JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Coronavirus Pandemic

Chest CT features and risk factors for patients with Omicron variant pneumonia: a multicenter retrospective clinical study

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Abstract

Introduction: Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) Omicron variant infection has become widespread in China as a result of the alterations in epidemic control and prevention policies. We identified the clinical characteristics and lung computed tomography (CT) imaging characteristics of patients infected during the early stage of the Omicron BA.5 wave in Shanghai to provide a guide to the diagnosis, treatment, and prognosis of infection.

Methodology: Clinical information and lung CT imaging characteristics of patients with Omicron variant infection admitted to three designated hospitals in Shanghai from March to June 2022 were analyzed retrospectively.

Results: A total of 958 patients were included in the analysis. Among the patients, 169 (17.64%) had pneumonia confirmed by CT, of whom 70.41% (119/169) had lesions in < 10% of the lung area. Older age, unvaccinated status, and comorbid chronic lung disease, cerebrovascular disease, kidney disease, or Alzheimer's disease were associated with poor prognosis. In patients with coronavirus disease 2019 (COVID-19) pneumonia, a large lesion size was associated with a poor prognosis. Age ≥ 65 years, unvaccinated status, fever > 5 days, and lymphocyte count < 0.5×10^9/L were risk factors for pneumonia.

Conclusions: Age ≥ 65 years, unvaccinated status, fever > 5 days, and lymphocyte count < 0.5×10^9/L can be used to identify high-risk individuals who warrant a CT scan to screen for COVID-19 pneumonia, especially during the period of Omicron variant predominance. Concurrently, the importance of immunization should be emphasized to help people withstand the effects of Omicron variant infection.

Key words: COVID-19; SARS-CoV-2; Omicron; pneumonia; computed tomography.

J Infect Dev Ctries 2024; 18(9.1):S18-S26. doi:10.3855/jidc.19818

(Received 07 January 2024 – Accepted 25 March 2024)

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Introduction

COVID-19 pneumonia has been steadily spreading in several Chinese cities as a result of changes in the epidemic prevention and control strategies. The predominant strain of SARS-CoV-2 is currently Omicron BA.5 [1], which poses a major threat to human life and health due to its high infectivity and rapid transmission rate. Large cities have large populations and a disproportionate number of senior citizens. A large number of individuals were affected by the Omicron variant infection outbreak due to its rapid transmission. However, studies on the particular clinical characteristics of Omicron variant infection in China are lacking. Diagnosis, treatment, and prevention of the disease are under a lot of pressure as a result of these factors. Fear of COVID-19 pneumonia has significantly increased the demand for computed tomography (CT) scans in hospitals [2].

Pneumonia is one of the typical manifestations of SARS-CoV-2 infection [3]. The clinical disease caused by SARS-CoV-2 infection is called COVID-19. Chest CT is a crucial tool for the diagnosis of Omicron variant COVID-19 pneumonia, that helps track the course of illness. Omicron variant infection is typically asymptomatic, and the incidence of pneumonia is very low. According to some published reports [4], the COVID-19 Reporting and Data System (CO-RADS) developed by the Dutch Radiological Society, has shown excellent diagnostic performance for COVID-19 by interpreting chest CT images with a 5-point suspicion scale. However, previous studies only included community cases [5]. Further research on the

clinical features and prognosis of Omicron variant COVID-19 pneumonia is required, focusing on individuals who require hospitalization.

From March to June 2022, Shanghai experienced an epidemic of Omicron BA.2 and BA.5 subvariant infection [6]. We conducted a study focusing on the risk factors for COVID-19 pneumonia in individuals infected with the Omicron variant, and the indications for chest CT screening to provide a guide for the diagnosis, treatment, prevention, and control of Omicron infection by summarizing the clinical and chest CT imaging characteristics of hospitalized patients with infection during the Omicron variant epidemic in Shanghai [7].

