Article

Discovery Medicine 2023; 35(178): 815–822
https://doi.org/10.24976/Discov.Med.202335178.76

Associating Serum IgM, IgA Levels with Thoracic CT Indicators and Pulmonary Function Indexes in Acutely Exacerbated Chronic Obstructive Pulmonary Disease Patients

Mengmeng Ji[1], Yong Li[1], Xiaolong Zhu[1], Dianjun Zou[1], Fei Yang[1], Hequn Geng[1], Shujun Cui[1,*]

[1]Medical Imaging Department, The First Affiliated Hospital of Hebei North University, 075000 Zhangjiakou, Hebei, China
*Correspondence: 15612305152@163.com (Shujun Cui)
Published: 1 October 2023

Background: Chronic Obstructive Pulmonary Disease (COPD) is a respiratory condition characterized by acute exacerbations and reduced lung function. This study investigates the link between serum markers (Immunoglobulin M (IgM) and Immunoglobulin A (IgA)), thoracic computed tomography (CT) scan findings, and pulmonary function indexes during these episodes, aiming to improve our understanding and identify new diagnostic indicators.

Methods: From the First Affiliated Hospital of Hebei North University, we selected 89 COPD patients experiencing acute exacerbation within the past two years for our Acute Exacerbation Group (AG). Meanwhile, 96 COPD patients, initially treated at the same hospital and currently deemed stable, were chosen for the Stable Group (SG). Both groups underwent serum IgM and IgA tests, thoracic CT examinations, and pulmonary function assessments.

Results: In the AG Group, the serum IgM levels were marginally lower than in the Stable Group (SG), though the difference wasn't statistically significant ($p = 0.097$). Conversely, serum IgA levels in the AG were significantly lower than in the SG ($p < 0.001$). The AG also showed markedly reduced lung volume, inspiratory lung density, and pulmonary function indexes compared to the SG while having considerably higher values for emphysema index (EI) and air trapping index (ATI) (all $p < 0.001$). Pearson correlation analysis revealed that lung volume, average inspiratory lung density, and IgA levels had strong positive correlations with one-second forced expiratory volume (FEV1), FEV1/forced vital capacity (FVC), and diffuse carbon monoxide (DLCO) (with respective r-values of 0.824, 0.841, and 0.829; all $p < 0.001$). In contrast, EI and ATI exhibited significantly negative correlations with FEV1, FEV1/FVC, and DLCO (with r-values ranging from –0.837 to –0.885; all $p < 0.001$).

Conclusions: The assessment of serum IgA combined with thoracic CT parameters offers valuable insights for diagnosing and evaluating acute exacerbations of COPD, presenting a straightforward clinical utility.

Keywords: Chronic Obstructive Pulmonary Disease; CT parameters; immunoglobulin; pulmonary function

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a respiratory condition where airway inflammation arises primarily from inhaling toxic agents. This inflammation leads to restricted airflow [1,2]. Clinically, COPD is marked by consistent pulmonary inflammation and only partial reversibility. The disease doesn't just adversely affect the lungs; it can also cause harm to extrapulmonary tissues, which may lead to immune dysfunction. Such complications often result in recurrent infections in patients [3], escalating the severity of the condition and posing serious risks to their well-being.

While pulmonary function indexes are widely recognized as critical indicators to gauge the progression of COPD, they have their limitations. Changes in physiological functions impact these indexes and often suffer from inconsistency and significant influence from subjective factors [4]. Prior studies [5,6] have identified infections as a primary trigger for acute exacerbations in COPD, suggesting that an underlying abnormal immune function may be responsible for the recurrent infections in these patients. Consequently, the levels of certain immunoglobulins, such as Immunoglobulin M (IgM) and Immunoglobulin A (IgA), undergo corresponding shifts in their expression. The observation of the above indicators is expected to clarify the relationship between immune indicators and pulmonary function indexes. The advancements in medical imaging, particularly thoracic computed tomography (CT) scans, provide valuable insights into the morphological transformations occurring within the lungs [7]. However, the potential correlation between these CT scan parameters and pulmonary function indexes remains an area awaiting deeper exploration and validation.

Given this backdrop, our study aims to elucidate the interplay between serum IgM, IgA levels, thoracic CT parameters, and pulmonary function indexes. Our findings aspire to enhance clinical diagnostic procedures and refine evaluations of COPD during acute exacerbations.

Materials and Methods

Clinical Data

We conducted a retrospective analysis of 89 COPD patients who had experienced acute exacerbations and were admitted to the First Affiliated Hospital of Hebei North University within the last two years. Based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification, the breakdown was as follows: 12 patients were categorized as moderate (GOLD-2), 59 as severe (GOLD-3), and 18 as extremely severe (GOLD-4). For comparison, we also studied 96 COPD patients from the same hospital who, after initial treatment, transitioned to and currently maintain a stable phase—designated as the Stable Group (SG).

