JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Coronavirus Pandemic

Association between vaccination and days of hospitalization in adult patients with non-severe COVID-19

Xiao Ding[1 #], Jiru Ye[2 #], Yao Tang[3], Feng Zhu[1]

[1] Department of Respiratory and Critical Care Medicine, Wuxi Fifth People's Hospital, Wuxi 214000, China
[2] Department of Respiratory and Critical Care Medicine, the Third Affiliated Hospital of Soochow University, Changzhou 213003, China
[3] Tuberculosis Department, Huai'an No. 4 People's Hospital, HuaiAn 223000, China

# Authors contributed equally to this work.

Abstract

Introduction: To explore the association between vaccination status and the days of hospitalization in non-severe adult COVID-19 patients.
Methodology: We retrospectively analyzed the 368 non-severe adult COVID-19 patients which were divided into three groups according to their vaccination status. Univariate and multivariate linear regression analysis were performed to determine the correlation between vaccination and the days of hospitalization. A generalized additive model and hierarchical linear regression model were used for outcome analysis.
Results: In the regression equation, the increase in the number of vaccine shots was significantly correlated with the decrease in the days of hospitalization (all $p < 0.001$). Particularly, the reduction of the days of hospitalization in patients with 3 injections of the vaccine was more significant than that of the 0-1 injection group (β: -2.810, -2.525, and -2.831; $p < 0.001$). Curve fitting showed that the relationship between the number of vaccination injections and the days of hospitalization was approximately linear, and the β value was -1.522 (95% CI: -2.091 − -0.954; $p < 0.001$). Among various laboratory indexes, only the monocyte ratio significantly affected the correlation between the number of vaccination injections and the days of hospitalization, indicating an interaction (p =0.027). The β values of the monocyte ratio in normal and elevated groups were -2.230 (95% CI: -3.048 − -1.412; $p < 0.001$) and -0.763 (95% CI: -1.520 − -0.005; $p = 0.050$), respectively.
Conclusions: In non-severe adult COVID-19 patients, there was a negative linear correlation between the vaccination status and the days of hospitalization.

Key words: COVID-19 patients; non-severe; vaccination; days of hospitalization; association.

J Infect Dev Ctries 2024; 18(1):34-43. doi:10.3855/jidc.18255

(Received 22 March 2023 – Accepted 21 July 2023)

Introduction

COVID-19 is a serious acute respiratory syndrome caused by coronavirus 2 (SARS-CoV-2). Since the first case was reported in 2019, COVID-19 has spread rapidly worldwide and significantly impacted human beings [1,2]. As of August 11, 2022, SARS-CoV-2 had caused more than 584 million infections and 6.41 million deaths worldwide [3]. During the pandemic, SARS-CoV-2 has produced many variants, especially the recently appeared Omicron variant, which is highly infectious and has caused multiple waves of infections [4].

Therefore, in the absence of effective preventive medicines and treatment methods, the COVID-19 vaccine is considered to help reduce transmission, prevent infection, and control disease [5]. Currently, the COVID-19 vaccine has become an important strategy for dealing with the pandemic. Many countries are carrying out large-scale vaccination campaigns and actively implementing the vaccination plan of booster vaccines [3,6]. The vaccines currently used in China mainly include inactivated vaccines, adenovirus vector vaccines, and recombinant subunit vaccines, of which inactivated vaccines are the main type [7]. Studies have shown that inactivated vaccines have good tolerability, immunogenicity, and immune persistence [8], and three injections of inactivated vaccines can significantly improve the IgG-positive rate in the population, which plays an important role in avoiding serious symptoms, hospitalization, and deaths [9]. Although the inactivated vaccines elicited strong antibody responses, some fully vaccinated people can still be infected with SARS-CoV-2, called breakthrough infection [10]. However, patients with breakthrough infections are mainly asymptomatic or only exhibit mild symptoms [11], and the virus clearance time is shorter [12,13]. The impact

of the vaccine on SARS-CoV-2 is complicated, some studies proposed that the COVID-19 vaccine may reduce the severity of the disease, but it will lead to the long-term spread of infectious viruses, which will have an important impact on public health [14]. Moreover, most COVID-19 vaccines were developed to target early epidemic variants [15]. Therefore, it is necessary to continuously evaluate the effectiveness of the vaccines against newly emerged COVID-19 variants.

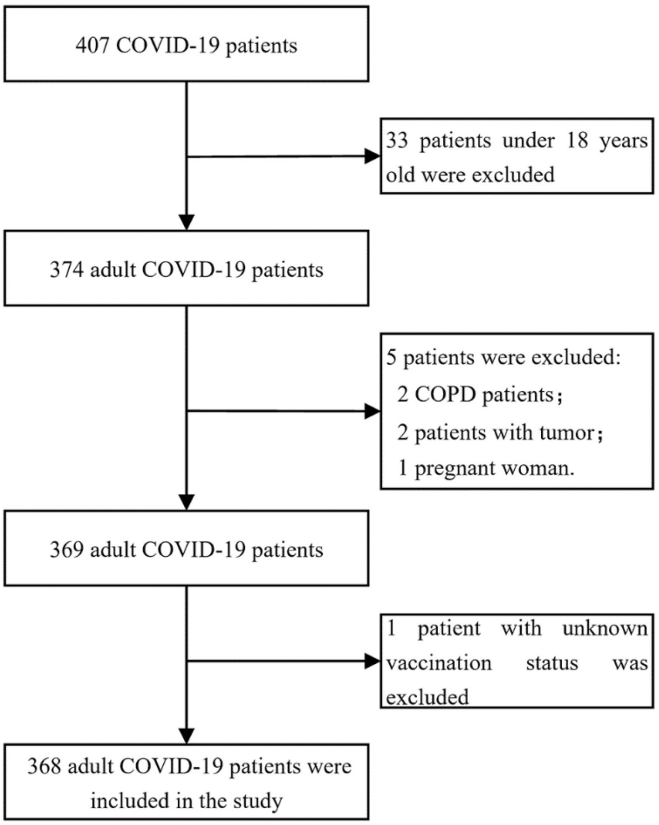
In this study, we analyzed the relationship between the vaccination status and clinical characteristics of hospitalized, non-severe adult COVID-19 patients. Specifically, we explored the association between the vaccination status and the length of hospital stay of COVID-19 patients to evaluate the effectiveness of the COVID-19 vaccine and provide important information for the control of COVID-19 transmission and vaccination policies.

Methodology

General data

We retrospectively analyzed the data of 407 patients hospitalized in the negative pressure ward of Wuxi Fifth People's Hospital from May 2, 2022, to May 14, 2022, to treat novel coronavirus infection. Genetic sequencing results showed that the virus was the Omicron variant BA. 2.2. Patient inclusion criteria: 1) The novel coronavirus nucleic acid was detected by real-time fluorescent RT-PCR. 2) The manifestation of the disease met the diagnostic criteria of Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 9) [16], it mainly includes asymptomatic infections and mild and moderate patients. Patient exclusion criteria: 3) Patients under the age of 18. 4) Patients with chronic obstructive pulmonary disease (COPD) or tumor. 5) Pregnant women. 6) Patients with unknown COVID-19 vaccination status. The general clinical data and test results of laboratory indexes of patients were collected. This study was conducted in compliance with the Helsinki Declaration and was approved by the Institutional Ethics Committee (Ethics No.: Lunzi No. 2022-016-1). The data were anonymous, and thus no informed consent was required. The research flow chart is shown in Figure 1.

