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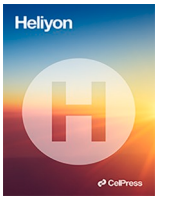

Research article

Clinical characteristics of SARS-CoV-2 Omicron pneumonia in immunocompromised and immunocompetent patients: A retrospective cohort study

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ABSTRACT

Objective: Previous studies evaluating the differences in COVID-19 mortality rates between immunocompromised patients and other patient groups have shown conflicting findings. This research aimed to compare the mortality rates of immunocompromised and immunocompetent patients during the Omicron-dominant period of the SARS-CoV-2 pandemic, and to identify factors associated with prognosis.

Methods: We conducted a retrospective analysis of 1085 adult patients (aged ≥18 years) admitted with COVID-19 pneumonia to the China-Japan Friendship Hospital between December 1, 2022, and January 31, 2023. We assessed the prevalence of comorbidities, incidence of co-infections and nosocomial infections, and 30-day mortality.

Results: Among the 1085 patients, 254 were immunocompromised, and 831 were immunocompetent. Immunocompromised patients had higher rates of non-invasive ventilation use (30.3 % vs. 21.1 %), invasive ventilation (12.2 % vs. 5.3 %), and 30-day mortality (19.7 % vs. 13.7 %) compared to immunocompetent patients. However, overall mortality rates did not significantly differ based on immunocompromised status. Cox regression analysis identified that elevated troponin T (≥0.15 ng/mL), respiratory failure, high lactate dehydrogenase (≥272.5 U/L), elevated D-dimer (≥1.295 mg/L), increased C-reactive protein (≥90 mg/L), elevated interleukin-6 (>11.67 ng/L), high peripheral blood neutrophil count (>9.84 × 10^9/L), and immunocompromised status were independent predictors of poor COVID-19 prognosis. In the immunocompetent group, current smoking and a history of interstitial lung disease were related to a worse prognosis.

Conclusions: COVID-19 pneumonia due to the Omicron variant may lead to worse outcomes in immunocompromised patients. In immunocompetent patients, careful monitoring is essential for those with respiratory failure, smoking history, or interstitial lung disease to prevent adverse outcomes.

1. Introduction

Due to their underlying medical conditions and treatments, immunocompromised patients are at a higher risk for respiratory viral

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infections compared to those with normal immune function [1,2]. Previous studies on COVID-19 mortality in immunocompromised individuals have yielded conflicting results. Some studies have reported increased mortality [3,4]; for instance, patients with both cancer and COVID-19 face a heightened risk of severe outcomes, including higher rates of intubation and mortality [5]. Conversely, other studies have reported no obvious difference in mortality between immunocompromised and immunocompetent patients [6,7]. Most clinical research to date has focused on patients with cancer or those who have received solid organ transplants, with limited data available on other types of immunocompromised individuals.

The Omicron variant, first identified in November 2021, quickly spread worldwide and has been linked to a decreased risk of hospitalization and death compared to earlier SARS-CoV-2 variants [8,9]. However, its spread to Beijing at the end of 2021 led to a high mortality rate among older adults with pre-existing conditions. This research aimed to compare the 30-day mortality rates between immunocompromised and immunocompetent patients hospitalized with COVID-19 pneumonia due to the Omicron variant, and to characterize the clinical features of immunocompromised patients admitted with COVID-19 pneumonia during this period.

2. Materials and methods

2.1. Study cohort

A retrospective analysis was performed on all consecutive adult patients (aged ≥18 years) admitted with COVID-19 pneumonia to the China-Japan Friendship Hospital, a tertiary academic hospital in Beijing, China, from December 1, 2022, to January 31, 2023. COVID-19 diagnosis was confirmed through both chest computed tomography scans and real-time reverse-transcription polymerase chain reaction (RT-PCR) testing. The Omicron variant was the predominant strain of SARS-CoV-2 circulating in China during the study period.

Immunocompromised patients were identified based on the following criteria: (1) use of corticosteroids at a dose greater than 10 mg for more than 3 weeks; (2) prolonged low-dose corticosteroid therapy for over 6 months with a cumulative dose of ≥750 mg; (3) use of other immunosuppressive or cytotoxic drugs such as azathioprine, methotrexate, mycophenolate mofetil, tacrolimus, anti-tumor necrosis factor (TNF) alpha agents, or other biologics in the past 6 months; (4) history of bone marrow or solid organ transplantation; (5) presence of hematologic malignancies in the past 6 months, with or without chemotherapy; (6) chemotherapy in the past 6 months or chest radiation therapy in the past 3 months for solid organ cancer; or (7) diagnosis of a primary immunodeficiency such as chronic granulomatous disease or common variable immunodeficiency [10,11]. Patients were excluded if they were (1) under 18 years of age; (2) did not show pneumonia on imaging; or (3) tested positive for HIV.

