group ($CD4^+/CD8^+\geq1.4$) ($p<0.05$), and there was no interaction between the groups ($p>0.05$).

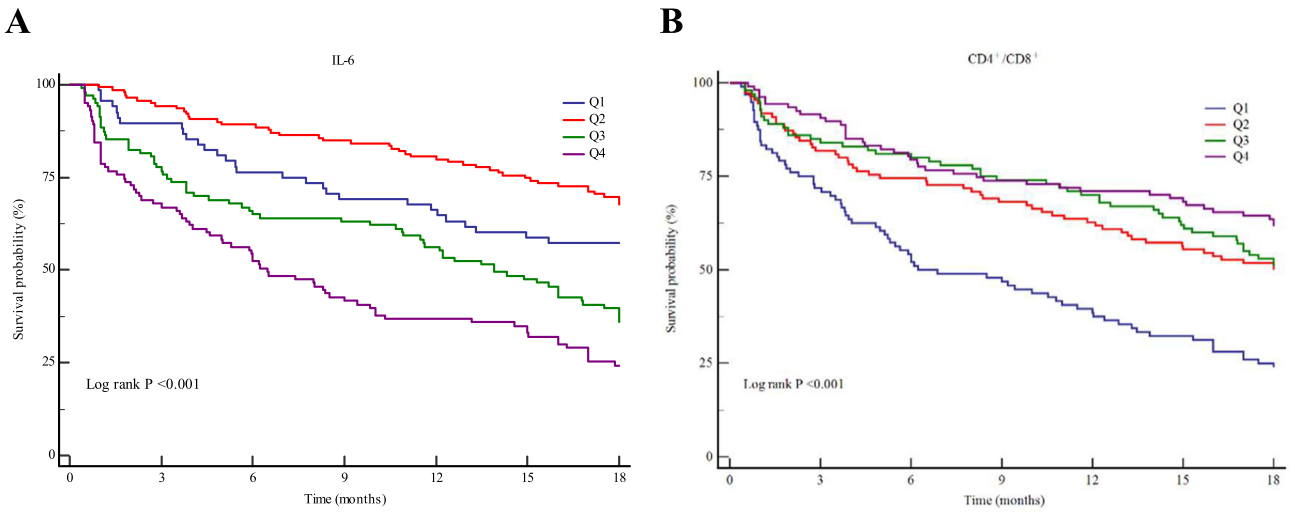

Figure 2 Survival curves of AECOPD patients at 18-month follow-up. (**A**) grouped by quartiles of IL-6; (**B**) grouped by quartiles of $CD4^+/CD8^+$.

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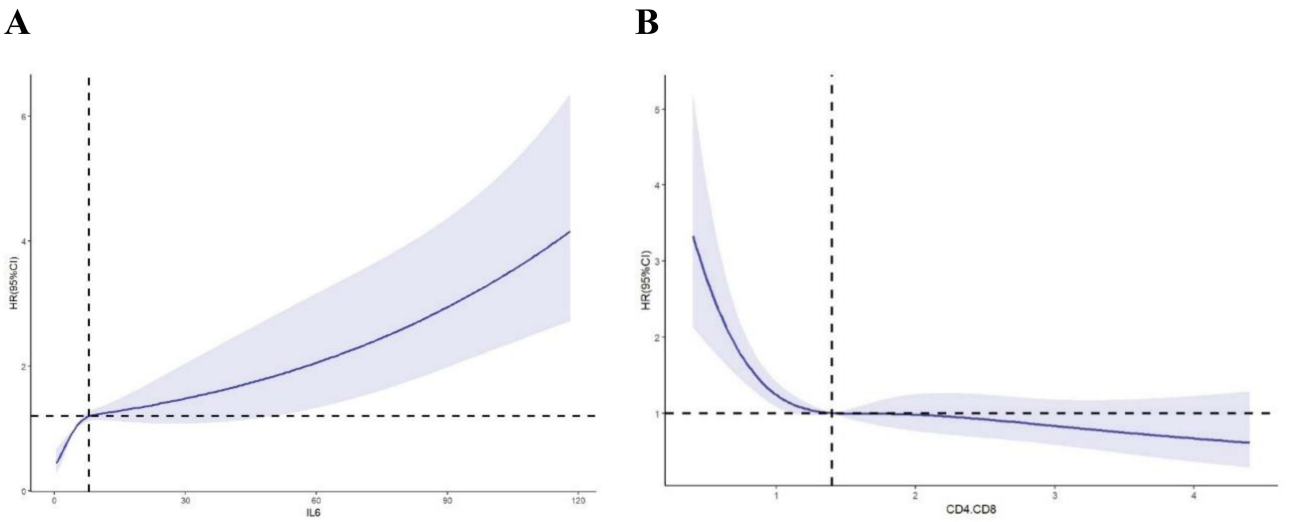