Figure 1. The research flow chart.



COVID-19 diagnosis, treatment, and discharge criteria

Diagnosis and treatment of COVID-19

A novel coronavirus nucleic acid test positive was the primary standard for COVID-19 diagnosis, and the final diagnosis was made according to a comprehensive analysis of epidemiological history, clinical manifestations, and laboratory test results. According to the Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 9) published by the General Office of the National Health Commission of China, COVID-19 patients were divided into mild (mild clinical symptoms, no pneumonia feature on imaging), moderate (with low fever, mild fatigue and other symptoms, and pneumonia feature on imaging), severe (patients met any of the following criteria: shortness of breath, RR ≥ 30 times/minute; in resting state, oxygen saturation ≤ 93%; arterial partial pressure of oxygen/inspired oxygen concentration ≤ 300 mmHg; clinical symptoms worsened progressively and pulmonary imaging showed that the lesions had significantly progressed > 50% within 24-48 hours), and critical cases (patients met any of the following criteria: respiratory failure that required mechanical ventilation; shock; combined with other organ failures that required ICU monitoring and treatment). Patients who had no obvious clinical symptoms after novel coronavirus infection were defined as asymptomatic infected patients. The treatment plan of all patients was implemented according to the Diagnosis and Treatment Protocol of Novel Coronavirus Pneumonia (Trial Version 9).

Discharge criteria

Body temperature returned to normal for more than 3 days. Respiratory symptoms improved significantly. Pulmonary imaging showed that the acute exudative lesions were improved considerably. The cycle threshold (Ct) of virus N gene and ORF gene was ≥ 35 in two consecutive novel coronavirus nucleic acid tests (fluorescent quantitative PCR method with the threshold value of 40, and sampling interval was at least 24 hours), or novel coronavirus nucleic acid test was negative in two consecutive trials (fluorescent quantitative PCR method with the threshold value of lower than 35, and sampling interval was at least 24 hours). The patient can be discharged if all the above criteria are met.

Laboratory tests

Patients' throat or nose swab samples were collected for RT-PCR tests. The ORF gene and N gene of SARS-CoV-2 were detected according to the kit's instructions, and the results showed the Ct values of the two genes.

The patient's venous blood was collected for various laboratory tests. The blood routine was analyzed using the Sysmex XN9000 blood analyzer (Sysmex, Hyogo, Japan). The liver function indexes of patients were determined using the automatic biochemical analyzer (Beckman Coulter AU5800, Brea, CA, USA). The high-sensitivity C-reactive protein (hs-CRP) was detected using the specific protein analyzer HP-083/4 (Hipro Biotechnology, Shijiazhuang, China). The blood coagulation function was detected by Sysmex CS5100 automatic blood coagulation analyzer (Sysmex, Kobe, Japan). COVID-19 IgG and IgM antibodies were detected using the colloidal gold method with the reagents produced by Nanjing Vazyme Medical Technology Co., Ltd.

Statistical analysis

R software (version 4.2.0; http://www.R-project.org) was used to analyze the data statistically. The continuous variables were expressed as the mean (standard deviation) (normal distribution) or the median (Q1-Q3) (skewed distribution). Categorical variables were expressed as the frequency or percentage (%). The χ^2 test (categorical variables), T-test (normal distribution), or Mann-Whitney U test (skewed distribution) were used to detect the difference in general clinical data and laboratory indexes between different vaccination groups.

Univariate and multivariate linear regression analyses were performed to determine the correlation between the number of vaccination injections and the days of hospital stay and further generate three different models, including an unadjusted model, a preliminary adjusted model, and a fully adjusted model. For multivariate regression analysis, the confounding variables were the clinical indexes such as gender, age, and complications before vaccination. Afterward, the vaccination status was used as categorical data to calculate *p* values for the trend.

After the confounding factors were fully adjusted, the generalized additive model (GAM) was used for curve fitting, and the piecewise linear regression model was used to evaluate whether the fitting curve had a threshold effect. In different subgroups of laboratory indexes (normal group vs. elevated group), a stratified linear regression model was used to evaluate whether there was an interaction between vaccination and the number of days of hospitalization. The effect value with a 95% confidence interval was recorded. All statistical analyses were two-tailed, and $p < 0.05$ was considered statistically significant.

Results

The vaccination status of the patients was as follows: 12 patients were unvaccinated (0 injections, 3.3%), 12 patients received one injection (3.3%), 51 patients received two injections (12.9%), and 293 patients received three injections (79.6%). The vaccines were all injected. Those who received 1 injection were all inactivated vaccines. Only 3 of those who received 2 injections used adenovirus vector vaccine for both injections (3/51), and only 5 of those who received 3 injections used 2 inactivated vaccines and 1 adenovirus vector vaccine (5/293). At admission, 51 patients had a fever (13.9%), and imaging examination showed that one patient had unilateral pneumonia (0.3%) and three patients had bilateral pneumonia (0.8%). The clinical classification of the patients included 359 cases of asymptomatic type (97.6%), 5 cases of mild type (1.4%), and 4 cases of moderate type of COVID-19 (1.1%). The patients' average length of hospital stay was 12.9 ± 3.2 days (range: 7-21 days). The patients were divided into three groups according to the vaccination status: 0-1 injection group, 2 injections group, and 3 injections group.

General clinical data and laboratory indexes of the three groups of COVID-19 patients

A comparison of the general clinical data and laboratory tests of the three groups is shown in Table 1. The results showed that the patients in the 0-1 injection group were older ($p < 0.001$), and the proportion of patients with high blood pressure and cardio-

cerebrovascular diseases was higher in this group ($p < 0.001$). In the three groups, the 0-1 injection group was more likely to have fever symptoms once infected with coronavirus ($p = 0.002$). Therefore, this group's proportion of mild-moderate COVID-19 was also higher ($p = 0.026$). The positive rate of IgM antibody in all three groups was low and had no significant difference between groups ($p = 1.000$). In contrast, the positive rate of IgG antibody in the three groups gradually increased and had significant differences ($p < 0.05$). The positive IgG rate in the 0-1 needle group was the lowest (4.2%). In all three groups, the Ct values of N and ORF genes decreased gradually before admission. The difference in N gene was insignificant ($p = 0.054$), while the difference in ORF gene was significant ($p = 0.045$). The D-dimer of the three groups also decreased gradually and had a significant difference ($p = 0.019$). Regarding the number of days of hospitalization, the three groups gradually decreased and had significant differences ($p < 0.001$).

Univariate analysis of patient's general clinical data, laboratory indexes, and days of hospitalization

Univariate linear regression analysis was conducted with the number of days in the hospital as the dependent variable and general clinical data and laboratory tests as the independent variables (Table 2). The age, gender, vaccination status, fever, IgG antibody, neutrophil ratio, lymphocyte ratio, monocyte ratio, lymphocyte count, and monocyte count of patients were all possible related factors for the days of hospitalization ($p < 0.05$), of which age, fever, neutrophil ratio, monocyte ratio, and monocyte count were risk factors (β values: 0.034−1.623), whereas male, vaccination status, IgG

Table 1. Comparison of general clinical data and laboratory indexes of patients with different numbers of COVID-19 vaccine injections.