All group participants underwent tests to detect serum IgM and IgA levels, X-ray/thoracic CT examinations, and assessments of pulmonary function indexes (PFT). These tests were closely spaced, ensuring a maximum 2-day gap between examinations. The acute exacerbation diagnosis for patients was firmly established using the PFT, adhering to the stringent diagnostic criteria for COPD diagnosis, treatment, and management [8]. Specifically, the acute exacerbation diagnosis was defined by an acute surge in respiratory symptoms, a short-term rise in purulent or mucinous sputum volume, intensified wheezing, fever, and other systemic manifestations [9]. This study conforming to the principle of the Declaration of Helsinki (2013) [10] has been approved by the ethical committee of the First Affiliated Hospital of Hebei North University (approval No.: 202103005), and the procedural flow is illustrated in Fig. 1.

Inclusion and Exclusion Criteria

Participants were included in the study if they were aged over 18, could tolerate pulmonary function examinations, and if both they and their families had given informed consent with a clear understanding of the study's objectives. However, patients were excluded if they had diseases of the blood or immune system, cardiac abnormalities, infectious or malignant diseases, mental confusion or psychiatric disorders, or abnormalities in the liver or kidneys.

Methods

Detection of Immune Indexes

Fasting venous blood (10 mL) was taken from all subjects to detect serum levels of IgM and IgA. The Beckman automatic biochemical analyzer (manufacturer: Beckman Coulter Commercial Enterprise (China) Co., Ltd.; model: AU5831; origin: Shanghai, China) was adopted. Beckman Coulter Commercial Enterprise (China) Co., Ltd. provided detection kits of serum IgM and IgA. The serum levels of IgM and IgA were determined by immunoturbidimetry, and the operations were strictly per the instructions of kits provided by Wuhan Enfei Biotechnology Co., Ltd. (Wuhan, China).

Thoracic CT Detection

Thoracic scanning was performed on all patients through a lung scanner (manufacturer: Japan Canon Corporation; location: Tokyo, Japan; model: Aquilion one 320-row volume CT scanner), with scanning settings including collimation as 64 mm $\times$ 0.5 mm, tube voltage as 120 kVp, tube current as automatic milliampere, rotation time as 0.5 s, and beam spacing as 0.828. The patients put their arms on their heads in a supine position, and the scanning direction was from head to foot. The detection parameters included lung volume, average inspiratory lung density, pulmonary emphysema index (EI), and CT air trapping index (ATI), and all images were analyzed by CT pulmonary image analysis software (the CT image analysis software of lung, version: NeuLungCARE-QA, Neusoft Medical Systems Co., Ltd., Shenyang, China).

Detection of Pulmonary Function Indexes

Using the MasterScreen model from Jaeger (produced by CareFusion Germany 234 GmbH, Würzburg, Germany), a skilled technician accurately assessed patients' pulmonary functions. Before testing, GlaxoSmithKline Group gave each patient a bronchodilator, specifically salbutamol. After allowing a 15-minute resting interval, the technician conducted three successive measurements to ascertain the peak respiratory value. The range between these tests' maximum and minimum values had to stay within a 5% threshold or be less than 100 mL. The evaluation mainly centered on documenting key metrics like the one-second forced expiratory volume (FEV1), its proportion to the total lung capacity (FEV1/forced vital capacity (FVC)), and the ability to diffuse carbon monoxide (DLCO).

Statistical Analysis

The data processing software selected in this study was SPSS 26.0 (IBM corporation, Armonk, NY, USA) for statistical analysis. Prism 8.0 software (GraphPad Software, San Diego, CA, USA) was used to plot the pictures. The measurement data were tested by t-test, indicated by ($\bar{x} \pm s$), and enumeration data were tested by χ^2 test, expressed as (n, %). Pearson was used for correlation analysis. $p < 0.05$ was considered statistically significant.

Results

Clinical Data

Table 1 showed no statistical significance in gender, body mass index (BMI), course of disease, age, and other clinical data between the two groups ($p > 0.05$).