Figure 3 Dose–response relationship between IL-6 or $CD4^+/CD8^+$ and adverse events in elderly patients with AECOPD from RCS analysis. IL-6 and adverse events (**A**); $CD4^+/CD8^+$ and adverse events (**B**).

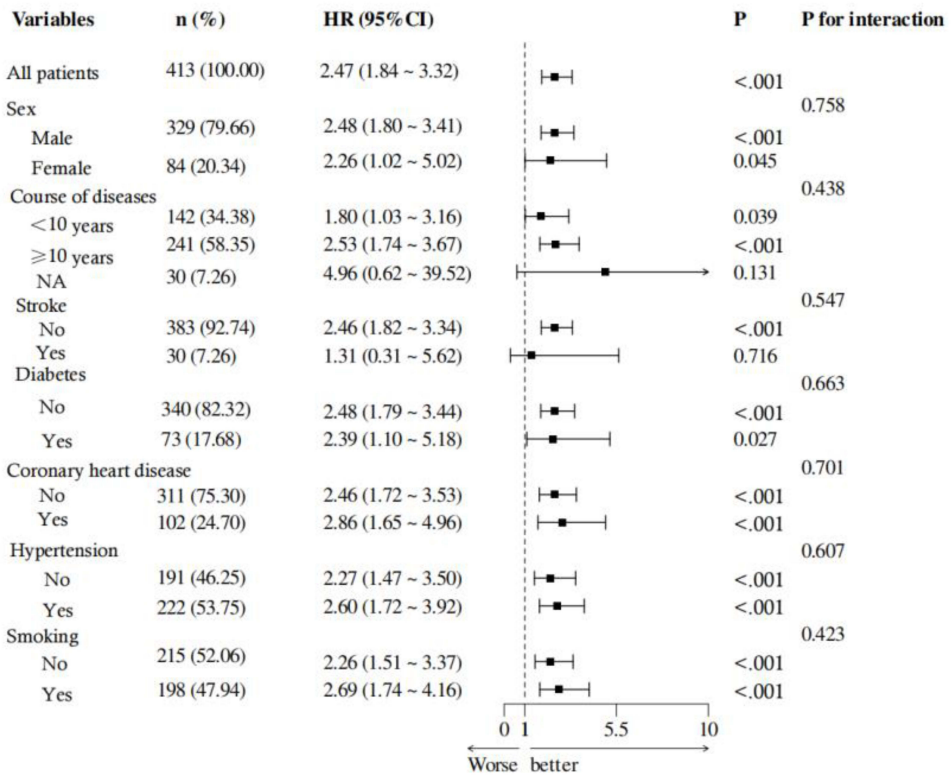

Figure 4 Hazard ratios of the IL-6 for predicting adverse events in the subgroup analysis.