Vaccination status	Total	0-1 injection	2 injections	3 injections	*p* value
N	368	24	51	293	
Age	47.0 (11.7)	53.1 (19.2)	42.3 (12.5)	47.4 (10.4)	< 0.001
Gender					
Female	167 (45.4%)	12 (50.0%)	26 (51.0%)	129 (44.0%)	**0.586**
Male	201 (54.6%)	12 (50.0%)	25 (49.0%)	164 (56.0%)	
Smoking	76 (20.7%)	6 (25.0%)	9 (17.7%)	61 (20.8%)	0.755
Complications					
High blood pressure	45 (12.2%)	10 (41.7%)	3 (5.9%)	32 (10.9%)	< 0.001
Diabetes	20 (5.4%)	2 (8.3%)	3 (5.9%)	15 (5.1%)	0.791
Cardio-cerebrovascular diseases	9 (2.5%)	5 (20.8%)	0 (0.0%)	4 (1.4%)	< 0.001
Chronic liver and kidney diseases/cirrhosis	7 (1.9%)	1 (4.2%)	0 (0.0%)	6 (2.1%)	0.298
Fever	51 (13.9%)	9 (37.5%)	8 (15.7%)	34 (11.6%)	0.002
Highest body temperature	38.1 (0.6)	38.0 (0.5)	38.4 (0.7)	38.1 (0.6)	0.346
Imaging (pneumonia)	4 (1.1%)	1 (4.2%)	0 (0.0%)	3 (1.0%)	0.318
Typing					**0.026**
Asymptomatic	359 (97.6%)	21 (87.5%)	50 (98.0%)	288 (98.3%)	
Mild-moderate	9 (2.4%)	3 (12.5%)	1 (2.0%)	5 (1.7%)	
N gene	29.20 (5.84)	31.09 (5.57)	30.40 (5.78)	28.83 (5.84)	0.054
ORF gene	28.09 (6.02)	29.89 (5.86)	29.50 (5.60)	27.70 (6.06)	0.045
IgM					1.000
Negative	361 (98.1%)	24 (100.0%)	50 (98.0%)	287 (98.0%)	
Positive	7 (1.9%)	0 (0.0%)	1 (2.0%)	6 (2.0%)	
IgG					< 0.001
Negative	168 (45.7%)	23 (95.8%)	43 (84.3%)	102 (34.8%)	
Weak positive	54 (14.7%)	0 (0.0%)	1 (2.0%)	53 (18.1%)	
Positive	146 (39.7%)	1 (4.2%)	7 (13.7%)	138 (47.1%)	
Laboratory tests at admission					
white blood cell (10^9/L)	5.44 (1.96)	5.19 (2.06)	5.31 (1.94)	5.48 (1.96)	0.697
Neutrophil ratio (%)	61.64 (11.84)	59.27 (13.18)	60.75 (13.74)	61.99 (11.38)	0.473
Lymphocyte ratio (%)	26.13 (10.34)	27.23 (10.74)	26.98 (11.91)	25.89 (10.04)	0.680
Monocyte ratio (%)	10.33 (3.99)	11.81 (4.79)	10.91 (4.25)	10.11 (3.85)	0.072
Neutrophil count (10^9/L)	3.49 (1.79)	3.25 (2.06)	3.39 (1.86)	3.52 (1.76)	0.702
Lymphocyte count (10^9/L)	1.32 (0.52)	1.29 (0.59)	1.32 (0.55)	1.32 (0.51)	0.975
Monocyte count (10^9/L)	0.54 (0.23)	0.57 (0.22)	0.54 (0.24)	0.53 (0.23)	0.664
High-sensitivity C-reactive protein (mg/L)	0.50 (0.20-132.60)	0.50 (0.50-34.60)	0.50 (0.50-33.40)	0.50 (0.20-132.60)	0.613
D-dimer (ug/mL)	0.22 (0.22-9.30)	0.29 (0.22-1.73)	0.25 (0.22-9.30)	0.22 (0.22-2.35)	0.019
Glutamic pyruvic transaminase (U/L)	18.0 (5.0-396.0)	17.5 (8.0-72.0)	19.0 (7.0-396.0)	18.0 (5.0-135.0)	0.996
Glutamic oxaloacetic transaminase (U/L)	20.0 (10.0-257.0)	23.0 (12.0-144.0)	22.0 (15.0-257.0)	20.0 (10.0-108.0)	0.235
Days of hospitalization	12.9 (3.2)	15.3 (3.3)	14.0 (3.4)	12.4 (3.1)	< 0.001

Results in the table: Mean (SD), Median (Min-Max) / N (%).

antibody, lymphocyte ratio, and lymphocyte count were protective factors (β values: -0.056 − -2.810).

Multivariate linear regression analysis of vaccination status and days of hospitalization

Multivariate linear regression analysis was conducted to evaluate the correlation between vaccination status and days of hospitalization by adjusting the confounding variables, which were clinical indexes before vaccination, including gender, age, high blood pressure, and cardio-cerebrovascular diseases. Unadjusted confounding variables were equivalent to univariate linear regression analysis, and preliminarily adjusted confounding variables included gender and age. Fully adjusted confounding variables included gender, age, high blood pressure, and cardio-cerebrovascular diseases. In the regression equations with unadjusted, preliminarily adjusted, and fully adjusted confounding variables, the increase in the number of vaccinations was significantly correlated with the decrease in the number of days of hospital stay ($p < 0.001$). The reduction in the days of hospitalization was especially significant in 3 injections group compared with that in 0-1 injection group (β values were -2.810, -2.525, and -2.831, respectively; all $p < 0.001$) (Table 3).

Smooth curve fitting

After fully adjusting the confounding variables (gender, age, high blood pressure, cardio-cerebrovascular diseases), with the increase in vaccination times, the length of hospitalization of patients was 15.3 days (95% CI: 13.9-16.6), 14.2 days (95% CI: 13.2-15.1), and 12.4 days (95% CI: 12.0-12.9) respectively (Figure 2), showing a linear relationship. The β value was -1.522 (95% CI: -2.091 − -0.954; $p < 0.001$) (Table 4). Furthermore, the piecewise linear regression model was used to evaluate whether the

Table 2. Univariate analysis of general clinical data, laboratory indexes, and days of hospitalization.