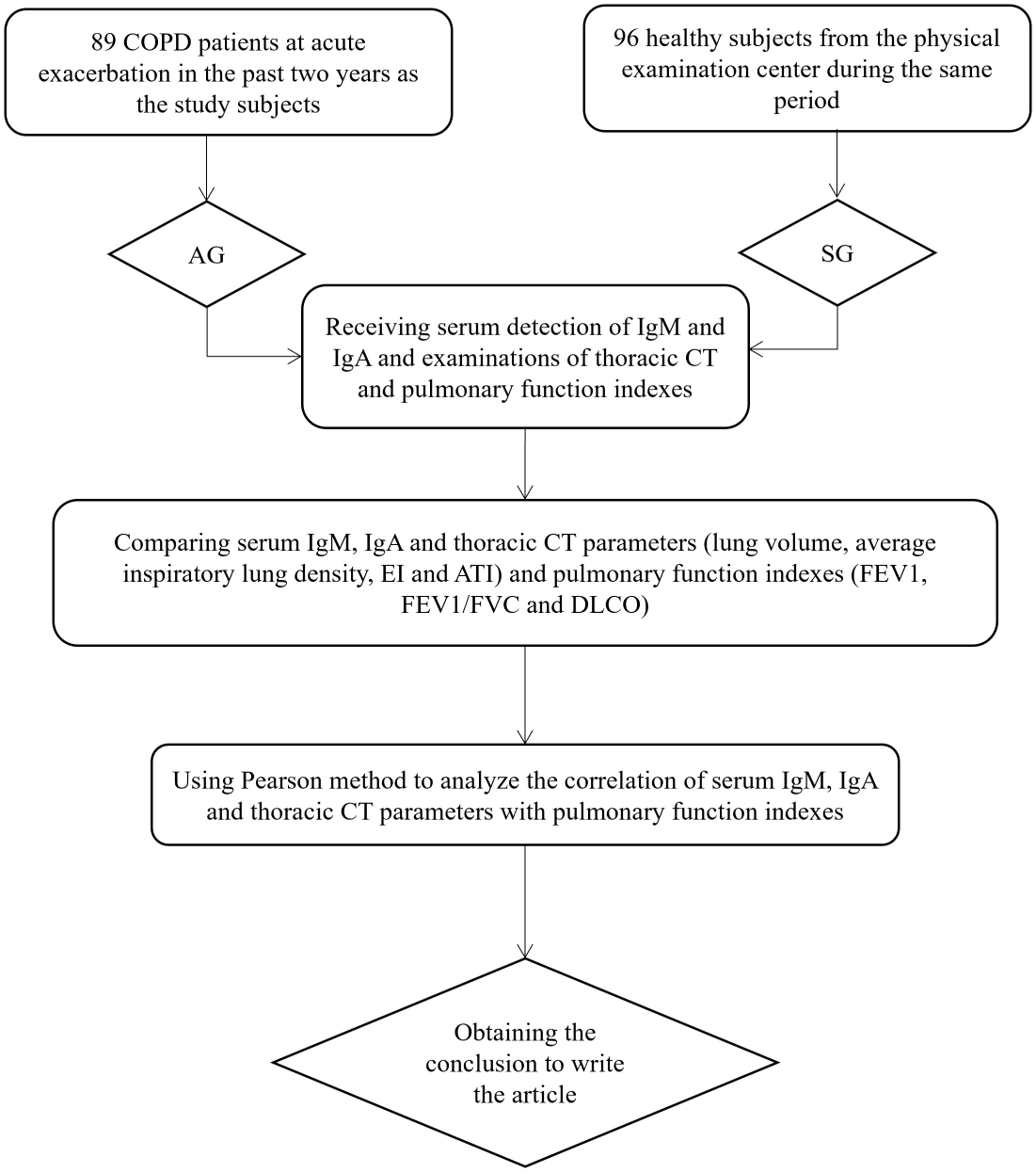

Fig. 1. Technical route. COPD, Chronic Obstructive Pulmonary Disease; AG, Acute Exacerbation Group; SG, Stable Group; IgM, Immunoglobulin M; IgA, Immunoglobulin A; CT, computed tomography; EI, emphysema index; ATI, air trapping index; FEV1, forced expiratory volume; FVC, forced vital capacity; DLCO, diffuse carbon monoxide. (Drawn with Microsoft Office Word, version 2019, Microsoft Corporation, Redmond, WA, USA.)

Comparison of Immune Indexes

In the Acute Exacerbation Group (AG), the serum IgM level was (1.28 ± 0.39) g/L, slightly lower than the SG's (1.38 ± 0.43) g/L. However, the difference was not statistically significant between the two groups (t = –1.671, p = 0.097). Conversely, the serum IgA level in the AG was measured at (1.44 ± 0.34) g/L, which was markedly lower than the SG's (2.62 ± 0.35) g/L. This difference was statistically significant (t = 23.214, $p < 0.001$) and is illustrated in Fig. 2.