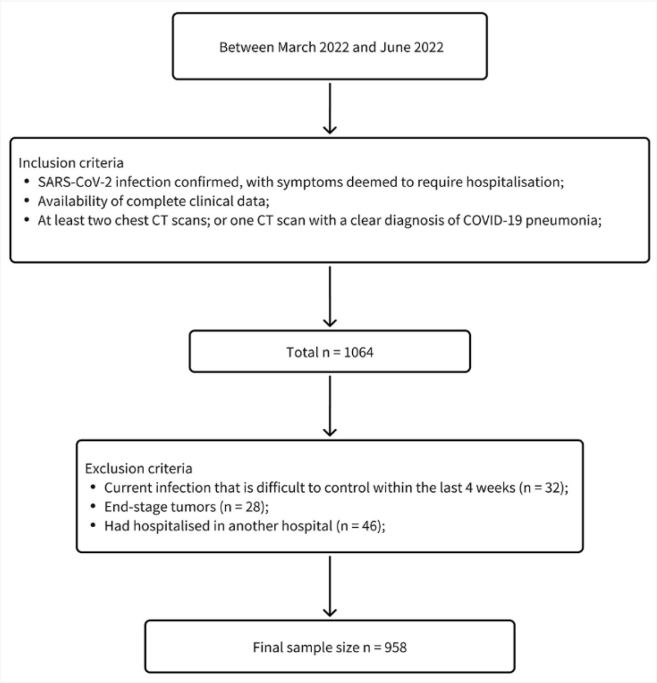
Methodology

Clinical data

A retrospective review was conducted of the clinical records of patients admitted to three facilities in Shanghai; Shanghai Changzheng Hospital, The 905th Hospital of PLA Navy, and Shanghai Jing'an District Zhabei Central Hospital; between March 2022 and June 2022, during the Omicron variant epidemic (Figure 1).

The inclusion criteria were: (1) SARS-CoV-2 infection confirmed by the real-time fluorescence reverse transcriptase polymerase chain reaction (RT-PCR) of a throat swab specimen, with symptoms such as fever and chest tightness deemed to require hospitalization by the medical staff; (2) availability of complete clinical data; (3) complete data on at least two chest CT scans, performed at least two days apart, with the last CT scan performed at least five days after the onset; or one CT scan with a clear diagnosis of COVID-19 pneumonia made by two imaging experts.

Figure 1. Flowchart of participant inclusion and exclusion.



COVID-19, coronavirus disease 2019; CT, computed tomography; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2.

The exclusion criteria were: (1) current infection that had been difficult to control within the last four weeks; (2) end-stage tumors; (3) hospitalized in another hospital.

The study was reviewed and approved by the ethical committees of the three facilities. An unfavorable outcome (poor prognosis) was defined by the need for a transfer to the intensive care unit for non-invasive mechanical ventilation including continuous positive airway pressure, and/or high flow nasal cannula, and/or invasive mechanical ventilation and/or death.

CT scan

All patients underwent chest CT scans. Multi-slice spiral CT (GE Light Speed VCT 64-slice CT, GE Discovery CT750 HD, United Imaging uCT 510 16-slice CT) with low-dose technology (50-80 mAs) was used. All patients underwent CT scans in the supine position and the scans were performed while they were holding their breath, after a deep inhalation.

Image analysis

Two experienced doctors, who had almost three years of experience managing patients with COVID-19 pneumonia, independently evaluated all CT scans without having access to patient information.

Interpretation of the CT images focused on the following aspects: (1) features of lesions: ground-glass opacities, consolidation, sheet or nodular lesions, grid-like changes, and interlobular septal thickening; (2) distribution and extent of lesions: location of lesions in the upper, middle, and lower lobes of the right lung or the upper and lower lobes of the left lung; subpleural or central distribution. The artificial intelligence program, the InferRead CT Pneumonia (Infervision Medical Technology Co., Ltd. Beijing, China), was applied to automatically identify and outline the lesions in the two lungs before the doctors reviewed and verified the results. At the same time, for patients with a history of respiratory diseases, the CT images were compared with previous CT images to exclude old lesions. The volume of the pneumonia lesions and the proportion of the entire lung affected by pneumonia were then quantified using the software. Based on the volume of lung lesions, CT scores were assigned as follows: 3

points for > 30%, 2 points for 10-30%, and 1 point for < 10%.

Statistical analysis

All data were analyzed using the IBM SPSS statistics version 26.0 (IBM Corp, Armonk, NY, USA) and the GraphPad Prism version 9 statistical software (GraphPad Software, San Diego, CA, USA). Frequencies and proportions were used to describe categorical data; means and standard deviations were used to describe continuous data with a normal distribution; and medians and interquartile ranges were used to describe continuous data without a normal distribution. In the case of continuous data such as age and lymphocyte count, the distribution pattern and homogeneity of variance between groups were initially assessed. Student's t-test was used to assess the difference between two independent groups for quantitative data showing a normal distribution and homogeneity of variance. Data with a normal distribution and unequal variances were compared using the Satterthwaite method. Data that did not follow a normal distribution were compared using the Kruskal-Wallis rank-sum test. To compare differences between different groups, non-normally distributed data were rank-transformed before being subjected to the Student-Newman-Keuls (SNK) approach for pairwise comparisons. Fisher's exact test or the Chi square test was used to compare categorical data. Multivariable logistic regression was used to study the risk variables associated with poor prognosis, and univariate analysis followed by multivariable logistic regression analysis was used to evaluate the risk factors associated with pneumonia (odds ratio and confidence Interval). *p values* < 0.05 were considered statistically significant.