	Statistics	β (95%CI)	*p* value
Age	47.0 ± 11.7	0.040 (0.012, 0.068)	0.006
Gender			
Female	167 (45.4%)	0	
Male	201 (54.6%)	-1.007 (-1.666, -0.349)	0.003
Smoking	76 (20.7%)	-0.369 (-1.187, 0.450)	0.378
Complications			
High blood pressure	45 (12.2%)	-0.001 (-1.014, 1.012)	0.999
Diabetes	20 (5.4%)	0.957 (-0.503, 2.417)	0.200
Cardio-cerebrovascular diseases	9 (2.4%)	1.070 (-1.075, 3.215)	0.329
Chronic kidney disease/chronic liver disease/liver cirrhosis	7 (1.9%)	1.323 (-1.102, 3.748)	0.286
Vaccination status			
0-1 injection	24 (6.5%)	0	
2 injections	51 (13.9%)	-1.211 (-2.735, 0.313)	0.120
3 injections	293 (79.6%)	-2.810 (-4.117, -1.503)	< 0.001
Fever	51 (13.9%)	1.136 (0.183, 2.089)	0.020
Highest body temperature	38.1 ± 0.6	1.050 (-0.479, 2.579)	0.185
Imaging (pneumonia or not)	4 (1.1%)	1.420 (-1.776, 4.617)	0.384
Classification (two categories)			
Asymptomatic	359 (97.6%)	0	
Mild-moderate	9 (2.4%)	1.070 (-1.075, 3.215)	0.329
N gene	29.20 ± 5.84	-0.005 (-0.062, 0.052)	0.866
ORF gene	28.10 ± 6.02	0.007 (-0.048, 0.062)	0.807
IgM			
Negative	361 (98.1%)	0	
Positive	7 (1.9%)	-1.444 (-3.869, 0.981)	0.244
IgG			
Negative	168 (45.7%)	0	
Weak positive	54 (14.7%)	-1.205 (-2.162, -0.248)	0.014
positive	146 (39.7%)	-1.955 (-2.647, -1.263)	< 0.001
Laboratory tests at admission			
White blood cell (10^9/L)	5.44 ± 1.96	-0.002 (-0.172, 0.167)	0.980
Neutrophil ratio (%)	61.64 ± 11.84	0.034 (0.006, 0.062)	0.016
Lymphocyte ratio (%)	26.13 ± 10.34	-0.056 (-0.088, -0.025)	< 0.001
Monocyte ratio (%)	10.33 ± 3.99	0.144 (0.062, 0.226)	< 0.001
Neutrophil count (10^9/L)	3.49 ± 1.79	0.115 (-0.071, 0.300)	0.226
Lymphocyte count (10^9/L)	1.32 ± 0.52	-1.476 (-2.098, -0.855)	< 0.001
Monocyte count (10^9/L)	0.54 ± 0.23	1.623 (0.167, 3.079)	0.030
High-sensitivity C-reactive protein (mg/L)	3.11 ± 8.65	0.014 (-0.025, 0.054)	0.480
D-dimer (ug/mL)	0.34 ± 0.53	0.256 (-0.377, 0.889)	0.428
Glutamic pyruvic transaminase (U/L)	25.25 ± 27.74	0.002 (-0.010, 0.014)	0.760
Glutamic oxaloacetic transaminase (U/L)	24.37 ± 17.83	0.008 (-0.010, 0.027)	0.379

Results in the table: Mean ± SD / N (%).

Table 3. Multiple regression equations of the impact of vaccination on the days of hospital stay.

Exposure	Unadjusted	Preliminary adjusted	Fully adjusted
Vaccination status			
0-1 injection	0	0	0
2 injections	-1.211 (-2.735, 0.313) 0.120	-0.787 (-2.311, 0.738) 0.313	-1.098 (-2.679, 0.482) 0.174
3 injections	-2.810 (-4.117, -1.503) < 0.001	-2.525 (-3.817, -1.233) < 0.001	-2.831 (-4.190, -1.472) < 0.001
P for trend	< 0.001	< 0.001	< 0.001

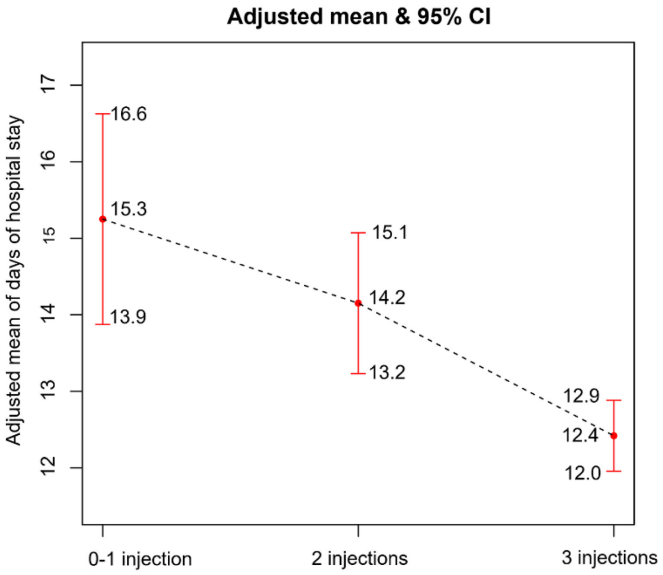
Data in the table: β (95% CI), *p* value. Unadjusted model adjust for: None; Preliminary adjusted model adjust for: gender, age; Fully adjusted model adjust for: gender, age, high blood pressure, cardio-cerebrovascular diseases.

fitting curve had a threshold effect. The log-likelihood ratio test results showed that at breakpoint 2, there was no statistical significance ($p = 0.569$). Model I should be selected as a linear effect.

Interaction analysis

After adjusting the confounding variables, the correlation between vaccination status and the number of days of hospitalization was compared in different laboratory indexes subgroups, and the results showed that the interaction only existed in the monocyte ratio subgroup ($p = 0.027$) (Table 4, Figure 3A). GAM test results showed that in the normal monocyte ratio subgroup (≤ 10%), with the increase of vaccination injections, the patients' hospital stay was 15.3 days (0-1 injection, 95% CI: 13.3-17.2), 14.7 days (2 injections, 95% CI: 13.5-15.9), and 11.9 days (3 injections, 95% CI: 11.3-12.4), respectively (Figure 3B), showing a nearly linear relationship (log-likelihood ratio test $p = 0.301$), with the β value of -2.230 (95% CI: -3.048 − -1.412; $p < 0.001$) (Table 4). In the monocyte ratio elevated subgroup (> 10%), with the increase of vaccination injections, the hospital stay of patients was 15.2 days (0-1 injection, 95% CI: 13.4-16.9), 13.5 days (2 injections, 95% CI: 12.2-14.8) and 13.1 days (3 injections, 95% CI: 12.5-13.7), respectively (Figure 3C), showing an approximately linear relationship (log-likelihood ratio test $p = 0.691$), with the β value of -0.763 (95% CI: -1.520− -0.005; $p = 0.050$) (Table 4).

Figure 2. The association between vaccination status and days of hospital stay.



The black dotted line represents the fitting line of the number of days in hospital and vaccination; the red line is the 95% confidence interval; the curve was adjusted for gender, age, high blood pressure, and cardio-cerebrovascular diseases.

Table 4. Analysis of the threshold effect between vaccination status and the number of days of hospitalization (different monocyte ratio subgroups).

Monocyte ratio (%) subgroup	Normal group (≤ 10%)	Elevated group (> 10%)	Total
Model I			P-interaction: 0.027
One line effect	-2.230 (-3.048, -1.412) <0.001	-0.763 (-1.520, -0.005) 0.050	-1.522 (-2.091, -0.954) < 0.001
Model II			P-interaction: 0.025
Breakpoint (K)	2	2	2
< K-segment effect 1	-1.090 (-3.432, 1.252) 0.363	-1.149 (-3.237, 0.940) 0.283	-1.098 (-2.679, 0.482) 0.174
> K-segment effect 2	-2.749 (-4.040, -1.458) < 0.001	-0.554 (-1.850, 0.742) 0.403	-1.733 (-2.659, -0.806) < 0.001
Difference in effect between 2 and 1	-1.659 (-4.852, 1.535) 0.310	0.594 (-2.400, 3.589) 0.698	-0.634 (-2.840, 1.571) 0.574
Predicted value of equation at the breakpoint	14.444 (13.244, 15.645)	13.583 (12.382, 14.785)	14.039 (13.177, 14.901)
Log-likelihood ratio tests	0.301	0.691	0.569

Data in the table: β (95% CI), *p* value; Adjusted variables: gender, age, high blood pressure, and cardio-cerebrovascular diseases.