Incremental Predictive Performance of IL-6 and CD4+/CD8+ in the Adverse Outcomes of Elderly Patients with AECOPD

In the analysis of elderly patients, the ROC curves were constructed to assess the predictive power of the basic model (sex, smoking, course of disease, D-dimer, C-reactive protein, procalcitonin, T3, T4), and the basic model plus IL-6, $CD4^+/CD8^+$, or a combination of both, respectively (Figure 6, Table 3). The results showed that the addition of IL-6 or

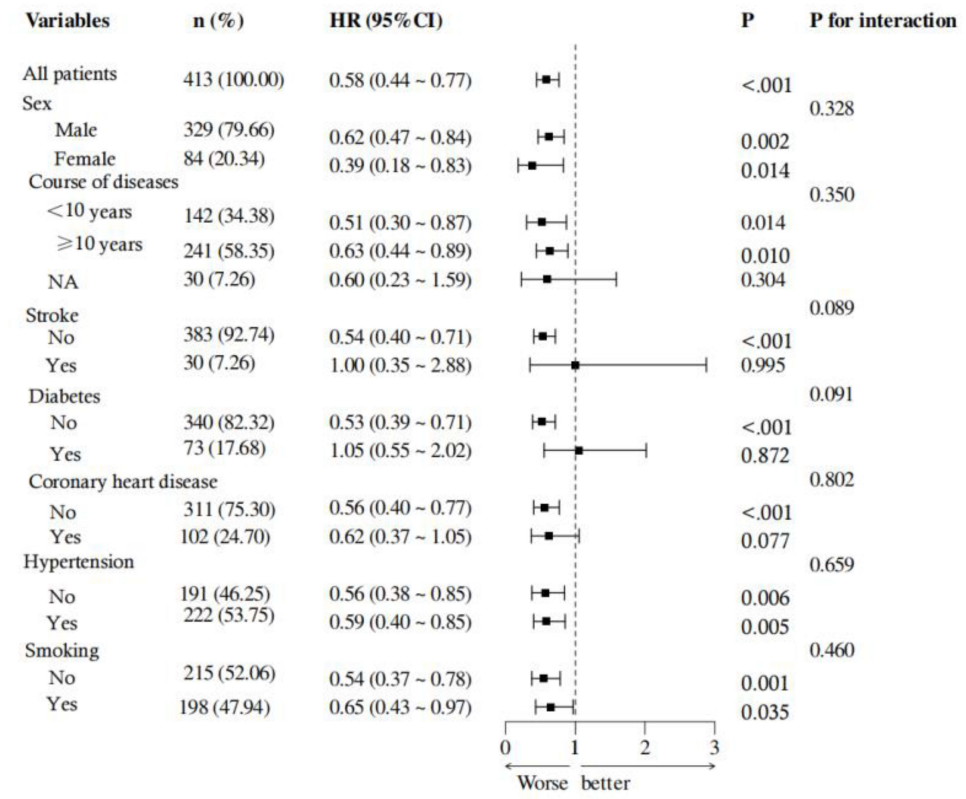

Figure 5 Hazard ratios of the $CD4^+/CD8^+$ for predicting adverse events in the subgroup analysis.

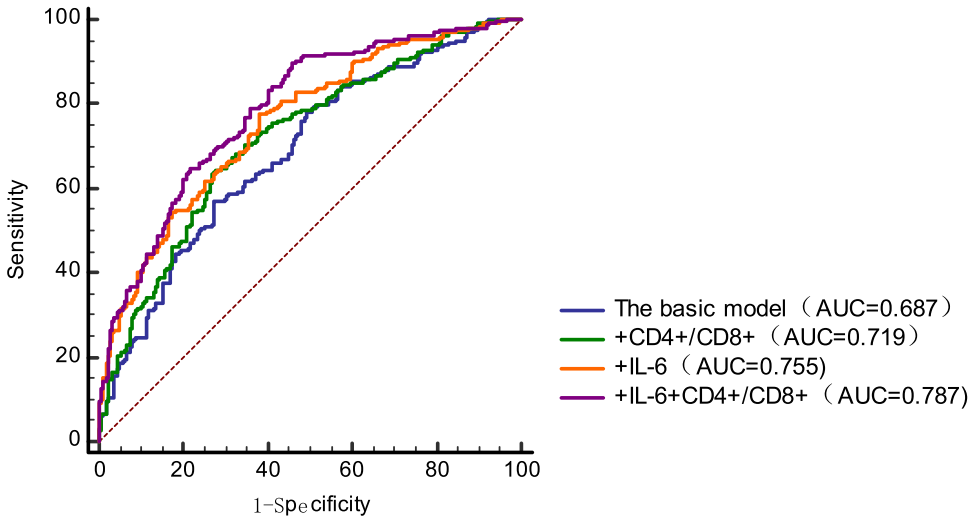

Figure 6 ROC curves for the prediction of adverse events. The basic model vs +the IL-6+ $CD4^+/CD8^+$ in the elderly patients.