Comparison of Thoracic CT Parameters and Pulmonary Function Indexes in AG and SG Groups

The AG exhibited considerably lower lung volume and average inspiratory lung density than the SG. Furthermore, the AG displayed higher EI and ATI values and significantly reduced pulmonary function indexes. The differences between the AG and SG groups were statistically significant ($p < 0.001$) and are elaborated upon in Table 2.

Table 1. Comparison of clinical data between AG and SG groups [($\bar{x} \pm s$), (n, %)].

Groups	AG (n = 89)	SG (n = 96)	t/χ^2	p
Gender			0.051	0.822
Male	57 (64.04)	63 (65.63)		
Female	32 (35.96)	33 (34.38)		
BMI ($\bar{x} \pm s$, kg/m^2)	21.77 ± 2.23	22.26 ± 2.54	–1.388	0.167
Age ($\bar{x} \pm s$, years)	58.09 ± 4.25	58.43 ± 4.41	0.528	0.598
Marital status			0.790	0.674
Unmarried	6 (6.74)	10 (10.42)		
Married	57 (64.04)	59 (61.46)		
Divorced	26 (29.21)	27 (28.13)		
Education level			0.112	0.945
Illiteracy	16 (17.98)	19 (19.79)		
Junior high school and primary school	49 (55.06)	51 (53.13)		
Senior high school and above	24 (26.97)	26 (27.08)		
Smoking history			0.021	0.885
Yes	51 (57.30)	54 (56.25)		
No	38 (42.70)	42 (43.75)		
Place of residence			0.018	0.894
Urban area	50 (56.18)	53 (55.21)		
Rural area	39 (43.82)	43 (44.79)		

BMI, body mass index.

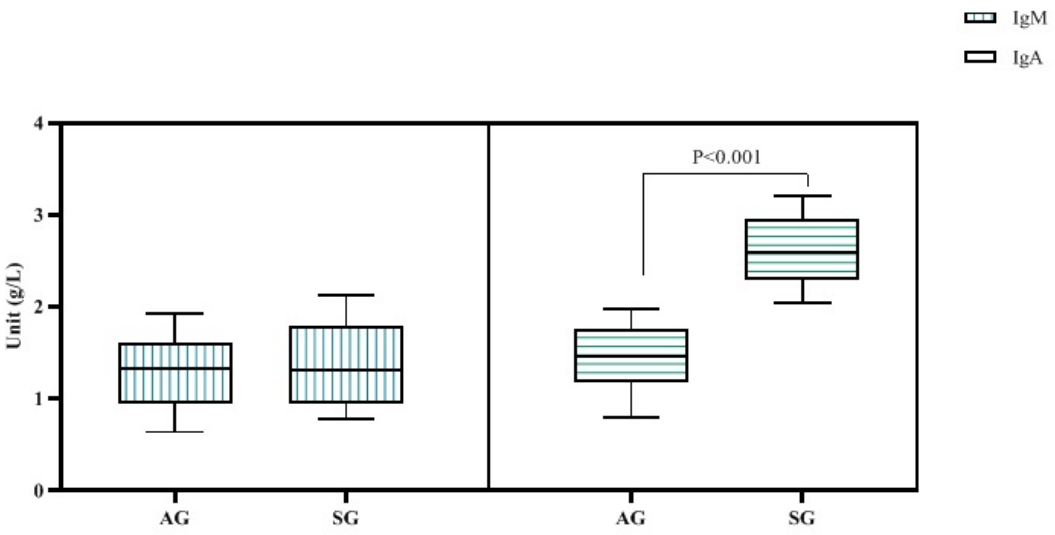

Fig. 2. Comparison of IgM and IgA indicators between the AG and SG.

Correlation Analysis of Immune Indexes, CT Parameters, and Pulmonary Function Indexes

Pearson correlation analysis denoted a significant positive association between lung volume, average inspiratory lung density, and IgA levels with FEV1, FEV1/FVC, and DLCO (r = 0.824, $p < 0.001$; r = 0.841, $p < 0.001$, r = 0.829, $p < 0.001$). In contrast, EI and ATI demonstrated a substantial negative correlation with FEV1, FEV1/FVC, and DLCO (r = –0.850, $p < 0.001$; r = –0.837, $p < 0.001$, r = –0.855, $p < 0.001$; r = –0.879, $p < 0.001$; r = –0.885, $p < 0.001$, r = –0.878, $p < 0.001$). These relationships are further detailed in Table 3 and illustrated in Fig. 3.