Discussion

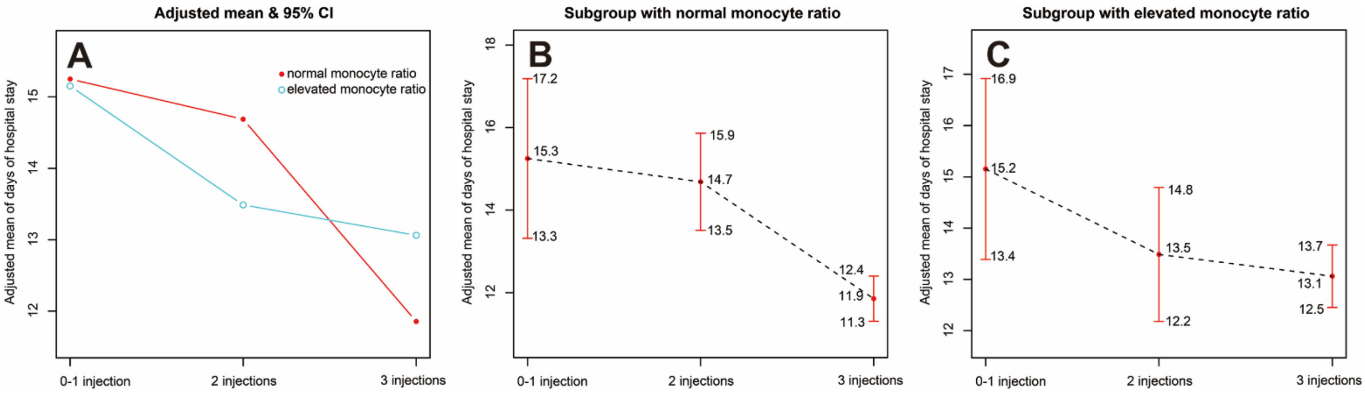
With the continuous spread and mutation of SARS-CoV-2, various SARS-CoV-2 variants have emerged. The Omicron variant has become the main epidemic strain [17,18]. It has higher infectivity and immune escape ability [19] and is prone to cause breakthrough infections, which poses a new challenge to the effectiveness of vaccines [3]. Our study found that with the increase in vaccination times, the length of hospital stay of non-severe adult COVID-19 patients gradually decreased, and the decrease was more significant in patients with a normal monocyte ratio at admission.

In our study, most the patients with COVID-19 had received booster injections. Most of the patients had asymptomatic infections, the proportion of mild and moderate COVID-19 was high among the patients who had not been vaccinated or partially vaccinated, and no patients had developed serious diseases. These data demonstrate that the COVID-19 vaccine was very effective in preventing serious infections, which is consistent with most research results [6,11,20-22]. We found that the Ct values of the N gene and ORF gene of patients who received booster injections were both low at admission, which was different from other results. Although the Ct value is not a direct measure of viral load, it is negatively correlated with the viral load. A lower Ct value indicated that patients had higher infectivity [23-25]. Some studies believe that the Ct values of the samples from vaccinated and unvaccinated patients at the initial admission are similar [7,26]. However, Accorsi et al. [27] believed that vaccinated patients' Ct value was higher when admitted to the hospital, which may be related to the heterogeneity of the patient's course of disease. In addition, at grouping, because the number of unvaccinated and partially vaccinated patients was small, we combined them into one group and subdivided the vaccinated patients into a complete vaccination group and enhanced vaccination with a booster injection group, which may lead to different results.

Vaccination can reduce the risk of SARS-CoV-2 infection and accelerate the elimination of the virus [28,29]. Our research also showed that with the increased number of vaccinations, the number of days of patients' hospital stay decreased gradually, which was especially significant in patients who received the booster vaccination. This relationship is not affected by confounding factors, consistent with the findings of Kissler *et al.* [23] and Havers *et al.* [30]. It can be seen that among breakthrough infection patients, although vaccination may not reduce the viral load in the upper respiratory tract of patients, it can shorten the time needed to eliminate the virus, effectively reduce the transmissibility of patients, and is conducive to the rapid recovery of COVID-19 patients.

Tian *et al.* [7] pointed out that, compared with patients without vaccination, patients infected with SARS-CoV-2 after vaccination can rapidly produce IgG antibodies at the early stage of the disease. Yang *et al.* [9] also found that the level of IgG antibodies in the enhanced vaccination with booster injection group was higher than in other groups, and the positive IgG rate could reach up to 100%. Our study also confirmed that the positive rate of IgG antibodies was the highest in patients who received booster injections, and this humoral immune response was attributed to the function of the vaccine [8]. Cellular immunity is also an

Figure 3. The association between vaccination status and days of hospitalization in the monocyte ratio subgroup.



The black dotted line represents the fitting line of the number of days in hospital and vaccination; the red line is the 95% confidence interval; the curve was adjusted for gender, age, high blood pressure, cardio-cerebrovascular diseases. **A:** the relationship between vaccination status and the number of days of hospitalization in the population with normal and elevated monocyte ratio. **B:** the subgroup with normal monocyte ratio. **C:** the subgroup with elevated monocyte ratio).

important part of the immune response [31], but the cellular immunity induced by SARS-CoV-2 infection does not necessarily have a protective effect [32]. The pathogenesis of COVID-19 is associated with immune overactivity [33]. As one of the primary immune cells, monocytes have been demonstrated to play an important role in excessive immune response and inflammation, which can lead to cytokine storms and serious clinical symptoms [34,35]. The increase in the monocyte population has been considered a risk factor for disease progression and death caused by COVID-19 [36]. Our research conducted a hierarchical analysis of the monocyte ratio and found that the positive rate of IgG was higher in the population with a normal monocyte ratio at admission (Supplementary Table 1). With the increased vaccination injections, the hospital stay was shortened more significantly in patients with normal monocyte ratio, indicating that patients with an appropriate cellular immune response after SARS-CoV-2 infection have greater vaccine benefits.

Our research still has some limitations. First, this is a retrospective single-center study. There may be bias in the enrollment of patients (for example, the number of patients with 2 vaccine injections is too small). Secondly, we did not subdivide the vaccination time and vaccine type, which may affect the analysis results. Finally, our research population was adults, and the results may not apply to children.

Conclusions

In conclusion, in non-severe COVID-19 adult patients, with the increase of vaccination injections, the days of patients' hospital stay decreases gradually, and the hospital stay was shorter in patients with normal monocyte ratio on admission. It can be seen that for the Omicron variant, COVID-19 vaccine injection is effective for protection, especially with booster injection, which provides valuable information for controlling virus transmission and vaccination policy.

Ethics approval and informed consent

This study was approved by the Institutional Ethics Committee of Wuxi Fifth People's Hospital for retrospective analysis (Lunzi No. 2022-016-1). The data were anonymous, and thus no informed consent was required.

Funding

This study was supported by Young Talent Development Plan of Changzhou Health Commission (CZQM2020039).

Availability of data and material

All data generated or analyzed during this study are available from the corresponding author upon reasonable request.

Authors' contributions

Conceptualization, YT and FZ; methodology, JY; software, FZ; validation, XD, JY, YT and FZ; formal analysis, XD; investigation, XD; resources, JY; data curation, XD; writing—original draft preparation, XD and JY; writing—review and editing, YT and FZ; project administration, FZ; funding acquisition, FZ. All authors have read and agreed to the published version of the manuscript.

