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Original article

## Clinical characteristics and risks of the convalescent COVID-19 patients with re-detectable positive RNA test: a 430 patients with Omicron infected cross-sectional survey in Tianjin, China



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### ABSTRACT

*Background:* The outbreak of severe acute respiratory syndrome coronavirus (SARS-CoV-2) Omicron variant occurred in Tianjin, China, at the beginning of 2022. In the present study, we identified risk factors that may affect positive (RP) RNA re-testing in recovered patients infected with Omicron variants during recovery in hospital.

*Methods:* We retrospectively analyzed the medical records of 425 patients with Omicron variant infection admitted to our medical center from January 21, 2022 to February 24, 2022, based on the recurrence of RT-PCR positive results for SARS-CoV-2 after cure and discharge. Patients were divided into re-tested positive (RP) and non-re-detectable positive patients (NRP) groups, and clinical data from both groups were analyzed to investigate the characteristics and risk factors of RP patients.

*Results:* Univariate analysis showed significant differences in age, vaccination rate and dose, partial signs and symptoms, most co-existing disorders, and levels of CRP and IL-6 between the RP and NRP groups (all P < 0.05), while multifactorial logistic regression analysis showed that vaccination status and levels of IL-6 were independent risk factors for RP patients.

*Conclusion:* Our results suggested that clinicians should assess the probability of "re-positive" nucleic acid tests after discharge, taking the following indicators into account: pre-admission underlying diseases, unvaccinated status, and high levels of CRP and IL-6. Post-discharge isolation and follow-up should also be strengthened.

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### Introduction

During the past two years, COVID-19 infection has swept the world, continuing to mutate. World Health Organization (WHO) classified COVID-19 variants into alpha (B.1.1.7), Beta (B.1.351), Gamma, Delta, and Omicron (B.1.1.529). Among the five variants, Omicron has accumulated the most mutations in the stinger protein; thus, its emergence has raised worldwide concern about infection, immune escape capacity, and risk of COVID-19 re-infection.

On January 8, 2022, an epidemic outbreak of the Omicron variant occurred in Tianjin, which is the first time that appeared in China. Up to February 24, 2022, a total 430 cases were reported in Tianjin. It remains unclear whether epidemiological and clinical characteristics differences continue between patients who suffered from the Omicron variant and other variants. In addition, whether patients who recovered from the Omicron variant have a potential risk of SARS-CoV-2 spread [1], recurrence, and risk factors, and underlying mechanisms need to be addressed further [2]. Some studies reported that residual virus during convalescence, intermittent virus release, and cyclical changes in virus replication lead to recurrence [3]. Furthermore, in the context of rapid virus mutation, the effectiveness of the vaccine and whether it can reduce the risk of recurrence remains to be confirmed.

In the present study, we collected information from 430 patients with COVID-19 who recovered after infection with the Omicron

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variant and analyzed their data to identify the characteristics and determine relevant risk factors.

## Methods

## Study design

This retrospective study analyzed data that were consecutively collected from patients treated at our medical center. A total of 425 patients with complete clinical data who were identified as RT-PCR positive for SARS-CoV-2 Omicron variant after being hospitalized and having recovered from Omicron variant between January 21, 2022 and February 24, 2022 were consecutively recruited. All patients met the following criteria at the time of admission to our medical center: (1) normal temperature for more than 3 days; (2) no significant respiratory symptoms; (3) significant improvement in acute exudative lesions on chest CT images; (4) two consecutive RT-PCR tests negative for SARS-CoV-2 (separated by at least one day). RT-PCR for SARS-CoV-2 was performed on a daily basis during the recovery period.

All patients signed an informed consent form to participate in this study. The study protocol was approved by the Medical Ethics Committee of our medical center and conformed to the principles outlined in the Declaration of Helsinki.

## Data acquisition

Demographic, epidemiological, and clinical characteristics such as age, sex, contact information, symptoms, comorbidities, lung involvement, and lesion pattern on computed tomography (CT) images, clinical classification, red blood cell count, white blood cell count, lymphocyte count, T-lymphocyte subpopulation monitoring, plasma IL-6 concentration, and anti-SARS-CoV-IgG/IgM data were obtained from the medical records of 425 patients.

## RT-PCR

Nasopharyngeal specimens from patients were collected, and total nucleic acids were extracted using RNA virus kits (Zybio, China), after which they were analyzed for RT-PCR. Sample of each patient was tested using commercial kits for SARS-CoV-2 provided by three different manufacturers (Zybio/Zhijiang, Zhejiang/Bo Jie, China). Ct value for each sample was calculated according to the manufacturing instructions, and the threshold for positive Ct value was set at 40 according to China Technical Guidelines for Laboratory Testing for COVID-19 (https://www.chinacdc.cn/jkzt/crb/zl/szkb\_11803/jszl\_11815/202003/t20200309\_214241.html).

### Flow cytometry

Each patient's sample was placed in a BD Trucount tube labeled with the sample registration number, 10  $\mu$ L of Cyto-STAT stain reagent was added followed by 50  $\mu$ L of well-mixed EDTA-anticoagulated whole blood sample. The tube was then capped and gently vortexed. The samples were incubated at room temperature (20–25 °C) for 15 min at room temperature and protected from light. Thereafter, 450  $\mu$ L 1 × BD Fluorescence Activated Cell Sorter (FACS) lysis solution was added. The sample was capped and gently vortexed, after which it was incubated for 10 min at room temperature (20–25 °C) protected from light. Samples were obtained within 1 h of lysis. Live samples were analyzed, and CytExpert for DxFLEX software was used for data analysis.