Discussion

A recent study has highlighted the pivotal role of immune dysfunction in causing recurrent infections among patients with COPD [11]. This dysfunction is instrumental in triggering the acute exacerbation of COPD. Patients with COPD, often characterized by limited airflow, experience irregular respiratory patterns and prolonged oxygen insufficiency. Such conditions contribute to the inadequate development of immune cells, leading to a steady decline in overall immunity [12]. While it's evident that viral infections suppress immune functions, the exact mechanisms

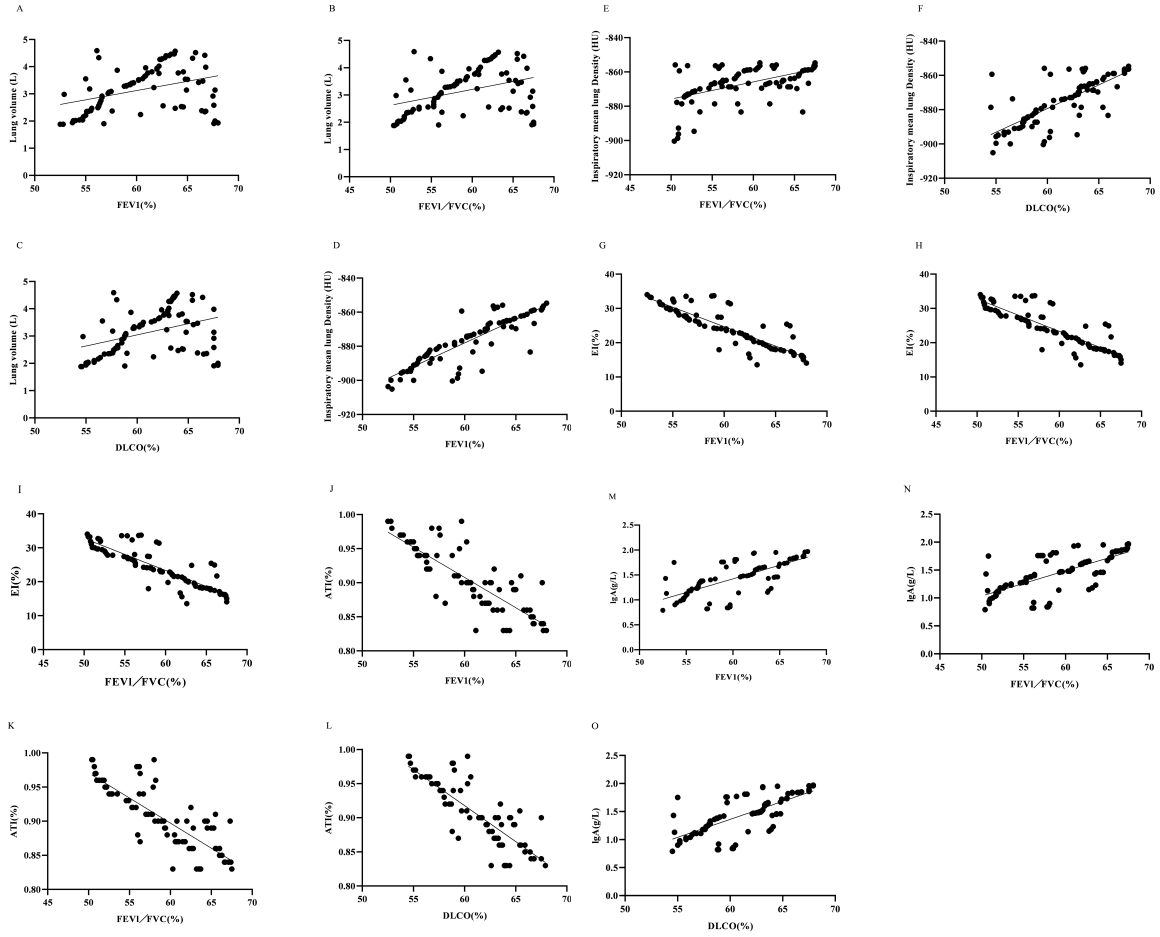

Fig. 3. Scatter plots depicting the correlation between lung volume, average inspiratory lung density, EI, ATI, IgA, and pulmonary function indexes (PFT) metrics in AG patients. (A–C) Scatter plots on correlation of lung volume with FEV1, FEV1/FVC and DLCO. (D–F) Scatter plots on correlation of average inspiratory lung density with FEV1, FEV1/FVC and DLCO. (G–I) Scatter plots on correlation between EI with FEV1, FEV1/FVC and DLCO. (J–L) Scatter plots on correlation of ATI with FEV1, FEV1/FVC and DLCO. (M–O) Scatter plots on correlation of IgA with FEV1, FEV1/FVC and DLCO.

remain ambiguous in clinical settings. Potential factors include immune cell damage, macrophage inhibition, and T-cell activation [13].