References

1. Buturovic L, Zheng H, Tang B, Lai K, Kuan WS, Gillett M, Santram R, Shojaei M, Almansa R, Nieto JA, Munoz S, Herrero C, Antonakos N, Koufargyris P, Kontogiorgi M, Damoraki G, Liesenfeld O, Wacker J, Midic U, Luethy R, Rawling D, Remmel M, Coyle S, Liu YE, Rao AM, Dermadi D, Toh J, Jones LM, Donato M, Khatri P, Giamarellos-Bourboulis EJ, Sweeney TE (2022) A 6-mRNA host response classifier in whole blood predicts outcomes in COVID-19 and other acute viral infections. Sci Rep 12: 889. doi: 10.1038/s41598-021-04509-9.
2. Huang CL, Fei L, Li W, Xu W, Xie XD, Li Q, Chen L (2021) A novel prediction model for long-term SARS-CoV-2 RNA shedding in non-severe adult hospitalized patients with COVID-19: a retrospective cohort study. Infect Dis Ther 10: 897-909. doi: 10.1007/s40121-021-00437-3.
3. Shao W, Chen X, Zheng C, Liu H, Wang G, Zhang B, Li Z, Zhang W (2022) Effectiveness of COVID-19 vaccines against SARS-CoV-2 variants of concern in real-world: a literature review and meta-analysis. Emerg Microbes & Infect 11: 2383-2392. doi: 10.1080/22221751.2022.2122582.
4. Servellita V, Syed AM, Morris MK, Brazer N, Saldhi P, Garcia-Knight M, Sreekumar B, Khalid MM, Ciling A, Chen PY, Kumar GR, Gliwa AS, Nguyen J, Sotomayor-Gonzalez A, Zhang Y, Frias E, Prostko J, Hackett J, Jr., Andino R, Wadford DA, Hanson C, Doudna J, Ott M, Chiu CY (2022) Neutralizing immunity in vaccine breakthrough infections from the SARS-CoV-2 Omicron and Delta variants. Cell 185: 1539-1548 e1535. doi: 10.1016/j.cell.2022.03.019.
5. Bose S, Adapa S, Aeddula NR, Roy S, Nandikanti D, Vupadhyayula PM, Naramala S, Gayam V, Muppidi V, Konala VM (2020) Medical management of COVID-19: evidence and experience. J Clin Med Res 12: 329-343. doi: 10.14740/jocmr4201.
6. Lauring AS, Tenforde MW, Chappell JD, Gaglani M, Ginde AA, McNeal T, Ghamande S, Douin DJ, Talbot HK, Casey JD, Mohr NM, Zepeski A, Shapiro NI, Gibbs KW, Files DC, Hager DN, Shehu A, Prekker ME, Erickson HL, Exline MC, Gong MN, Mohamed A, Johnson NJ, Srinivasan V, Steingrub JS, Peltan ID, Brown SM, Martin ET, Monto AS, Khan A, Hough CL, Busse LW, Ten Lohuis CC, Duggal A, Wilson JG, Gordon AJ, Qadir N, Chang SY, Mallow C, Rivas C, Babcock HM, Kwon JH, Halasa N, Grijalva CG, Rice TW, Stubblefield WB, Baughman A, Womack KN, Rhoads JP, Lindsell CJ, Hart KW, Zhu Y, Adams K, Schrag SJ, Olson SM, Kobayashi M, Verani JR, Patel MM, Self WH, Influenza, Other Viruses in the Acutely Ill N (2022) Clinical severity of, and effectiveness of mRNA vaccines against, covid-19 from omicron, delta, and