2.2. Data collection

The following data were acquired from the medical records: (1) Demographics: Age, sex, and other baseline characteristics. (2) Underlying conditions: Including hypertension, coronary heart disease, details on immunosuppression in immunocompromised patients, and use of corticosteroids and immunosuppressants. (3). Symptoms and signs: Clinical manifestations at presentation. (4). Laboratory examinations: Complete blood count, blood gas analysis, liver and kidney function tests, and cardiac enzyme levels. (5). Microbiological tests: Results of bacterial and fungal cultures from sputum and bronchoalveolar lavage fluid (BALF), and other viral nucleic acid and gut microbiota test results. (6). Treatment information: Use of antiviral drugs, corticosteroids, high-flow oxygen therapy, and ventilator support. (7). Outcomes: In-hospital mortality and 30-day mortality.

2.3. Pathogen detection

Respiratory viruses, including SARS-CoV-2, cytomegalovirus, influenza A and B, human rhinovirus, and human metapneumovirus, were detected in sputum, endotracheal aspirate, bronchoalveolar lavage fluid (BALF), or nasopharyngeal swab specimens using RT-PCR assays (Shanghai Bojie Medical Technology or Zhijiang Biological Technology, China).

2.4. Pathogen-specific diagnostic criteria

The diagnosis of Aspergillus-related pneumonia required at least one of the following criteria: (1) identification of Aspergillus species based on culture characteristics and microscopic examination; (2) galactomannan optical index ≥0.8 in BALF; (3) galactomannan optical index ≥0.5 in serum; or (4) detection of Aspergillus by next-generation sequencing [12–14].

2.5. Statistical analysis

Patient demographics, clinical features, and pathogen testing data were presented as means (±standard deviation), medians (interquartile range), or frequencies (percentage). Continuous data were compared between groups using parametric or non-parametric tests, based on their distribution. Categorical data were compared using the χ^2 test. Cox regression analysis was employed to identify independent predictors of mortality, with data reported as hazard ratio (HR) and 95 % confidence interval (CI). Kaplan–Meier survival curves were generated to compare 30-day survival rates between patient groups using the log-rank test. All statistical tests were conducted using SPSS v26.0. Two-sided $P < 0.05$ was deemed statistically significant.

Table 1
Clinical characteristics of COVID-19 patients between immunocompetent and immunocompromised group.