In an effort to delve deeper, this study assessed the immune functions of COPD patients during acute exacerbation phases. The results showed that the serum IgM levels were similar between the AG and SG groups ($p > 0.05$), but the serum IgA levels in the AG were notably lower than those in the SG ($p < 0.001$). An intriguing observation from the Pearson correlation analysis highlighted that IgA levels shared a positive relationship with FEV1, FEV1/FVC, and DLCO (r = 0.824, $p < 0.001$; r = 0.841, $p < 0.001$; r = 0.829, $p < 0.001$). Within the immune system, Secretory IgA plays a crucial role in defending the respiratory mucosa against infections.

Supporting this, research by Sneh Arora and colleagues [14] postulated that the levels of IgA in respiratory tract secretions (like sputum and bronchoalveolar lavage fluid) of COPD patients were noticeably diminished. This aligns with the current study's findings. The plausible explanation is the erratic and diminished humoral immune function seen in COPD patients during acute exacerbations. As the disease advances and lung function deteriorates, there's a consequent decline in serum-type IgA levels [15,16]. Interestingly, the disparity in IgM levels between both groups was not profound ($p > 0.05$). Given that the IgM antibody is the initial responder in the immune reaction, its concentration dwindles, or even vanishes, as the infection duration extends [17]. Hence, there is negligible variance in the IgM data between the groups.

CT scans are more straightforward and efficient than invasive tests like pathological tissue analysis and airway ultrasound. As advancements in CT imaging technology continue and with the widespread use of processing soft-

Table 2. Comparison of thoracic CT parameters and pulmonary function indexes in AG and SG groups ($\bar{x} \pm s$).

Groups	AG (n = 89)	SG (n = 96)	t	p
Lung volume ($\bar{x} \pm s$, L)	3.14 ± 0.82	5.45 ± 0.31	–25.716	<0.001
Average inspiratory lung density ($\bar{x} \pm s$, Hounsfield Unit (HU))	–877.14 ± 13.99	–785.62 ± 43.40	–18.997	<0.001
EI ($\bar{x} \pm s$, %)	24.31 ± 5.81	8.81 ± 1.03	25.747	<0.001
ATI ($\bar{x} \pm s$, %)	0.90 ± 0.05	0.57 ± 0.10	29.176	<0.001
FEV1 ($\bar{x} \pm s$, %)	60.32 ± 4.45	83.58 ± 1.28	–49.125	<0.001
FEV1/FVC ($\bar{x} \pm s$, %)	58.95 ± 5.35	86.49 ± 1.94	–47.212	<0.001
DLCO ($\bar{x} \pm s$, %)	61.22 ± 3.80	84.39 ± 1.97	–52.595	<0.001

Table 3. Correlation analysis of immune indexes, CT parameters, and pulmonary function indexes.

Indexes		FEV1	FEV1/FVC	DLCO
Lung volume	r-value	0.845**	0.861**	0.862**
	p-value	<0.001	<0.001	<0.001
Average inspiratory lung density	r-value	0.777**	0.786**	0.807**
	p-value	<0.001	<0.001	<0.001
EI	r-value	–0.850**	–0.837**	–0.855**
	p-value	<0.001	<0.001	<0.001
ATI	r-value	–0.879**	–0.885**	–0.878**
	p-value	<0.001	<0.001	<0.001
IgA	r-value	0.824**	0.841**	0.829**
	p-value	<0.001	<0.001	<0.001

Notes: ** indicates a significant correlation at 0.01.

ware, it's increasingly becoming a key method for detailed examination and analysis of lung abnormalities. Okuma Tomohisa *et al.* [18] have shown that some thoracic CT parameters are correlated with lung function in quantitative studies on CT and asthma, bronchial pneumonia, and so on. Therefore, this study selected COPD patients at acute exacerbation as the study subjects to analyze the relationship of lung volume, average inspiratory lung density, EI, and ATI with pulmonary function indexes. Pearson correlation analysis showed that the lung volume of patients was positively correlated with FEV1, FEV1/FVC, and DLCO (r = 0.845, $p < 0.001$; r = 0.861, $p < 0.001$; r = 0.862, $p < 0.001$), revealing a correlation between lung volume and impaired lung function in COPD patients during acute exacerbation phases, which was also one of the characteristics of COPD [19].

This research identified a pronounced positive correlation between the average inspiratory lung density and FEV1, FEV1/FVC, and DLCO (r = 0.777, $p < 0.001$; r = 0.786, $p < 0.001$; r = 0.807, $p < 0.001$). This aligns with the perspective of Staub Leonardo Jönck *et al.* [20], which suggests a strong association between FEV1/FVC and average lung density. CT imaging provides a vivid representation of the morphological features of a patient's bronchi and pulmonary vessels. By employing specialized image processing software to quantify lung density and lesion severity, we can gain precise insight into the extent of a patient's lung tissue and functional impairment [21,22].