alpha SARS-CoV-2 variants in the United States: prospective observational study. BMJ 376: e069761. doi: 10.1136/bmj-2021-069761.
7. Tian D, Song Y, Zhang M, Pan Y, Ge Z, Zhang Y, Ren X, Wen J, Xu Y, Guo H, Yang P, Chen Z, Xu W (2022) Genomic, immunological, and clinical analysis of COVID-19 vaccine breakthrough infections in Beijing, China. J Med Virol 94: 2237-2249. doi: 10.1002/jmv.27636.
8. Xia S, Duan K, Zhang Y, Zhao D, Zhang H, Xie Z, Li X, Peng C, Zhang Y, Zhang W, Yang Y, Chen W, Gao X, You W, Wang X, Wang Z, Shi Z, Wang Y, Yang X, Zhang L, Huang L, Wang Q, Lu J, Yang Y, Guo J, Zhou W, Wan X, Wu C, Wang W, Huang S, Du J, Meng Z, Pan A, Yuan Z, Shen S, Guo W, Yang X (2020) Effect of an inactivated vaccine against SARS-CoV-2 on safety and immunogenicity outcomes: interim analysis of 2 randomized clinical trials. JAMA 324: 951-960. doi: 10.1001/jama.2020.15543.
9. Yang H, Ma J, Li A, Lei J, Shang F, Cheng Y, Han B, Li H, Chen Y, Yang Y, Xu Y (2022) Inactivated vaccine injection and immunoglobulin G levels related to severe coronavirus disease 2019 (Delta) pneumonia in Xi'an, China: a single-centered, retrospective, observational study. Front Cell Infect Microbiol 12: 933100. doi: 10.3389/fcimb.2022.933100.
10. Munigela A, Sowpati DT, M S, Banu S, Siva AB, V JK, Nutalapati C, Vishnubhotla R, Kulkarni A, Mukherjee P, Zaveri L, Rao GV, Tallapaka KB, Nageshwar Reddy D, Ccmb Covid-19 Team AIGHC-VST (2022) Clinical outcomes in individuals hospitalized with SARS-CoV-2 Delta variant (B.1.617.2) who had been vaccinated with Covishield (ChAdOx1) and Covaxin (BBV-152). IJID Reg 5: 104-110. doi: 10.1016/j.ijregi.2022.08.016.
11. Bergwerk M, Gonen T, Lustig Y, Amit S, Lipsitch M, Cohen C, Mandelboim M, Levin EG, Rubin C, Indenbaum V, Tal I, Zavitan M, Zuckerman N, Bar-Chaim A, Kreiss Y, Regev-Yochay G (2021) Covid-19 breakthrough infections in vaccinated health care workers. N Engl J Med 385: 1474-1484. doi: 10.1056/NEJMoa2109072.
12. Chia PY, Ong SWX, Chiew CJ, Ang LW, Chavatte JM, Mak TM, Cui L, Kalimuddin S, Chia WN, Tan CW, Chai LYA, Tan SY, Zheng S, Lin RTP, Wang L, Leo YS, Lee VJ, Lye DC, Young BE (2022) Virological and serological kinetics of SARS-CoV-2 Delta variant vaccine breakthrough infections: a multicentre cohort study. Clin Microbiol Infect 28: 612-617. doi: 10.1016/j.cmi.2021.11.010.
13. Jung J, Kim JY, Park H, Park S, Lim JS, Lim SY, Bae S, Lim YJ, Kim EO, Kim J, Park MS, Kim SH (2022) Transmission and infectious SARS-CoV-2 shedding kinetics in vaccinated and unvaccinated individuals. JAMA Netw Open 5: e2213606. doi: 10.1001/jamanetworkopen.2022.13606.
14. Hodgson SH, Mansatta K, Mallett G, Harris V, Emary KRW, Pollard AJ (2021) What defines an efficacious COVID-19 vaccine? A review of the challenges assessing the clinical efficacy of vaccines against SARS-CoV-2. Lancet Infect Dis 21: e26-e35. doi: 10.1016/S1473-3099(20)30773-8.
15. Moore JP, Offit PA (2021) SARS-CoV-2 vaccines and the growing threat of viral variants. JAMA 325: 821-822. doi: 10.1001/jama.2021.1114.
16. Comprehensive Group of the State Council's Joint Prevention and Control Mechanism (2020) Diagnosis and treatment protocol for novel coronavirus Pneumonia (trial version 9). Available at: http: //www.nhc.gov.cn/yzygj/s7653p/202203/b74ade1ba44945838 05a3d2e40093d88/files/ef09aa4070244620b010951b088b8a2 7.pdf. Accessed: 27 June 2022.
17. Abu-Raddad LJ, Chemaitelly H, Ayoub HH, AlMukdad S, Yassine HM, Al-Khatib HA, Smatti MK, Tang P, Hasan MR, Coyle P, Al-Kanaani Z, Al-Kuwari E, Jeremijenko A, Kaleeckal AH, Latif AN, Shaik RM, Abdul-Rahim HF, Nasrallah GK, Al-Kuwari MG, Butt AA, Al-Romaihi HE, Al-Thani MH, Al-Khal A, Bertollini R (2022) Effect of mRNA vaccine boosters against SARS-CoV-2 Omicron I nfection in Qatar. N Engl J Med 386: 1804-1816. doi: 10.1056/NEJMoa2200797.
18. Sheikh A, Kerr S, Woolhouse M, McMenamin J, Robertson C, Collaborators EI (2022) Severity of omicron variant of concern and effectiveness of vaccine boosters against symptomatic disease in Scotland (EAVE II): a national cohort study with nested test-negative design. Lancet Infect Dis 22: 959-966. doi: 10.1016/S1473-3099(22)00141-4.
19. Cao Y, Wang J, Jian F, Xiao T, Song W, Yisimayi A, Huang W, Li Q, Wang P, An R, Wang J, Wang Y, Niu X, Yang S, Liang H, Sun H, Li T, Yu Y, Cui Q, Liu S, Yang X, Du S, Zhang Z, Hao X, Shao F, Jin R, Wang X, Xiao J, Wang Y, Xie XS (2022) Omicron escapes the majority of existing SARS-CoV-2 neutralizing antibodies. Nature 602: 657-663. doi: 10.1038/s41586-021-04385-3.
20. Andrews N, Stowe J, Kirsebom F, Toffa S, Rickeard T, Gallagher E, Gower C, Kall M, Groves N, O'Connell AM, Simons D, Blomquist PB, Zaidi A, Nash S, Iwani Binti Abdul Aziz N, Thelwall S, Dabrera G, Myers R, Amirthalingam G, Gharbia S, Barrett JC, Elson R, Ladhani SN, Ferguson N, Zambon M, Campbell CNJ, Brown K, Hopkins S, Chand M, Ramsay M, Lopez Bernal J (2022) Covid-19 vaccine effectiveness against the Omicron (B.1.1.529) Variant. N Engl J Med 386: 1532-1546. doi: 10.1056/NEJMoa2119451.
21. Hacisuleyman E, Hale C, Saito Y, Blachere NE, Bergh M, Conlon EG, Schaefer-Babajew DJ, DaSilva J, Muecksch F, Gaebler C, Lifton R, Nussenzweig MC, Hatziioannou T, Bieniasz PD, Darnell RB (2021) Vaccine breakthrough infections with SARS-CoV-2 Variants. N Engl J Med 384: 2212-2218. doi: 10.1056/NEJMoa2105000.
22. Higdon MM, Wahl B, Jones CB, Rosen JG, Truelove SA, Baidya A, Nande AA, ShamaeiZadeh PA, Walter KK, Feikin DR, Patel MK, Deloria Knoll M, Hill AL (2022) A systematic review of coronavirus disease 2019 vaccine efficacy and effectiveness against severe acute respiratory syndrome coronavirus 2 infection and disease. Open Forum Infect Dis 9: ofac138. doi: 10.1093/ofid/ofac138.
23. Kissler SM, Fauver JR, Mack C, Tai CG, Breban MI, Watkins AE, Samant RM, Anderson DJ, Metti J, Khullar G, Baits R, MacKay M, Salgado D, Baker T, Dudley JT, Mason CE, Ho DD, Grubaugh ND, Grad YH (2021) Viral dynamics of SARS-CoV-2 variants in vaccinated and unvaccinated persons. N Engl J Med 385: 2489-2491. doi: 10.1056/NEJMc2102507.
24. Al Bayat S, Mundodan J, Hasnain S, Sallam M, Khogali H, Ali D, Alateeg S, Osama M, Elberdiny A, Al-Romaihi H, Al-Thani MHJ (2021) Can the cycle threshold (Ct) value of RT-PCR test for SARS CoV2 predict infectivity among close contacts? J Infect Public Health 14: 1201-1205. doi: 10.1016/j.jiph.2021.08.013.
25. Singanayagam A, Patel M, Charlett A, Lopez Bernal J, Saliba V, Ellis J, Ladhani S, Zambon M, Gopal R (2020) Duration of infectiousness and correlation with RT-PCR cycle threshold values in cases of COVID-19, England, January to May 2020.