Variables	Total, N = 1085	Immunocompromised group, n = 254	Immunocompetent group, n = 831	*P*-Value
Sex, female, n (%)	389 (35.9)	95 (37.4)	294 (35.4)	0.556
Age, median (IQR)	73.0 (64.0, 82.0)	64.0(56.0, 72.0)	76.0(67.0, 84.0)	<0.001
Symptoms and signs, n (%)				
Fever	935 (86.2)	221 (87.0)	714 (85.9)	0.660
Cough	924 (88.9)	216 (85.0)	708 (85.2)	0.950
Expectoration	861 (79.4)	202 (79.5)	659 (79.3)	0.938
Dyspnoea	604 (55.7)	144 (56.7)	460 (55.4)	0.707
Consciousness disturbance	60 (5.5)	7 (2.8)	53 (6.4)	0.027
Poor appetite	426 (39.3)	80 (31.5)	346 (41.6)	0.004
Laboratory examination				
White blood cell≥9.84 × 10^9/L	217 (20.0)	47 (18.5)	170 (20.5)	0.496
Neutrophils≥8.0 × 10^9/L	241 (22.2)	56 (22.0)	185 (22.3)	0.942
Lymphocyte≤0.865 × 10^9/L	556 (51.2)	150 (59.1)	406 (48.9)	0.004
Eosinophilic granulocyte≥0.15 × 10^9/L	106 (97.7)	19 (7.5)	87 (10.5)	0.160
Platelet, × 10^9/L (IQR)	200.5 (147.0,266.0)	170 (135,226)	208 (152,275)	<0.001
Mean hemoglobin, g/L (IQR)	124.0 (110.0,136.0)	116.0 (101.0,132.5)	125.0(113.0,137.0)	<0.001
Blood urea nitrogen, mmol/L	6.69 (4.94, 10.04)	7.68 (5.55, 11.12)	6.34 (4.83, 9.68)	<0.001
Lactic dehydrogenase (LDH)≥272.5U/L	300/718 (41.8)	71/133 (53.4)	229/585 (40.7)	0.191
Troponin T ≥ 0.15 ng/ml	519/1048 (49.5)	109/247 (44.1)	410/801 (51.2)	0.052
Interleukin-6≥11.67 ng/L	420/766 (54.8)	107/171 (62.6)	313/595 (52.6)	0.021
NT-proBNP≥585 pg/ml	375/1078 (34.8)	79/252 (31.3)	296/826 (35.7)	0.191
C-reactive protein (CRP) ≥90 mg/L	274/1061 (25.8)	61/246 (24.8)	213/815 (26.1)	0.674
D-Dimer≥1.295 mg/L	470/1064 (44.2)	111/251 (44.2)	359/813 (44.2)	0.985
Procalcitonin≥0.135 ng/ml	293/986 (29.7)	75/230 (32.6)	218/756 (28.8)	0.273
Severe pneumonia index score	86.0 (70.0, 109.0)	81.0 (64.0, 104.0)	87.0 (72.0, 111.0)	0.042
CURB65 score>1	457 (42.1)	84 (33.1)	373 (44.9)	0.001
Underlying Diseases, n (%)				
Hypertension	601 (55.4)	132 (52.0)	469 (56.4)	0.210
Coronary Heart Disease	270 (24.9)	40 (15.7)	230 (27.7)	<0.001
Chronic heart failure	107 (9.9)	18 (7.1)	89 (10.7)	0.090
Cerebrovascular disease	167 (15.4)	25 (9.8)	142 (17.1)	0.005
Diabetes mellitus	401 (40.0)	85 (33.5)	316 (38.0)	0.187
Tumor	89(10.8)	52 (20.5)	37 (4.5)	<0.001
Anemia	421 (38.8)	128 (50.4)	293 (35.3)	<0.001
Connective tissue disease[a]	84 (7.7)	75 (29.5)	9 (1.1)	<0.001
Interstitial lung disease	128 (11.8)	65 (25.6)	63 (7.6)	<0.001
Bronchiectasis	25 (2.3)	6 (2.4)	19 (2.3)	0.944
Bronchial asthma	31 (2.9)	7 (2.8)	24 (2.9)	0.912
Chronic obstructive pulmonary disease	76 (7.0)	16 (5.2)	60 (7.2)	0.615
Leukemia	7 (0.6)	7 (6.3)	0 (0)	<0.001
Lymphoma	32 (1.6)	32 (12.6)	0 (0)	<0.001
Nephritic syndrome	5 (0.5)	2 (0.8)	3 (0.4)	0.380
Chronic renal failure	147 (13.5)	67 (26.4)	80 (9.6)	<0.001
Solid organ transplant	93 (8.6)	93 (36.6)	0 (0)	<0.001
Current smoker	59 (5.4)	7 (2.8)	52 (6.3)	0.031
Ex-smoker	250 (23.0)	59 (23.2)	191 (23.0)	0.936
Disease severity				
Severe pneumonia	582 (53.6)	133 (52.4)	449 (54.0)	0.641
Co-pathogens				
Bacterium	113 (10.4)	44 (17.3)	69 (8.3)	<0.001
Aspergillosis	67 (6.2)	32 (12.6)	35 (4.2)	<0.001
Other viruses	21 (1.9)	13 (5.1)	8 (0.9)	<0.001
Mycobacterium	3 (0.3)	1 (0.4)	2 (0.2)	0.684
Treatment, n (%)				
Glucocorticoids	803 (74.0)	224 (88.2)	579 (69.7)	<0.001
Antiviral drug	415 (26.5)	133(52.4)	282 (33.9)	<0.001
Azvudine	65 (6.0)	16 (6.3)	49 (5.9)	0.813
Paxlovid	348 (32.1)	116 (45.7)	232 (27.9)	<0.001
Molnupiravir	2 (0.2)	1 (0.4)	1 (0.1)	0.374
Baricitinib	107 (9.9)	34 (13.4)	73 (8.8)	0.031
Tocilizumab	42 (3.9)	14 (5.5)	28 (3.4)	0.121
Complications, n (%)				
Noninvasive ventilation	252 (23.2)	77 (30.3)	175 (21.1)	0.002
Invasive mechanical ventilation	75 (6.9)	31 (12.2)	44 (5.3)	<0.001
Respiratory failure during admission	503 (46.4)	122 (48.0)	381 (45.8)	0.541
Extracorporeal membrane oxygenation	9 (8.3)	1 (0.4)	8 (0.9)	0.382
30-day mortality	164 (15.0)	50 (19.7)	114 (13.7)	0.020

[a] Connective tissue disorders: rheumatoid arthritis, systemic lupus erythematosus, dermatomyositis, polymyositis, systemic sclerosis, Sjogren's syndrome, etc.