$CD4^+/CD8^+$ alone to the basic model increased its predictability ($p<0.001$), while the addition of both significantly increased the predictive value, with the AUC value increasing from 0.687 to 0.787 ($p<0.001$) and the incremental change value being 10% ($p<0.001$).

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Table 3 Improvement in Discrimination for Adverse Events After Adding IL-6, $CD4^+/CD8^+$ in Elderly Patients

	AUC (95% CI)	P	ΔChanges	P
The basic model	0.687(0.640–0.732)	<0.001		Reference
+$CD4^+/CD8^+$	0.719(0.673–0.762)	<0.001	0.032	0.024
+IL-6	0.755(0.710–0.796)	<0.001	0.068	0.001
+IL-6+$CD4^+/CD8^+$	0.787(0.744–0.825)	<0.001	0.1	<0.001

Notes: The basic model includes sex, smoking, course of disease, PCT, CRP, T3, T4 and D-dimer.

Abbreviations: PCT, procalcitonin; CRP, C-reactive protein; T3, triiodothyronine; T4, thyroxine.

Discussion

In the elderly population, the immune response is easily activated uncontrollably, resulting in the release of large amounts of cytokines and tissue damage, but the inability to trigger an effective adaptive immune response may lead to uncontrollable disease and potential clinical consequences.[18] Therefore, the search for effective predictors is essential for early clinical management. In this study, 413 elderly patients with AECOPD were retrospectively studied to explore the association between IL-6 or $CD4^+/CD8^+$ and the prognosis of elderly patients with AECOPD. We found that, even after adjusting for potential confounders, higher IL-6 levels and lower $CD4^+/CD8^+$ were significantly associated with poor outcomes with a significant dose–response relationship, and subgroup analysis further confirmed the robustness of the association. In addition, it was found that IL-6 combined with $CD4^+/CD8^+$ significantly improved the predictive power of the underlying model.

Previous studies have shown that IL-6 responds rapidly and rapidly activates the airway inflammatory response during an acute exacerbation of COPD, which is associated with the severity of COPD and has important value in predicting the mortality of patients.[19,20] This study also confirmed this conclusion, even after adjusting for multiple confounders, elevated IL-6 levels significantly increased the risk of adverse outcomes in patients, with patients in the high IL-6 group (Q3, Q4) having significantly shorter survival times than those in the low IL-6 group (Q1).

Building on this, we focused on analyzing the dose–response relationship between the two variables and found that when IL-6 levels are ≥8pg/mL, the risk of adverse outcomes in patients increases with rising IL-6 levels. Our results exceed the normal range (0–5.4pg/mL), but research by Hui Huang et al indicated that IL-6 levels ≥14.03pg/mL are a risk factor for experiencing ≥2 acute exacerbations of COPD in the following year.[9] Differences in results may be due to different suppliers of instruments or reagents that measure IL-6 concentrations, or different sample sizes. In addition, this study also found that the prognostic value of IL-6 alone in assessing patients was not obvious, and the AUC value of the improved base model in this study was only 0.068, which may be due to the fact that IL-6 was involved in the acute phase response to COPD exacerbations, which helped to identify potential acute exacerbations early but was not associated with persistent COPD exacerbations.[21] This implies that IL-6 is associated with prognosis in elderly AECOPD patients, but its predictive effect is poor.