Pearson correlation analysis underscored a notable negative correlation between EI and ATI with FEV1, FEV1/FVC, and DLCO (r = –0.850, $p < 0.001$; r = –0.837, $p < 0.001$; r = –0.855, $p < 0.001$; r = –0.879, $p < 0.001$; r = –0.885, $p < 0.001$; r = –0.878, $p < 0.001$). This implies that EI and ATI are potent indicators, objectively representing the extent of lung tissue damage in COPD patients during acute exacerbation phases. This observation parallels Zou Dianjun and Zhu Xiaolong's conclusion [23] that EI and ATI significantly correlate with reduced lung functionality in lung cancer patients. The underlying rationale is that during the rapid shifts experienced by COPD patients in acute exacerbations, bronchiolar tissue's elasticity decreases. Consequently, a considerable volume of gas remains trapped in the lungs post-expiration, leading to sustained alveolar distension, damage, or even rupture over time. As these compromised alveoli coalesce, emphysema formation [24,25] and pulmonary bullae culminate in irreversible damage to pulmonary function.

This study examined the relationship between immune markers and thoracic CT measurements with lung function in COPD patients during acute exacerbation. It revealed associations between serum IgA, lung volume, average inspiratory lung density, EI, and ATI with key pulmonary function indicators. Combining these immune markers with thoracic CT scans holds significant potential in diagnosing acute exacerbations of COPD. Such a combination can offer a data-driven foundation for precise clinical assessments and tailored medical treatments.

Conclusions

In summary, there's a stronger correlation between serum IgA and thoracic CT metrics (such as lung volume,

average inspiratory lung density, EI, and ATI) and pulmonary function indicators during acute COPD exacerbation. This aids in precisely assessing lung lesions in COPD patients during these flare-ups.

Availability of Data and Materials

Data to support the findings of this study are available on reasonable request from the corresponding author.

Author Contributions

MJ, YL and SC contributed to the concept and designed the research study. XZ and DZ performed the research. FY and HG provided help and advice on the experiments. MJ and SC contributed to the analysis and interpretation of the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

This study conforming to the principle of the Declaration of Helsinki (2013) has been approved by the ethical committee of the First Affiliated Hospital of Hebei North University (approval No.: 202103005).

Acknowledgment

Not applicable.

Funding

This research was funded by the Key Project Plan for Medical Science Research in Hebei Province (Grant Number: 20180873).

Conflict of Interest

The authors declare no conflict of interest.

References

[1] Vogelmeier CF, Román-Rodríguez M, Singh D, Han MK, Rodríguez-Roisin R, Ferguson GT. Goals of COPD treatment: Focus on symptoms and exacerbations. Respiratory Medicine. 2020; 166: 105938.

[2] Medrinal C, Bonnevie T. Physiotherapy during and after acute exacerbation of COPD. Revue Des Maladies Respiratoires. 2022; 39: 386–397.

[3] MacLeod M, Papi A, Contoli M, Beghé B, Celli BR, Wedzicha JA, *et al*. Chronic obstructive pulmonary disease exacerbation fundamentals: Diagnosis, treatment, prevention and disease impact. Respirology (Carlton, Vic.). 2021; 26: 532–551.

[4] Erhabor GE, Adeniyi B, Arawomo AO, Akinwalere O, Adetona G, Fagbohun FT, *et al*. Acute Exacerbation of COPD: Clinical Perspectives and Literature Review. West African Journal of Medicine. 2021; 38: 1129–1142.

[5] Li S, Zhao S, Wu Z, Wang F, Li W. Alteration of immune profiles is associated with pulmonary function and symptoms in patients with chronic obstructive pulmonary disease. Molecular Medicine Reports. 2021; 24: 742.

[6] Mathioudakis AG, Janssens W, Sivapalan P, Singanayagam A, Dransfield MT, Jensen JUS, *et al*. Acute exacerbations of chronic obstructive pulmonary disease: in search of diagnostic biomarkers and treatable traits. Thorax. 2020; 75: 520–527.

[7] Yang T, Chen C, Chen Z. The CT pulmonary vascular parameters and disease severity in COPD patients on acute exacerbation: a correlation analysis. BMC Pulmonary Medicine. 2021; 21: 34.

[8] Gentry S, Gentry B. Chronic Obstructive Pulmonary Disease: Diagnosis and Management. American Family Physician. 2017; 95: 433–441.