3. Results

The study included 1085 adult patients admitted with COVID-19 pneumonia between December 1, 2022, and January 31, 2023. Among them, 254 were immunocompromised and 831 were immunocompetent. In the immunocompromised group, 37.4 % (95/254) were women, with a median age of 64 years. The most common presenting symptoms were fever (87.0 %), cough (85.0 %), and dyspnea (56.7 %). The primary underlying immune-associated conditions were solid organ transplantation (36.6 %), connective tissue disease (CTD; 29.5 %), interstitial lung disease (ILD, 25.6 %), malignancy (20.5 %), and hematologic malignancies (18.9 %). Compared to the immunocompetent group, the immunocompromised patients were younger and had lower platelet counts, hemoglobin levels, PSI scores, and CURB-65 scores. However, they had significantly higher levels of blood urea nitrogen, a higher prevalence of lymphopenia, a greater proportion of patients with interleukin-6 (IL-6) levels ≥11.67 ng/L, and a higher prevalence of bacterial, fungal, or viral co-infections. Additionally, the use of glucocorticoids, antiviral drugs, non-invasive ventilation, invasive ventilation, and the 30-day mortality rate were remarkably higher in immunocompromised group than in immunocompetent group ($P < 0.05$) (Table 1).

In the immunocompromised group, bacterial co-infections occurred in 22.4 % of patients, with *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa* being the most frequently isolated pathogens, followed by fungal (16.2 %) and viral (5.2 %) co-infections. Among immunocompetent patients, bacterial co-infections were also the most common (11.1 %), followed by fungal (4.7 %) and viral (0.8 %) co-infections (Table 2).

In the immunocompromised cohort, the underlying conditions included CTD (72 patients), post-organ transplantation (94 patients), hematologic malignancies (36 patients), conditions requiring immunosuppressive therapy for idiopathic interstitial pneumonia or nephrotic syndrome (7 patients), and cancer with recent chemotherapy or radiation therapy (45 patients). Notably, age, sex, and PSI scores differed significantly across these subgroups ($P < 0.01$), but no obvious differences were found in in-hospital mortality rates or the incidence of complications between the subgroups (Table 3).

Cox regression analysis indicated that, in all patients, independent predictors of in-hospital mortality included elevated troponin T levels (≥0.15 ng/mL), respiratory failure, lactate dehydrogenase levels (≥272.5 U/L), D-dimer levels (≥1.295 mg/L), C-reactive protein levels (≥90 mg/L), interleukin-6 (IL-6) levels (>11.67 ng/L), peripheral blood neutrophil counts (>9.84 × 10^9/L), and immunocompromised status. Specifically, in immunocompromised patients, elevated lactate dehydrogenase levels (>272.5 U/L), respiratory failure, chronic heart failure, and elevated neutrophil counts were independent predictors of mortality. For the immunocompetent group, predictors of mortality included respiratory failure, ILD, elevated troponin T levels (≥0.15 ng/mL), high lactate dehydrogenase levels (≥272.5 U/L), elevated IL-6 levels (>11.67 ng/L), high pneumonia severity index, and current smoking (Table 4).

In the immunocompromised group, the 30-day mortality rate was 75.8 % for those receiving invasive mechanical ventilation and

Table 2
The pathogen results of pneumonia between immunocompetent and immunocompromised group.

Variables, n (%)	Immunocompromised group, n = 254	Immunocompetent group, n = 831	*P*-Value
Virus	13(5.2)	7 (0.8)	<0.001
Cytomegalovirus	11(4.3)	5 (0.6)	<0.001
Influenza A virus	0 (0)	1 (0.1)	–
Rhinovirus	1 (0.4)	0 (0)	–
Human herpesvirus 1	1 (0.4)	1 (0.1)	0.374
Bacteria	57 (22.4)	91 (11.0)	<0.001
Streptococcus pneumoniae	2 (0.8)	2 (0.2)	0.208
Haemophilus influenzae	1 (0.4)	2 (0.2)	0.684
Staphylococcus aureus	3 (1.2)	7 (0.8)	0.621
Escherichia coli	2 (0.8)	1 (0.1)	0.076
Enterobacter cloacae	4 (1.6)	0 (0)	<0.001
Klebsiella pneumoniae	9 (3.5)	14 (1.7)	0.072
Pseudomonas	14 (5.5)	13 (1.6)	<0.001
Serratia marcescens	0 (0)	2 (0.2)	0.434
Acinetobacter	13 (5.1)	22 (2.7)	0.051
Corynebacterium striatum	5 (2.0)	11 (1.3)	0.456
Burkholderia	0 (0.4)	1 (0.1)	–
Stenotrophomonas maltophilia	1 (0.4)	6 (0.7)	0.567
Enterococcus	1 (0.4)	6 (0.7)	0.567
Nocardia	1 (0.4)	1 (0.1)	0.374
Actinomycetes	1 (0.4)	0 (0)	–
Achromobacter xylosoxidans	0 (0)	1 (0.1)	–
Klebsiella aerogenes	0 (0)	1 (0.1)	–
Klebsiella acidogenes	0 (0)	1 (0.1)	–
Pneumocystis	2 (0.8)	0 (0.1)	0.010
Aspergillus	38 (15.0)	39(4.7)	<0.001
Rhizopus	1 (0.4)	0 (0)	–
Fusarium	1 (0.4)	0 (0)	–
Mycobacterium tuberculosis	1 (0.4)	1 (0.1)	0.374
Non-tuberculosis mycobacteria	0 (0)	1 (0.1)	–
Chlamydia psittaci	0 (0)	2 (0.2)	0.434

Table 3
Clinical characteristics of pneumonia with immunocompromised patients in different underlying disease.