Euro Surveill 25. doi: 10.2807/1560-7917.ES.2020.25.32.2001483.
26. Patterson BK, Francisco EB, Yogendra R, Long E, Pise A, Rodrigues H, Hall E, Herrera M, Parikh P, Guevara-Coto J, Triche TJ, Scott P, Hekmati S, Maglinte D, Chang X, Mora-Rodriguez RA, Mora J (2021) Persistence of SARS CoV-2 S1 protein in CD16+ monocytes in post-acute sequelae of COVID-19 (PASC) up to 15 months post-infection. Front Immunol 12: 746021. doi: 10.3389/fimmu.2021.746021.
27. Accorsi EK, Britton A, Fleming-Dutra KE, Smith ZR, Shang N, Derado G, Miller J, Schrag SJ, Verani JR (2022) Association between 3 doses of mRNA COVID-19 vaccine and symptomatic infection caused by the SARS-CoV-2 omicron and delta variants. JAMA 327: 639-651. doi: 10.1001/jama.2022.0470.
28. Kyriakidis NC, Lopez-Cortes A, Gonzalez EV, Grimaldos AB, Prado EO (2021) SARS-CoV-2 vaccines strategies: a comprehensive review of phase 3 candidates. NPJ Vaccines 6: 28. doi: 10.1038/s41541-021-00292-w.
29. Singanayagam A, Hakki S, Dunning J, Madon KJ, Crone MA, Koycheva A, Derqui-Fernandez N, Barnett JL, Whitfield MG, Varro R, Charlett A, Kundu R, Fenn J, Cutajar J, Quinn V, Conibear E, Barclay W, Freemont PS, Taylor GP, Ahmad S, Zambon M, Ferguson NM, Lalvani A, Investigators AS (2022) Community transmission and viral load kinetics of the SARS-CoV-2 delta (B.1.617.2) variant in vaccinated and unvaccinated individuals in the UK: a prospective, longitudinal, cohort study. Lancet Infect Dis 22: 183-195. doi: 10.1016/S1473-3099(21)00648-4.
30. Havers FP, Pham H, Taylor CA, Whitaker M, Patel K, Anglin O, Kambhampati AK, Milucky J, Zell E, Moline HL, Chai SJ, Kirley PD, Alden NB, Armistead I, Yousey-Hindes K, Meek J, Openo KP, Anderson EJ, Reeg L, Kohrman A, Lynfield R, Como-Sabetti K, Davis EM, Cline C, Muse A, Barney G, Bushey S, Felsen CB, Billing LM, Shiltz E, Sutton M, Abdullah N, Talbot HK, Schaffner W, Hill M, George A, Hall AJ, Bialek SR, Murthy NC, Murthy BP, McMorrow M (2022) COVID-19-associated hospitalizations among vaccinated and unvaccinated adults 18 years or older in 13 US States, January 2021 to April 2022. JAMA Intern Med 182: 1071-1081. doi: 10.1001/jamainternmed.2022.4299.
31. Bilich T, Nelde A, Heitmann JS, Maringer Y, Roerden M, Bauer J, Rieth J, Wacker M, Peter A, Horber S, Rachfalski D, Marklin M, Stevanovic S, Rammensee HG, Salih HR, Walz JS (2021) T cell and antibody kinetics delineate SARS-CoV-2 peptides mediating long-term immune responses in COVID-19 convalescent individuals. Sci Transl Med 13: eabf7517. doi: 10.1126/scitranslmed.abf7517.
32. Duarte LF, Galvez NMS, Iturriaga C, Melo-Gonzalez F, Soto JA, Schultz BM, Urzua M, Gonzalez LA, Vazquez Y, Rios M, Berrios-Rojas RV, Rivera-Perez D, Moreno-Tapia D, Pacheco GA, Vallejos OP, Hoppe-Elsholz G, Navarrete MS, Rojas A, Fasce RA, Fernandez J, Mora J, Ramirez E, Zeng G, Meng W, Gonzalez-Aramundiz JV, Gonzalez PA, Abarca K, Bueno SM, Kalergis AM (2021) Immune profile and clinical outcome of breakthrough cases after vaccination with an inactivated SARS-CoV-2 vaccine. Front Immunol 12: 742914. doi: 10.3389/fimmu.2021.742914.
33. Ruenjaiman V, Sodsai P, Kueanjinda P, Bunrasmee W, Klinchanhom S, Reantragoon R, Tunvirachaisakul C, Manothummetha K, Mejun N, Liengswangwong K, Torvorapanit P, Paitoonpong L, Putcharoen O, Palaga T, Hirankarn N, study team (2022) Impact of SARS-CoV-2 infection on the profiles and responses of innate immune cells after recovery. J Microbiol Immunol Infect 55: 993-1004. doi: 10.1016/j.jmii.2022.09.001.
34. Mann ER, Menon M, Knight SB, Konkel JE, Jagger C, Shaw TN, Krishnan S, Rattray M, Ustianowski A, Bakerly ND, Dark P, Lord G, Simpson A, Felton T, Ho LP, TRC NR, Feldmann M, Circo, Grainger JR, Hussell T (2020) Longitudinal immune profiling reveals key myeloid signatures associated with COVID-19. Sci Immunol 5: eabd6197. doi: 10.1126/sciimmunol.abd6197.
35. Arunachalam PS, Wimmers F, Mok CKP, Perera R, Scott M, Hagan T, Sigal N, Feng Y, Bristow L, Tak-Yin Tsang O, Wagh D, Coller J, Pellegrini KL, Kazmin D, Alaaeddine G, Leung WS, Chan JMC, Chik TSH, Choi CYC, Huerta C, Paine McCullough M, Lv H, Anderson E, Edupuganti S, Upadhyay AA, Bosinger SE, Maecker HT, Khatri P, Rouphael N, Peiris M, Pulendran B (2020) Systems biological assessment of immunity to mild versus severe COVID-19 infection in humans. Science 369: 1210-1220. doi: 10.1126/science.abc6261.
36. Yuan S, Pan Y, Xia Y, Zhang Y, Chen J, Zheng W, Xu X, Xie X, Zhang J (2021) Development and validation of an individualized nomogram for early prediction of the duration of SARS-CoV-2 shedding in COVID-19 patients with non-severe disease. J Zhejiang Univ Sci B 22: 318-329. doi: 10.1631/jzus.B2000608.

Corresponding authors

Feng Zhu
Department of Respiratory and Critical Care Medicine,
Wuxi Fifth People's Hospital,
Wuxi 214000, China.
Tel: +86-0-13914135026
Email: 181515688@qq.com

Yao Tang
Tuberculosis Department,
Huai'an No.4 People's Hospital,
HuaiAn 223000, China.
Tel: +86-0-18751264998
Email: 18751264998@163.com

Conflict of interests: No conflict of interests is declared.

Annex – Supplementary Items

Supplementary Table 1. Comparison of monocyte ratio subgroups general clinical data and laboratory indexes.

Monocyte ratio (%) subgroup	Normal group (≤ 10%)	Elevated group (> 10%)	*p* value
N	203	165	
Age	47.4 (12.3)	46.5 (11.0	0.465
Gender			0.281
Female	87 (42.9%)	80 (48.5%)	
Male	116 (57.1%)	85 (51.5%)	
Smoking	**44 (21.7%)**	**32 (19.4%)**	**0.591**
Complications			
High blood pressure	24 (11.8%)	21 (12.7%)	0.792
Diabetes	11 (5.4%)	9 (5.5%)	0.988
Cardio-cerebrovascular diseases	7 (3.5%)	2 (1.2%)	0.195
Chronic liver and kidney diseases/cirrhosis	1 (0.5%)	6 (3.6%)	0.049
Vaccination status			**0.803**
0-1 injection	12 (5.9%)	12 (7.3%)	
2 injections	27 (13.3%)	24 (14.6%)	
3 injections	164 (80.8%)	129 (78.2%)	
Fever	25 (12.3%)	26 (15.8%)	0.342
Highest body temperature	38.2 (0.6)	38.0 (0.6)	0.187
Typing			**0.195**
Asymptomatic	196 (96.6%)	163 (98.8%)	
Mild-moderate	7 (3.5%)	2 (1.2%)	
Imaging (pneumonia)	3 (1.5%)	1 (0.6%)	0.631
N gene	29.49 (5.79)	28.84 (5.90)	0.286
ORF gene	28.49 (6.23)	27.61 (5.74)	0.166
IgM			**0.382**
Negative	198 (97.5%)	163 (98.8%)	
Positive	5 (2.5%)	2 (1.2%)	
IgG			**< 0.001**
Negative	77 (37.9%)	91 (55.2%)	
Weak positive	27 (13.3%)	27 (16.4%)	
Positive	99 (48.8%)	47 (28.5%)	
Laboratory tests at admission			
white blood cell (10^9/L)	5.92 (2.04)	4.85 (1.69)	< 0.001
Neutrophil ratio (%)	64.77 (11.55)	57.78 (11.06)	< 0.001
Lymphocyte ratio (%)	25.75 (10.68)	26.60 (9.92)	0.431
Monocyte ratio (%)	7.51 (1.63)	13.81 (3.21)	< 0.001
Neutrophil count (10^9/L)	3.96 (1.93)	2.90 (1.40)	< 0.001
Lymphocyte count (10^9/L)	1.41 (0.56)	1.20 (0.44)	< 0.001
Monocyte count (10^9/L)	0.44 (0.17)	0.66 (0.23)	< 0.001
High-sensitivity C-reactive protein (mg/L)	0.50 (0.50-132.60)	0.50 (0.20-45.60)	0.103
D-dimer (ug/mL)	0.22 (0.22-1.90)	0.23 (0.22-9.30)	0.012
Glutamic pyruvic transaminase (U/L)	19.0 (5.0-145.0)	18.0 (8.0-396.0)	0.709
Glutamic oxaloacetic transaminase (U/L)	20.0 (10.0-144.0)	21.0 (12.0-257.0)	0.095
Days of hospitalization	12.5 (3.4)	13.3 (3.0)	0.012

Results in the table: Mean (SD), Median (Min-Max) / N (%).