Results

CT imaging features of Omicron variant COVID-19 pneumonia

A total of 958 individuals were included in the analysis, of which 169 patients (17.64%) had pneumonia confirmed by CT. Of the 958 patients, 660 (68.89%) were aged over 65 years. In patients with pneumonia, the lesions accounted for > 30% of the lung volume in 5 patients (3.0%), 10-30% in 45 patients (26.6%), and < 10% in 119 patients (70.4%).

Interstitial pneumonia, manifesting as one or more ground-glass density shadows in the shape of patches and small nodules, was the primary CT imaging feature. The lung marks in the lesion were also apparent as a grid (mostly due to thickening of the interstitium due to inflammation, accompanied by thickening of blood vessels). Some lesions displayed nodules with a peripheral halo sign. The long axis of certain lesions was parallel to the pleura, and their distribution was not consistent with the lung segments (Figures 2A, 2D, 2F and 2G). Most of the patients did not have cavities, pleural effusions, or mediastinal lymphadenopathy. Most bronchi inside the lesion were regular, without obvious distortion. Local consolidation of the lung

Table 1. Demographic and clinical characteristics of patients infected with the Omicron variant.

	Overall (N = 958)	Unfavorable outcome[a] (N = 36)	Favorable outcome (N = 922)	*p*
Age, mean (SD)	69.60 (17.44)	84.89 (9.59)	69.04 (17.42)	< 0.001
Gender				0.310
Female	510 (53.24)	16 (44.44)	494 (53.58)	
Male	448 (46.76)	20 (55.56)	428 (46.42)	
Fever	335 (34.97)	22 (61.11)	313 (33.95)	0.372
Cough	700 (73.07)	33 (91.67)	667 (72.34)	0.262
Chronic lung disease	152 (15.87)	30 (83.33)	122 (13.23)	< 0.001
Hypertension	478 (49.90)	25 (69.44)	453 (49.13)	0.018
Diabetes	234 (24.43)	10 (27.78)	224 (24.30)	0.692
Chronic kidney disease	54 (5.64)	12 (33.33)	42 (4.56)	< 0.001
Cerebrovascular disease	203 (21.19)	20 (55.56)	183 (19.85)	< 0.001
Chronic heart disease	192 (20.04)	15 (41.67)	177 (19.20)	0.002
Alzheimer's disease	42 (4.38)	8 (22.22)	34 (3.69)	< 0.001
pneumonia confirmed on CT	169 (17.64)	5 (13.89)	164 (17.79)	0.661
LDH (U/L)				< 0.001
> 400	89 (9.29)	25 (69.44)	64 (6.94)	
≤ 400	869 (90.71)	11 (30.56)	858 (93.06)	
Lymphocyte count (10^9/L)				< 0.001
≥ 0.5	780 (81.42)	7 (19.44)	773 (83.84)	
< 0.5	178 (18.58)	29 (80.56)	149 (16.16)	
Vaccination	346 (36.12)	1 (2.78)	345 (37.42)	< 0.001

Results are expressed as number (%) for categorical variables and as mean (standard deviation) for quantitative variables. CT: computed tomography; LDH: lactate dehydrogenase. An unfavorable outcome was defined as the need for a transfer to the intensive care unit for non-invasive mechanical ventilation including continuous positive airway pressure, and/or high flow nasal cannula, and/or invasive mechanical ventilation, and/or death.