Variables	Connective tissue disease, N = 72	Solid organ transplant, N = 94	Hematopoiesis diseases[a] N = 36	Idiopathic interstitial pneumonia or nephrotic syndrome, N = 7	Radiotherapy and chemotherapy of malignant solid tumor, N = 45	*P* value
Sex, female, n (%)	47 (65.3)	13 (13.8)	17 (47.2)	4 (57.1)	14 (31.1)	<0.001
Age, median (IGR)	65.0 (58.3, 80.0)	58.0 (48.3, 64.0)	70.0 (61.5, 78.8)	66.0 (58.0, 72.0)	70.0 (64.5, 76.0)	<0.001
Severe pneumonia index score	75.0 (56.3, 99.0)	81.0 (63.0, 99.3)	79.0 (68.0, 91.8)	92.0 (66.0, 104.0)	117.0 (90.5, 133.5)	<0.001
CURB65 score>1	24 (33.3)	26 (27.7)	13 (36.1)	3 (42.9)	18 (40.0)	0.614
Viral-aspergillus co-pathogen	3 (4.2)	22 (23.4)	2 (5.6)	2 (28.6)	3 (6.7)	0.001
Viral-bacteria co-pathogen	10 (13.9)	23 (24.5)	4 (11.1)	3 (42.9)	4 (8.9)	0.035
Other-virus co-pathogen	8 (11.1)	4 (4.3)	0 (0)	0 (0)	1 (2.2)	0.253
Treatment, n (%)						
Glucocorticoids	65 (90.3)	90 (95.7)	28 (77.8)	5 (71.4)	36 (80.0)	0.007
Antiviral drug						
Azvudine	5 (69.4)	7 (7.4)	1 (2.8)	1 (14.3)	2 (4.5)	–
Paxlovid	21 (29.2)	67 (71.3)	11 (30.6)	2 (28.6)	15 (33.3)	<0.001
Molnupiravir	0 (0)	0 (0)	0 (0)	0 (0)	1 (2.2)	–
Baricitinib	16 (22.2)	13 (13.8)	2 (5.6)	0 (0)	3 (6.7)	0.083
Tocilizumab	4 (5.6)	4 (4.3)	3 (8.3)	0 (0)	3 (6.7)	0.788
Complications, n (%)						
Noninvasive ventilation	20 (27.8)	35 (37.2)	5 (13.9)	3 (42.9)	14 (31.1)	0.112
Invasive mechanical ventilation	8 (11.1)	17 (18.1)	3 (8.3)	2 (28.6)	1 (2.2)	0.049
Respiratory failure	32 (44.4)	43 (45.7)	15 (41.7)	5 (71.4)	27 (60.0)	0.261
30-day mortality	15 (20.8)	18 (19.1)	8 (22.2)	1 (14.3)	8 (17.8)	0.978

[a] Hematopoiesis diseases: Leukemia, lymphoma, bone marrow or hematopoietic stem cell transplantation. In the connective tissue disease group, four patients received JAK-2 inhibitors, all of whom survived, while the rest were treated with methotrexate, tacrolimus, or corticosteroids.

46.8 % for those on non-invasive mechanical ventilation. In the immunocompetent group, the 30-day mortality rate was 25.0 % for current smokers and 23.8 % for patients with a history of ILD (Table 5.1, 5.2 and Fig. 1).

4. Discussion

This study retrospectively analyzed the characteristics and mortality risk factors in a large cohort of immunocompromised patients with COVID-19 pneumonia due to the Omicron variant. The key findings were: (1) immunocompromised patients experienced higher disease severity and 30-day mortality rates compared to immunocompetent patients; (2) bacterial infections were the most common co-infections in immunocompromised patients, followed by Aspergillus; (3) immunocompromised status was an independent predictor of COVID-19 prognosis, with current smoking and a history of ILD being poor prognostic factors in immunocompetent patients.

Comorbidities such as cardiovascular diseases, hypertension, diabetes, and cancer are well-established risk factors for severe COVID-19 [15,16], but the impact of immunodeficiency remains unclear. Given the association between COVID-19 and elevated cytokine production, immunosuppression might attenuate the excessive inflammatory response to infection [17]. Early studies

Table 4
Cox regression analysis of 30-d prognostic factors in COVID-19 patients.