In addition, we also found that $CD4^+/CD8^+$ affects the prognosis of elderly patients with AECOPD. Patients with a poor prognosis had lower $CD4^+/CD8^+$ level than those with a good prognosis. After adjusting for confounding factors, low $CD4^+/CD8^+$ level was still a risk factor for adverse outcomes. The survival time of low $CD4^+/CD8^+$ group (Q3, Q4) was significantly lower than that of high-level group (Q1, Q2). This may be because the airway or alveoli of low $CD4^+/CD8^+$ individuals are more sensitive to smoke stimulation, and the body is more prone to persistent airflow restriction,[22,23] which affects disease severity and increases mortality risk in COPD patients.[24–26] In this study, it was further observed that $CD4^+/CD8^+$ was nonlinearly associated with adverse outcomes, and when $CD4^+/CD8^+ \leq 1.4$, the risk of readmission or death increased linearly with the decrease of $CD4^+/CD8^+$ level. The median $CD4^+/CD8^+$ in our study was 1.4, which is similar to the median $CD4^+/CD8^+$ of 1.5 in AECOPD patients in a cross-sectional study of 1483 patients reviewed by Xiufang Hong et al.[27] Therefore, $CD4^+/CD8^+$ has a certain value in predicting the prognosis of elderly AECOPD patients. However, this study found that the AUC value of adding $CD4^+/CD8^+$ to the basic model to assess patient prognosis was only 0.719, which has poor potential as a clinical predictor for patients with AECOPD alone.

Considering the limited prognostic value of patients assessed by IL-6 or $CD4^+/CD8^+$ alone, the combination of both in this study was added to the base model and found that the predictive value of the prognosis in elderly patients was significantly improved (AUC: 0.787 vs 0.687). A systematic review assessing the prognosis of AECOPD showed AUC values ranging from 0.58 to 0.81 in 27 studies.[28] Although the present study falls within this range, variations in AUC values may be attributed to differences in the definitions of outcome events, time frames, statistical methods, and predictive factors. The combination of IL-6 and $CD4^+/CD8^+$ can effectively predict the prognosis of elderly patients with AECOPD, which is related to the interplay and mutual enhancement between inflammatory cell infiltration and immune dysregulation.[29] Elderly patients with AECOPD can have a large number of rapid activation of IL-6, which can aggravate the progression of the disease, and at the same time, some individuals with low $CD4^+/CD8^+$ cannot make the corresponding immune response, which will lead to the deterioration of the disease. IL-6, as a multifunctional cytokine, can regulate the occurrence and progression of immune-related responses by affecting $CD4^+$ T lymphocytes,[30] and also induce $CD8^+$ T lymphocytes to differentiate into cytotoxic T lymphocytes, participating in the body's elimination of pathogens.[31] Therefore, systemic inflammation and immune response are the main factors affecting the prognosis and quality of life in patients with AECOPD.[32] Building on the identification and validation of prognostic markers for AECOPD, this study explores the association between IL-6 or $CD4^+/CD8^+$, and prognosis in elderly patients with AECOPD from the perspectives of immune regulation and inflammatory response. We found that the combination of IL-6 and $CD4^+/CD8^+$ significantly enhances the ability to assess prognosis in elderly AECOPD patients.

This study has the following limitations: 1. this study is a retrospective study, and some data are missing; 2. The subjects of this study are all from one center, and the sample size is limited; 3. The normal range of IL-6 and $CD4^+/CD8^+$ values of patients varies from region to region and from hospital to hospital, and the detected data is affected by a variety of factors, so it is necessary to be cautious when interpreting them.

Conclusion

IL-6 or $CD4^+/CD8^+$ exhibits a nonlinear correlation with adverse outcomes in elderly patients with AECOPD, and the combination of both can significantly improve the predictive value of adverse events.

Data Sharing Statement

The dataset used in the present study is not currently publicly available but is available from the corresponding author (Juan Xie) upon reasonable request.

Ethics Statement

This study was designed in accordance with the Declaration of Helsinki and approved by the ethics committee of the Shanghai Fifth People's Hospital, Fudan University (NO.2024-198). Due to the study being a retrospective non-interventional design, the review committee waived the requirement for written informed consent. All patient data was maintained with confidentiality.

Consent for Publication

All authors accept and confirm publication.

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Disclosure

The authors declare no conflicts of interest related to this study.

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