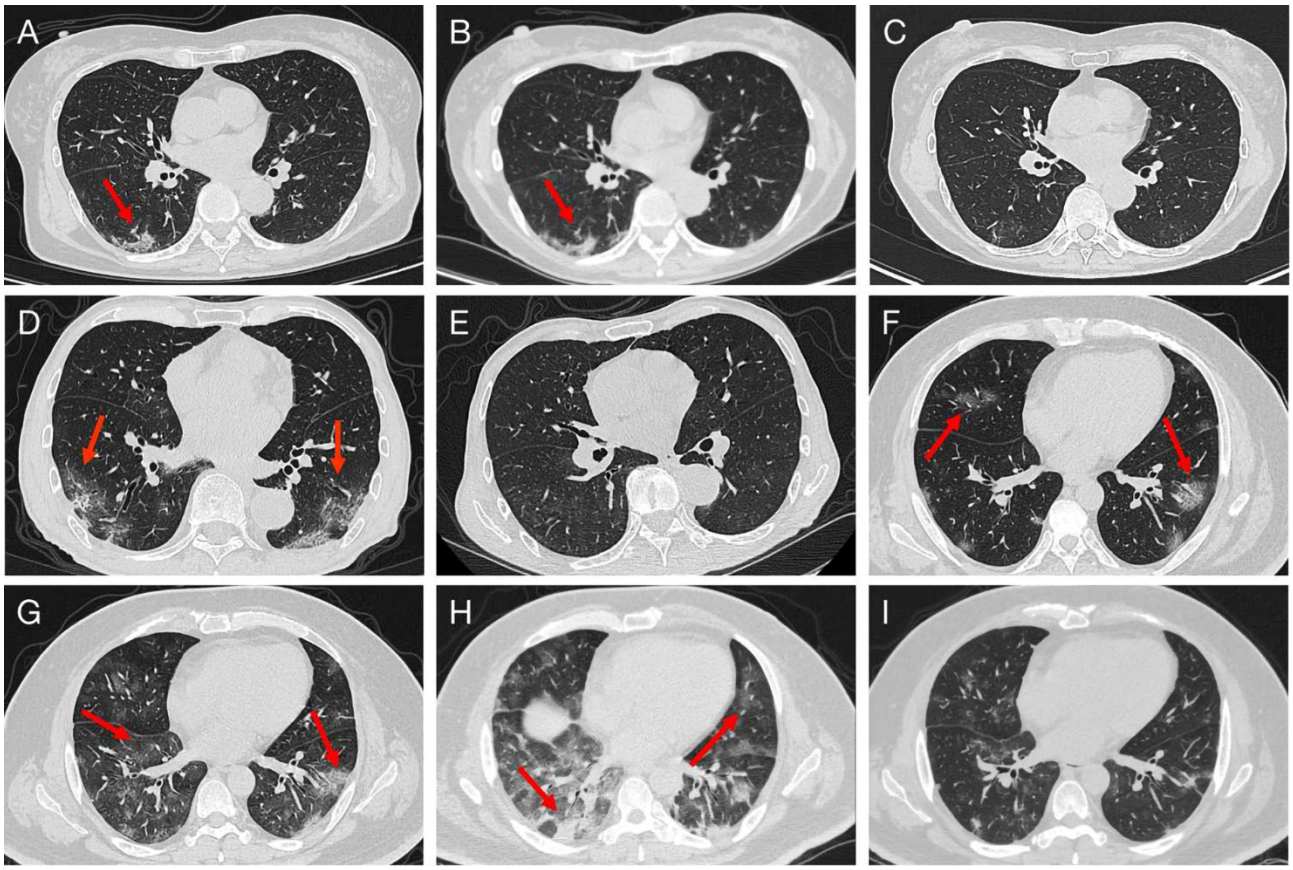
lesions appeared approximately two weeks after the onset of the disease, and the density of the lesion increased as fibrous exudation of the alveolar cavity increased (Figures 2B and 2H). The boundaries of the lesions became more distinct and the lesions shrank as the inflammation healed. The lesions subsequently became less dense and eventually disappeared after 3-4 weeks (Figures 2C, 2E and 2I).

Risk factors for an unfavorable outcome (poor prognosis)

A total of 36 of the 958 patients (3.8%) had an unfavorable outcome. The median time for the occurrence of the unfavorable outcome was 10 days after admission (interquartile range [IQR]: 7 to 12 days). The details for the patients with unfavorable outcomes and patients with a good prognosis are shown in Table 1.

The average age of patients with a poor prognosis was higher than that of patients with a good prognosis (84.89 vs 69.04 years, $p < 0.001$), and patients with a poor prognosis were more likely to have underlying illnesses, including hypertension (69.44% vs 49.13%, $p = 0.018$), chronic lung disease (83.33% vs 13.23%, $p < 0.001$), chronic renal disease (33.33% vs. 4.56%, $p < 0.001$), chronic heart disease (41.67% vs 19.20%, $p = 0.002$), cerebrovascular disease (33.33% vs 4.56%, $p < 0.001$), Alzheimer's disease (22.22% vs 3.69%, $p < 0.001$), lactate dehydrogenase (LDH) level > 400 U/L (69.44% vs 6.94%,$p < 0.001$), absolute lymphocyte count < 0.5×10^9/L (80.56% vs 16.16%, $p < 0.001$), and a lower vaccination rate (2.78% vs 37.42%, $p < 0.001$). Multivariable logistic regression analysis showed that an absolute lymphocyte count < 0.5×10^9/L (OR: 5.21, 95% CI: 1.41-22.44, $p = 0.017$), LDH level > 400 U/L

Figure 2. Pulmonary CT imaging of the three patients infected with the Omicron variant.