Variables	All COVID-19 patients			Immunocompromised group			Immunocompetent group		
	OR	95%CI	*P* value	OR	95%CI	*P* value	OR	95%CI	*P* value
Troponin T ≥ 0.15 ng/ml	3.226	1.588–6.557	0.001				5.104	1.790–14.554	0.002
Respiratory failure	8.237	2.552–26.581	<0.001	10.099	1.309–77.944	0.027	13.187	3.156–55.106	<0.001
Lactic dehydrogenase≥272.5U/L	3.366	1.578–7.178	0.002	7.841	1.020–60.272	0.048	2.172	1.042–4.527	0.038
D-Dimer≥1.295 mg/L	2.336	1.192–4.578	0.013						
Interleukin-6≥11.67 ng/L	3.566	1.672–7.609	0.001				6.577	2.555–16.930	0.001
C-reactive protein≥90 mg/L	1.950	1.176–3.233	0.010						
Peripheral white blood count≥9.84*10^9	2.067	1.223–3.493	0.007	5.036	1.808–14.030	0.002			
Immunocompromised host	1.781	1.009–3.146	0.047						
Chronic heart failure				4.424	1.058–18.504	0.042			
Interstitial lung disease							3.611	1.805–7.221	<0.001
Pneumonia severity index							1.015	1.005–1.024	0.003
Current smoker							3.742	1.579–8.866	0.003

Tables 5–1
Comparison of 30-day mortality rates among different patient groups.

Variables (%)	Immunocompromised group			Immunocompetent group		
	Survivors (n = 204)	non-survivors (n = 50)	P-Value	Survivors (n = 717)	non-survivors (n = 114)	P-Value
Invasive mechanical ventilation	6 (2.9)	25 (50.0)	<0.001	15 (2.1)	29 (25.4)	<0.001
Noninvasive ventilation	41 (20.1)	36 (72.0)	<0.001	103 (14.4)	72 (63.2)	<0.001
Respiratory failure	75 (36.8)	47 (94.0)	<0.001	270 (37.7)	111 (97.4)	<0.001
Chronic heart failure	8 (3.9)	10 (20.0)	<0.001	67 (9.3)	22 (19.3)	0.001
Interstitial lung disease	52 (25.5)	13 (26.0)	0.941	48 (6.7)	15 (13.2)	0.015
Current smoker	6 (2.9)	1 (2.0)	0.716	39 (5.4)	13 (11.4)	0.015
Ex-smoker	48 (23.50	11 (22.0)	0.818	157 (21.9)	34 (29.8)	0.062

Tables 5–2
Comparison of 30-day mortality rates among different patient groups.

Variables (%)	Total	Immunocompromised group	Immunocompetent group	*P*-Value
30-day mortality in patients with invasive mechanical ventilation (n = 75)	31/75 (41.3)	25/31 (75.8)	29/44 (65.9)	0.162
30-day mortality in patients with noninvasive ventilation (n = 252)	108/252 (42.9)	36/77 (46.8)	72/175 (41.1)	0.407
30-day mortality in patients with respiratory failure (n = 503)	158/503 (31.4)	47/122 (38.5)	111/381 (29.1)	0.052
30-day mortality in patients with interstitial lung disease(n = 128)	28/128(21.9)	13/65 (20.0)	15/63 (23.8)	0.602
30-day mortality in patients with current smoker(n = 252)	14/59 (23.7)	1/7 (14.3)	13/52(25.0)	0.532

reported no significant difference in mortality between immunocompromised and immunocompetent patients with COVID-19 pneumonia [6,7]. However, large-scale studies early in the pandemic indicated a higher COVID-19 mortality rate in immunocompromised patients compared to immunocompetent ones [18]. A recent study with a substantial sample size found that, after adjusting for age, gender, ethnicity, vaccination status, and comorbidities, in-hospital mortality remained higher in immunocompromised patients, with less improvement in outcomes over time. Notably, mortality risks vary among different immunocompromising conditions; for instance, cancer patients exhibit higher death rates compared to those with other immunocompromising conditions [19]. This study confirmed that immunocompromised patients had higher illness severity and 30-day mortality rates than immunocompetent patients. The slower decline in COVID-19 mortality among immunocompromised individuals during the pandemic may have contributed to this discrepancy. Additionally, as most patients in the study did not receive antiviral therapy, immunocompromised patients, who had to rely primarily on their limited immune response, may have been unable to clear the virus effectively, potentially leading to higher mortality rates.