[9] Baqdunes MW, Leap J, Young M, Kaura A, Cheema T. Acute Exacerbation of Chronic Obstructive Pulmonary Disease. Critical Care Nursing Quarterly. 2021; 44: 74–90.

[10] World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013; 310: 2191–2194.

[11] Adibi A, Sin DD, Safari A, Johnson KM, Aaron SD, FitzGerald JM, *et al*. The Acute COPD Exacerbation Prediction Tool (ACCEPT): a modelling study. The Lancet. Respiratory Medicine. 2020; 8: 1013–1021.

[12] El-Gazzar AG, Kamel MH, Elbahnasy OKM, El-Naggar MES. Prognostic value of platelet and neutrophil to lymphocyte ratio in COPD patients. Expert Review of Respiratory Medicine. 2020; 14: 111–116.

[13] Liu L, Luan Y, Xiao L, Wang N, Wang J, Cui Z. The predictive value of serum procalcitonin for non-invasive positive pressure ventilation in the patients with acute exacerbation of chronic obstructive pulmonary disease. Medicine. 2021; 100: e25547.

[14] Sneh A, Pawan T, Randeep G, Anant M, Mani K, Hadda V, *et al*. Acute Phase Proteins as Predictors of Survival in Patients With Acute Exacerbation of Chronic Obstructive Pulmonary Disease Requiring Mechanical Ventilation. COPD. 2020; 17: 22–28.

[15] Palikhe NS, Niven M, Fuhr D, Sinnatamby T, Rowe BH, Bhutani M, *et al*. Low immunoglobulin levels affect the course of COPD in hospitalized patients. Allergy, Asthma, and Clinical Immunology: Official Journal of the Canadian Society of Allergy and Clinical Immunology. 2023; 19: 10.

[16] Xiong XF, Zhu M, Wu HX, Fan LL, Cheng DY. Immunophenotype in acute exacerbation of chronic obstructive pulmonary disease: a cross-sectional study. Respiratory Research. 2022; 23: 137.

[17] Xue W, Ma J, Li Y, Xie C. Role of CD_4$^+$ T and CD_8$^+$ T Lymphocytes-Mediated Cellular Immunity in Pathogenesis of Chronic Obstructive Pulmonary Disease. Journal of Immunology Research. 2022; 2022: 1429213.

[18] Okuma T, Hamamoto S, Maebayashi T, Taniguchi A, Hirakawa K, Matsushita S, *et al*. Quantitative evaluation of COVID-19 pneumonia severity by CT pneumonia analysis algorithm using deep learning technology and blood test results. Japanese Journal of Radiology. 2021; 39: 956–965.

[19] Hua Q, Chen G, Yang Y, Leng S, Zhao Z, Bai F, *et al*. Quantitative Evaluation of Chronic Obstructive Pulmonary Disease and Risk Prediction of Acute Exacerbation by High-Resolution Computed Tomography. Evidence-based Complementary and Alternative Medicine: ECAM. 2022; 2022: 6015766.

[20] Staub LJ, Mazzali Biscaro RR, Kaszubowski E, Maurici R. Lung Ultrasound for the Emergency Diagnosis of Pneumonia, Acute Heart Failure, and Exacerbations of Chronic Obstructive Pulmonary Disease/Asthma in Adults: A Systematic Review and

Meta-analysis. The Journal of Emergency Medicine. 2019; 56: 53–69.

[21] Duffy SP, Criner GJ. Chronic Obstructive Pulmonary Disease: Evaluation and Management. The Medical Clinics of North America. 2019; 103: 453–461.

[22] Zhao J, Wu Y, Zhang K, Zhang H, Ren H, Wang Y. Computer Tomography (CT)-based Screening of Hospitalized Patients with Moderate to Severe Chronic Obstructive Pulmonary Disease Complicated by Bronchiectasis Phenotype During Acute Exacerbation: A Clinical Analysis. Current Medical Imaging. 2023. (online ahead of print)

[23] Zou D, Zhu X. Association of CT phenotype with pulmonary function in patients with chronic obstructive pulmonary disease and influencing factors of prognosis. American Journal of Translational Research. 2023; 15: 2164–2174.

[24] Nemoto M, Nei Y, Bartholmai B, Yoshida K, Matsui H, Nakashita T, *et al*. Automated computed tomography quantification of fibrosis predicts prognosis in combined pulmonary fibrosis and emphysema in a real-world setting: a single-centre, retrospective study. Respiratory Research. 2020; 21: 275.

[25] Li L, Liu Y, Li J, Gao JM. Values of Body Mass Index and Chest CT Features in the Assessment of Chronic Obstructive Pulmonary Disease. Zhongguo Yi Xue Ke Xue Yuan Xue Bao. 2020; 42: 55–61. (In Chinese)