Patient 1 (A-C): A 63-year-old female was admitted to the hospital with a sore throat and fever for 6 days. On the day of admission (day 6, D6), a CT examination revealed ground-glass opacities in the lower lobe of the right lung (red arrow, A). On the 12th day after the onset of the disease (D12), the density of lesions in the lower lobe of the right lung increased (red arrow, B). On D27, CT showed that the lesions were absorbed (C). Patient 2 (D-E): An 80-year-old male was admitted with a fever for 7 days. CT examination on the day of admission (D7) revealed subpleural patchy shadows in the lower lobes of both lungs, with the long axis of the lesion parallel to the pleura (red arrows, D). On D32, the reexamination showed that the lesions were absorbed (E). Patient 3 (F-I): Male, 44 years old, admitted with fever and cough for 5 days. On the day of admission (D5), a CT examination revealed multiple ground-glass opacities in both lungs, with visible lung markings in the lesion, showing grid-like changes (red arrows, F). On the 9th day after the onset of the disease, CT showed that the lesions were enlarged and increased (red arrows, G). On D12, the lesions were further enlarged and increased, and some of them showed consolidation (red arrow, H). On D23, the density of the lesions decreased and dissipated (I). CT, computed tomography.

Table 2. The clinical characteristics of patients with and without pneumonia confirmed on CT.

	Overall (N = 958)	Pneumonia confirmed on CT		*p*
		No (N = 789)	Yes (N = 169)	
Age ≥ 65 years	660 (68.89)	528 (66.92)	132 (78.11)	0.004
Fever > 5days	179 (18.68)	63 (7.98)	116 (68.64)	< 0.001
No vaccine	612 (63.88)	471 (59.70)	141 (83.43)	< 0.001
Lymphocyte count < 0.5×10^9/L	178 (18.58)	123 (15.59)	55 (32.54)	< 0.001
LDH > 400 U/L	89 (9.29)	75 (9.50)	14 (8.28)	0.770
Chronic lung disease	152 (15.87)	120 (15.21)	32 (18.93)	0.246
Hypertension	478 (49.90)	391 (49.56)	87 (51.48)	0.672
Diabetes	234 (24.43)	186 (23.57)	48 (28.40)	0.200
Chronic kidney disease	54 (5.64)	41 (5.20)	13 (7.69)	0.200
Cerebrovascular disease	203 (21.19)	152 (19.26)	51 (30.18)	0.002
Chronic heart disease	192 (20.04)	156 (19.77)	36 (21.30)	0.672
Alzheimer's disease	42 (4.38)	32 (4.06)	10 (5.92)	0.300

Results are expressed as numbers (%) for categorical variables. CT: computed tomography; LDH: lactate dehydrogenase.

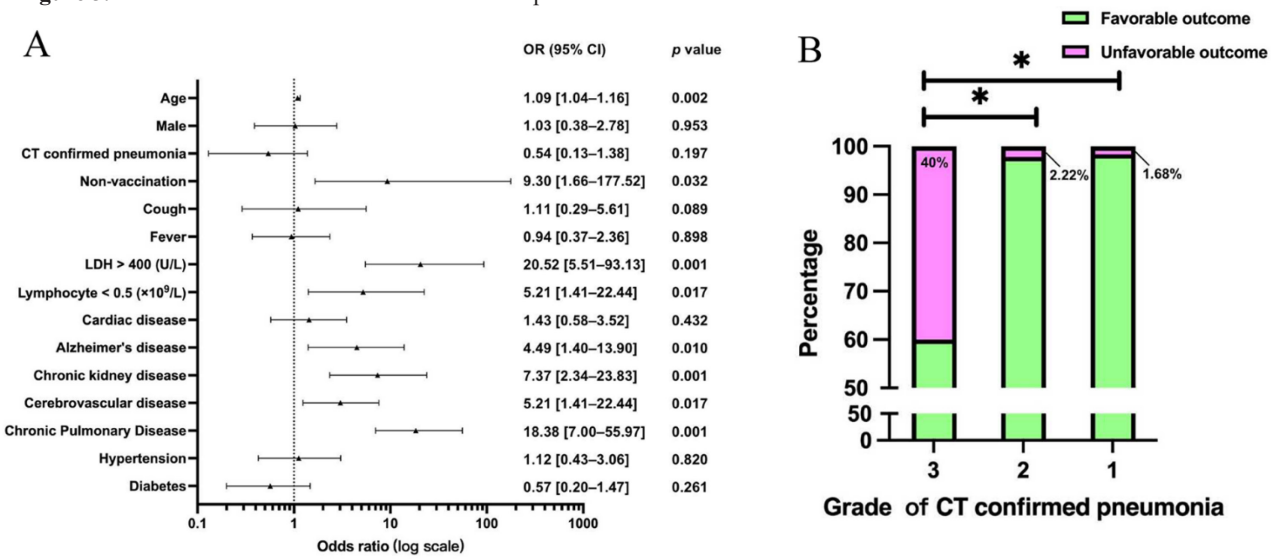
(OR: 20.52, 95% CI: 5.51-22.44, $p < 0.001$), age (OR: 1.09, 95% CI: 1.04-1.16, $p = 0.002$), unvaccinated status (OR: 9.30, 95% CI: 1.66-177.52, $p = 0.032$), comorbid chronic pulmonary disease (OR: 18.38, 95% CI: 7.00-55.97, $p < 0.001$), cerebrovascular disease (OR: 3.03, 95% CI: 1.24-7.62, $p = 0.016$), chronic kidney disease (OR: 7.37, 95% CI: 2.34-23.83, $p < 0.001$), and Alzheimer's disease (OR: 4.49, 95% CI: 1.40-13.90, $p = 0.010$) were all independent risk factors for a poor prognosis (Figure 3A).