Our findings align with other Chinese cohort studies examining patients with cancer and COVID-19, where case fatality rates (CFR) ranged from 11 % to 21 %, varying according to cancer subtype and treatment regimen [20,21]. In particular, patients with hematologic malignancies have reported significantly higher COVID-19 CFRs, ranging from 32 % to 62 % [22,23]. In comparison, stem cell transplant recipients had a lower overall CFR of 27 %, while a study of 90 solid organ transplant recipients in New York City found a mortality rate of 18 % [24]. The Global Rheumatology Alliance also reported that among 600 patients with underlying rheumatologic diseases who contracted COVID-19, 46 % were hospitalized and 9 % died. Of these, 39 % were receiving JAK inhibitors or biologics [25]. Interestingly, biologics or JAK inhibitors alone were related to a lower risk of hospitalization, largely due to the protective effect of anti-TNF therapies. Brodin et al. [26] found that patients with CTD and organ transplant recipients on high-dose glucocorticoids had increased risks of hospitalization, cardiac complications, pulmonary embolism, and death from COVID-19. In this study, immunocompromised status was a significant predictor of mortality among COVID-19 patients. However, no obvious differences in mortality rates were found among the different subgroups of immunocompromised patients, possibly due to the limited sample size within each subgroup.

Regarding co-infections, a retrospective study from Spain by Garcia-Vidal and co-workers [27] reported that 3.1 % (31 of 989) of patients hospitalized with COVID-19 had community-acquired co-infections, with 2.5 % and 0.6 % being bacterial and viral, respectively. Similarly, a retrospective study from North America found a 3.7 % incidence of co-infections in hospitalized COVID-19 patients [28]. A meta-analysis by Rawson and colleagues [29] estimated the prevalence of fungal or bacterial co-infections in hospitalized COVID-19 patients to be around 8 %. Specifically, *Aspergillus* co-infection in COVID-19 patients can lead to acute respiratory distress syndrome. Another meta-analysis of 28 studies, including 3184 ICU-admitted COVID-19 patients, reported a cumulative incidence of 12.3 % for COVID-19-associated pulmonary aspergillosis (CAPA) [30]. In the current study, the immunocompromised group exhibited a higher incidence of bacterial and fungal infections compared with the immunocompetent group, highlighting the importance of vigilant monitoring for fungal co-infections in these patients.

Lee et al. [31] reported that patients with ILD and COVID-19 experience more severe clinical courses and higher mortality rates compared to those without ILD. This increased vulnerability was observed irrespective of the presence of CTD. While CTD itself was not linked to severe COVID-19 in patients with ILD, idiopathic pulmonary fibrosis was associated with both a higher susceptibility to