Imaging-confirmed that pneumonia was not significantly associated with a poor outcome in either the univariate or multivariable analysis (13.89% vs 17.79%, $p = 0.661$; OR: 0.55, 95% CI: 0.13-1.38, $p = 0.197$). However, a high CT score was significantly associated with a poor prognosis ($p < 0.001$) (Figure 3B).

Risk factors for pneumonia

The clinical characteristics of patients with and without pneumonia are compared in Table 2. Patients in the pneumonia group were significantly more likely to have fever for >5 days (68.64% vs 7.98%, $p < 0.001$), have lymphocyte count < 0.5×10^9/L (32.54% vs 15.59%, $p < 0.001$), and be unvaccinated (83.43% vs 59.70%, $p < 0.001$). Patients with pneumonia were significantly more likely to have cerebrovascular disease than those without pneumonia (30.18% vs 19.26%, $p = 0.003$), but the prevalence of other underlying diseases did not differ significantly by pneumonia status. Lymphocyte count in the group with pneumonia confirmed on CT was significantly lower than that in the group without pneumonia (Figure 4A). Among patients who had received one or more doses of COVID-19 vaccine, there were no significant

Figure 3. Risk factors for an unfavorable outcome in patients with SARS-CoV-2 Omicron variant infection.



A: Forrest plot showing odds ratios (95% confidence interval) for the risk of unfavorable outcome (need of artificial ventilation and/or death) by multivariable analysis; B: A high CT score was significantly associated with a poor prognosis. CT, computed tomography; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2.

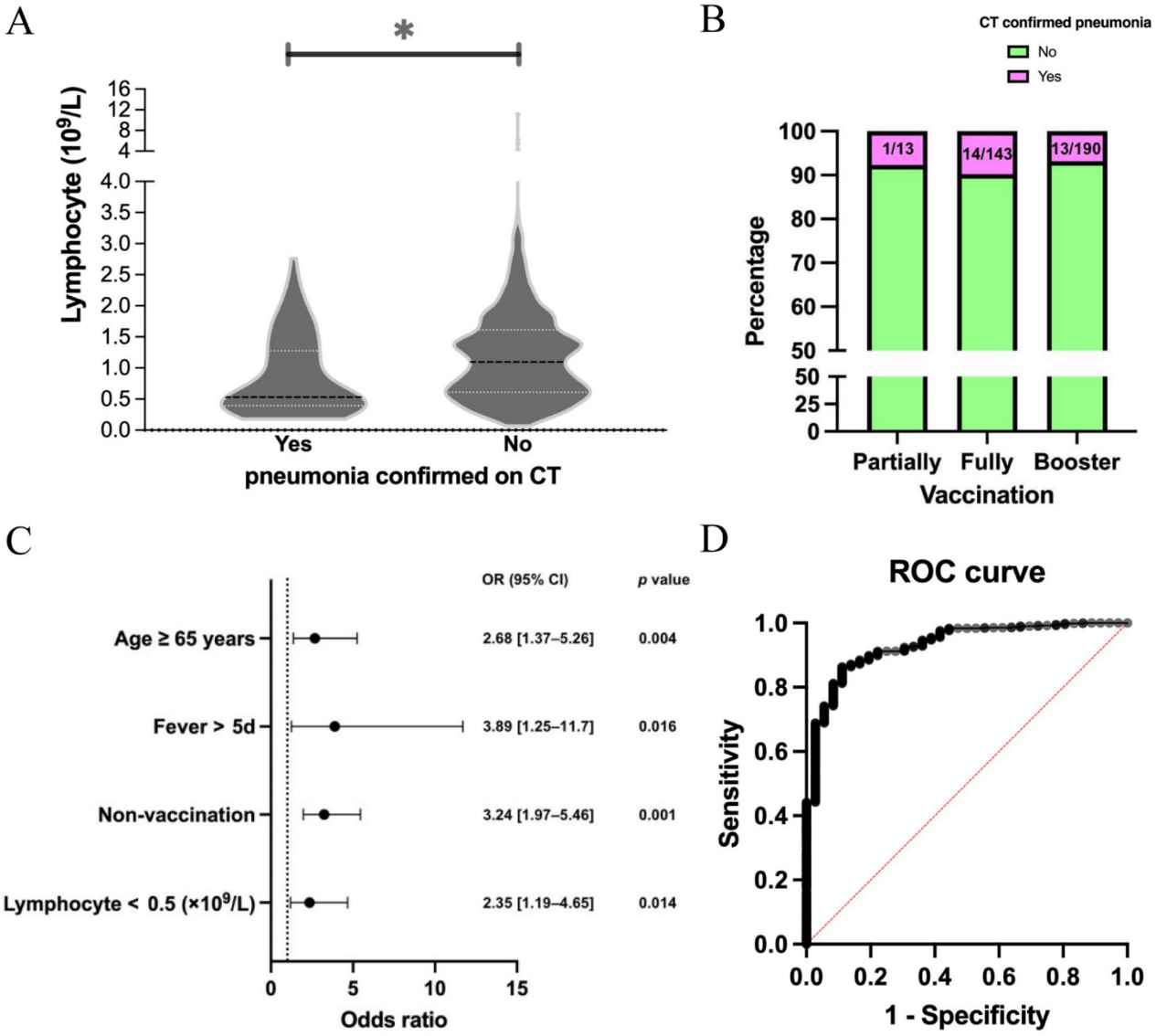
differences in the occurrence of pneumonia according to whether the patients were partially vaccinated, fully vaccinated, or fully vaccinated and had received a booster dose (Figure 4B).