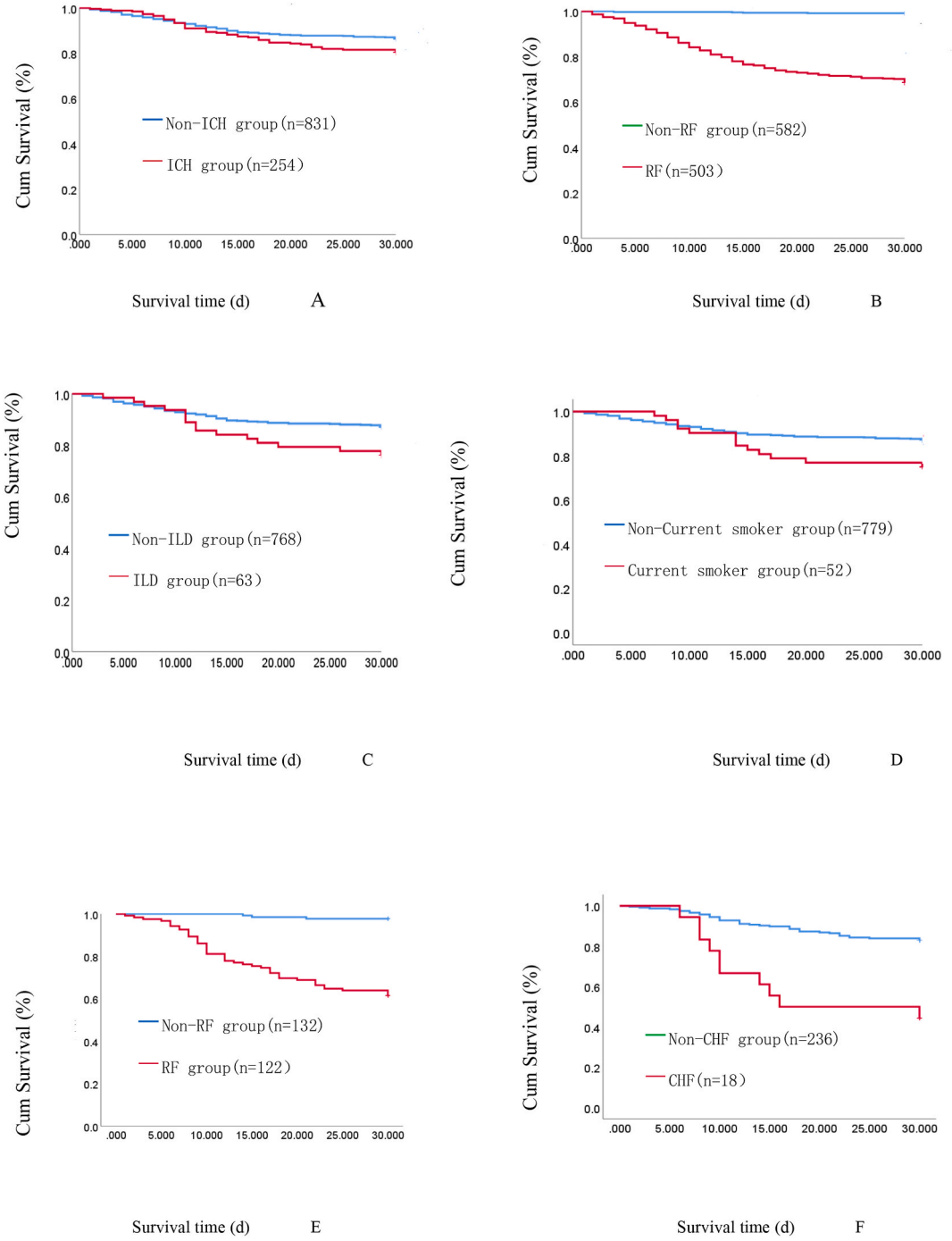

Fig. 1. A–B: Among all COVID-19 patients, the 30-day survival curve with the immunocompromised (ICH) group and respiratory failure (RF) group. C-D:Among immunocompetent COVID-19 patients, the 30-day survival curve for the group with interstitial lung disease (ILD) and current smoker group. E-F:Among the immunocompromised group, the 30-day survival curve for the group with respiratory failure(RF) and chronic heart failure(CHF).

COVID-19 and the greatest risk for severe disease outcomes. In our study, a history of interstitial pneumonia emerged as a poor prognostic factor among immunocompetent patients, highlighting the need for vigilance in this population during flu seasons. These patients should adopt preventive measures and seek timely antiviral and symptomatic treatment to reduce the risk of adverse outcomes. Tobacco use may exacerbate the severity of COVID-19. Early studies suggest that smokers are at a significantly increased risk of severe complications from COVID-19, including mechanical ventilation, intensive care unit admission, and severe health

consequences, compared to non-smokers [34]. Although smoking rates among COVID-19 patients appear to be lower than in the general population, the severity of disease and mortality is higher among smokers, highlighting the harmful impact of smoking on COVID-19 outcomes.

Nevertheless, this research has few limitations. It was carried out at a single center, and not all patients received early or effective antiviral therapy. Furthermore, data on COVID-19 vaccination status were not available for all participants, and metagenomic next-generation sequencing for co-infections was performed in only a few cases. Despite these limitations, our findings indicate that immunocompromised patients hospitalized with COVID-19 pneumonia due to the Omicron variant have higher mortality rates than immunocompetent patients. We identified several adverse prognostic factors, and future multicenter studies are necessary to validate these results.

5. Conclusions

In patients hospitalized with COVID-19 pneumonia caused by the Omicron variant, immunocompromised individuals exhibited greater illness severity and a higher 30-day mortality rate compared to their immunocompetent counterparts. Immunocompromised patients were particularly susceptible to bacterial co-infections, while immunocompetent patients had a higher prevalence of fungal co-infections. This study underscores the poor prognosis associated with COVID-19 pneumonia in immunocompromised patients, particularly those requiring invasive mechanical ventilation (IMV), who experienced significantly elevated 30-day mortality rates. These findings emphasize the critical need for vigilant monitoring and prompt intervention in immunocompromised patients with COVID-19 pneumonia.

CRediT authorship contribution statement

Xiaoyan Li: Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **Lijuan Li:** Writing – original draft, Project administration, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Ethics approval and consent to participate

The Ethics Committee of China-Japan Friendship Hospital (no. 2023-KY-286) granted approval for this retrospective study and facilitated the centralized collaboration and approval of all participating institutions.

Availability of data and materials

All data collected or analyzed throughout this research are presented in this article and its supplementary materials.

Transparency declarations

None to declare.

Data sharing statement

No other information is accesssible.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Abbreviations

Abbreviation	Definition
CFR	Case fatality rate
CI	Confidence interval
CTD	Connective tissue disease
HR	Hazard ratio
IL-6	Interleukin 6
ILD	Interstitial lung disease
IMV	Invasive mechanical ventilation
RT-PCR	Real-time reverse-transcription polymerase chain reaction
TNF	Tumour necrosis factor

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