Multivariable analysis showed that age ≥ 65 years (OR: 2.68, 95% CI: 1.37-5.26, $p = 0.004$), unvaccinated status (OR: 3.24, 95% CI: 1.97-5.46, $p < 0.0001$), fever > 5 days (OR: 3.89, 95% CI: 1.25-11.70, $p = 0.016$), lymphocyte count < 0.5×10^9/L (OR: 2.35, 95% CI: 1.19-4.65, $p = 0.014$) were all risk factors for Omicron variant COVID-19 pneumonia (Figure 4C). Using the above four factors to predict the occurrence of Omicron variant-associated pneumonia, the area under the curve was 0.931 (95% CI: 0.893-0.968, $p < 0.001$), the positive predictive value was 96.26%, and the negative predictive value was 63.16% (Figure 4D).

Discussion

Omicron was one of the predominant SARS-CoV-2 variants circulating worldwide [8,9]. From March to June 2022, Shanghai had a high incidence of infections caused by the Omicron BA.2 and BA.5 subvariants. The number of infected people surged rapidly due to changes in the epidemic prevention strategies in China. The BA.5 subvariant was the predominant SARS-CoV-2 variant in China at the time when this study was

Figure 4. Risk factors for pneumonia confirmed by CT



A: Lymphocyte count in the group with pneumonia was significantly lower than that in the group without pneumonia; B: Among patients who had received one or more doses of the COVID-19 vaccine, there were no significant differences in the occurrence of pneumonia according to whether the patients were partially vaccinated, fully vaccinated, or fully vaccinated and had received a booster dose; C: Forrest plot showing odds ratios (95% confidence interval) for the risk of pneumonia confirmed on CT; D: Receiver operating characteristic (ROC) curve of using the four risk factors to predict the occurrence of Omicron variant-associated pneumonia. COVID-19, coronavirus disease 2019; CT: computed tomography.

conducted [1]. It is essential to understand the clinical characteristics and lung imaging characteristics of patients infected with the SARS-CoV-2 Omicron variant to control the Omicron variant pandemic and provide focused diagnosis and therapy, and prognosis assessment.

Patients infected with the Omicron variant had milder symptoms and better prognosis than those infected with the Delta variant [10]. This study found that < 4% of the study patients had a poor prognosis, which is consistent with the low number of patients who experienced critical illnesses as a result of the Omicron variant infection. The pneumonia verified by chest CT was 17.64% (169/958), which is consistent with a report by Trunfio [11], and suggests that the Omicron variant had less impact on the lung than the Delta variant. Ground-glass opacities and consolidation shadows in the lungs, which were single or multiple patchy shadows, were the key characteristics of a chest CT for Omicron variant COVID-19 pneumonia [12]. The imaging characteristics of this kind of pneumonia are consistent with those of other pneumonia that were brought on by other SARS-CoV-2 variants. The virus invades the alveolar epithelium, and as a result of its inflammatory cells and exudate, the alveolar septum thickens and the alveoli partially collapse [13]. The pathological basis of pneumonia caused by the Omicron variant and the Delta variant is the same [14]. Based on our results, the pulmonary lesions brought on by COVID-19 pneumonia caused by the Omicron variant were minor and healed quickly. The lower lobes of the two lungs continued to have the highest percentage of lung lesions, in line with earlier reports [15]. One theory is that this is because coronavirus particles are tiny and spread widely once they enter the lungs [16]. Being the most peripheral structure of the lung, lesions frequently congregate in the subpleural area. This study showed that the lesion range was relatively small and that the lung lesions in the Omicron variant strain-infected patients were minimal. The proportion of patients with lesions of < 10% lung capacity was higher than that in patients with COVID-19 pneumonia caused by the Delta variant [17]. This suggests that the Omicron variant might cause less lung damage than other SARS-CoV-2 variants [18].

In this study, imaging-confirmed pneumonia in the lungs was not substantially associated with a poor prognosis, according to both univariate and multivariable analysis. Omicron variant infection is more likely to be asymptomatic than the Alpha and Delta variants and is less likely to cause pneumonia [19]. Absolute lymphocyte count < 0.5×10^9/L, LDH > 400 U/L; age; vaccination status; and comorbid conditions such as chronic lung disease, cerebrovascular disease, kidney disease, and Alzheimer's disease; were the primary risk factors linked to a poor prognosis. This is consistent with previous studies that found that Omicron variant infection damages multiple systems of the body, lung lesions are only one of the manifestations, and age and underlying illnesses were the main factors associated with a poor prognosis [20].

In this study, the prognosis was substantially associated with the pneumonia severity score on CT. There was a strong association between lesions exceeding 30% of the lung volume and an unfavorable outcome. This is consistent with previous reports [21,22] of patients with COVID-19 pneumonia caused by the SARS-CoV-2 wild strain, Alpha, and Delta variants, which found that in patients with increasing inflammation and a wide spectrum of infiltration, repeated CT screening was very valuable for directing disease treatment. Similarly, in patients with Omicron variant infection, COVID-19 pneumonia is an important indication for admission of patients with other risk factors (such as age ≥ 65 years and concomitant underlying illnesses). The risk factors for pneumonia were age ≥ 65 years, fever > 5 days, lymphocyte count < 0.5×10^9/L, and being unvaccinated. The analysis of vaccination found that partial vaccination as well as full vaccination and booster vaccination had a sizeable protective effect on the occurrence of pneumonia [23].

The present study has several limitations. The limited sample size may have affected model training. The limited sample size also led to the deviation between the predicted results and the actual outcome results. This paper study aimed to explore a simple and rapid method to predict the probability of Omicron variant-associated pneumonia in patients. Therefore, this article lacks the input of more clinical laboratory indicators. In the follow-up study, we will further explore the factors related to the poor prognosis of COVID-19 patients.

Conclusions

In this large, multicenter retrospective analysis of patients infected with the Omicron variant, the incidence of pneumonia was relatively low, the lesion volume was generally small, and COVID-19 pneumonia confirmed by imaging was not linked to a poor prognosis. The main risk factors for a poor prognosis were age, being unvaccinated, and having an underlying illness; specifically, comorbid chronic lung

disease, cerebrovascular disease, kidney disease, or Alzheimer's disease. In patients with COVID-19 pneumonia, only a minority had a substantial lung volume involved, and the severity of the lesion was strongly associated with a poor prognosis. Risk factors for pneumonia included age ≥ 65 years, fever > 5 days, lymphocyte count < 0.5×10^9/L, and lack of immunization. We recommend to the concerned authorities that in order to address the wave of the Omicron variant, these four risk factors can be used to identify patients at high high-risk who require CT examinations, to avoid wasting limited CT examination resources. At the same time, vaccination should be emphasized to improve the prognosis of individuals infected with the Omicron variant.

Data availability

The raw data supporting the conclusions of this article will be made available by the corresponding authors, without undue reservation. Please contact hangxfdoc@smmu.edu.cn.

Funding

This research was supported by the Innovative Clinical Research Project of Changzheng Hospital (2020YLCYJ-Y03), and the Discipline Construction Project of Jing'an District (2021BR04).

Ethics approval and consent to participate

The studies involving human participants were reviewed and approved by the Medical Ethical Committees of Shanghai Changzheng Hospital, the 905th Hospital of PLA Navy, and the Shanghai Jing'an District Zhabei Central Hospital. The requirement for written informed consent of participants was waived since no additional interventions and potential harm were posed to these patients. Therefore, written informed consent for participation was not provided by the participants' legal guardians. The waiver of need for informed consent was approved by the above three Medical Ethical Committees. All methods of the study were carried out in accordance with relevant guidelines and regulations.

Authors' contributions

HX and WZ, conception and design of the study; HH, XY, SR, LB, and YJ, organization of the database; HX, YY, and WJ, statistical analysis; YY and XY, writing the first draft of the manuscript; HX, critical revision of the manuscript. All authors contributed to the manuscript revision; and have read and approved the submitted version.

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Conflict of interests: No conflict of interests is declared.