### Statistical analysis

Group variables are represented by numbers (%), normally distributed continuous variables are represented by means ± standard deviations (SD), and non-normally distributed continuous variables are represented by medians (interguartile range). Group variables included sex, age range, vaccine strategy, COVID-19 vaccine, COVID-19 booster vaccination, clinical classification. Continuous variables included vaccination rate, signs and symptoms, and coexisting disorders. Non-normally distributed continuous variables included laboratory indicators. The student's t-test was used to compare two groups of continuous variables, and the  $\chi^2$  test was used to compare continuous variables. A logistic regression analysis was used to analyze the clinical characteristics that influenced patients' recurrence. Results are expressed as adjusted odds ratios (ORs) and 95 % confidence intervals (95 % CIs). SPSS 22.0 software (version 22.0; IBM Corp., Armonk, NY, USA) was used for all statistical analyses. All tests were two-sided, and P values < 0.05 were considered statistically significant.

### Results

### Study population

A total of 430 patients from January 21, 2022 to February 24, 2022 with identified infection with COVID-19 were quarantined for 14 days at our medical center. Up to March 20, 2022, 85 recovered patients (19.77 %) were with RT-PCR positive for SARS-CoV-2.

# Demographic and epidemiological characteristics of RP patients and NRP patients

Table 1 shows a comparative analysis of the relevant demographic, epidemiological, and clinical characteristics between the RP patients and the NRP patients. The age distribution significantly differed between NP patients and NRP patients, with a higher proportion of elderly RP patients (60 years) than NRP patients (24.71 % vs. 13.62 %), which suggested that older patients may be more likely to develop RP results after discharge. In contrast, a lower percentage of children showed RP outcomes. The proportion of heavy/critical patients in this study population was low. RP patients were predominantly common (61.18 %) and NRP patients were predominantly light (50.43 %). In terms of clinical typing, significantly greater proportion of RP occurred in the general type. In addition, RP patients were with more underlying diseases, which may be caused by the higher number of elderly patients in the RP group.

The vaccinated rate was higher in the NRP population than in the RP population (93.33 % vs. 82.35 %; P < 0.05), suggesting that vaccine could still have the protective effect on the body and reduce the occurrence of RP. Furthermore, we found that the vaccination rate had an impact on the occurrence of RP results, and the greater the vaccination rate, the lower the risk of RP.

# Differences in laboratory indicators between RP patients and NRP patients

In order to compare the differences in laboratory indicators between RP and NRP patients, a comparative analysis of their blood routine, biochemical indexes, and immune indexes at the time of discharge was performed. As shown in Table 2, the CRP and IL-6 levels were significantly higher in RP patients than in NRP patients [0.7 (0.26, 1.65) vs. 0.66 (0.26, 1.44), 1.5 (1.5, 1.97) vs. 1.5 (1.5, 1.5), P < 0.05]. Besides, there was no statistically significant difference in red blood cell count, white blood cell count, AST, ALT, CD3, CD4, and CD8 between RP and NRP patients.

#### Table 1

Baseline characteristics of RP and NRP patients.

	RP (n = 85)	NRP (n = 345)	All (n = 430)	P-value
Sex				0.161
Male	32 (37.64 %)	159 (46.09 %)	191 (44.42 %)	
Female	53 (62.35 %)	186 (53.91 %)	239 (55.58 %)	
Age range(years)				0.020 *
0–17 (juvenile)	14 (16.47 %)	100 (28.99 %)	114 (26.51 %)	
18–44 (youth)	28 (32.94 %)	121 (35.07 %)	149 (34.65 %)	
45-59 (middle-aged)	22 (25.88 %)	77 (22.32 %)	99 (23.02 %)	
$\geq 60$ (elderly)	21 (24.71 %)	47 (13.62 %)	68 (15.81 %)	
Vaccination Rate	70 (82.35 %)	322 (93.33 %)	392 (91.16 %)	0.001 *
Vaccine Strategy				0.230
Inactivated virus	58 (82.86 %)	283 (87.89 %)	341 (86.99 %)	
Virus vector (Ad5)	11 (15.71 %)	38 (11.80 %)	49 (12.5 %)	
Protein subunit (CHO)	1 (1.43 %)	1 (0.31 %)	2 (0.51 %)	
COVID-19 vaccine				0.009 *
None	15 (17.65 %)	23 (6.67 %)	38 (8.84 %)	
One dose	3 (3.53 %)	8 (2.32 %)	11 (2.56 %)	
Two dose	30 (35.29 %)	161 (46.67 %)	191 (44.42 %)	
Three dose	37 (43.53 %)	153 (44.35 %)	190 (44.19 %)	
COVID-19 booster vaccination				0.351
Yes	38(54.28 %)	155(48.14 %)	193(49.23 %)	
No	32(45.71 %)	167(51.86 %)	199(50.76 %)	
Clinical classification				0.086
Asymptomatic	1 (1.18 %)	6 (1.74 %)	7 (1.63 %)	
Mild	31 (36.47 %)	174 (50.43 %)	205 (47.67 %)	
Moderate	52 (61.18 %)	164 (47.53 %)	216 (50.23 %)	
Severe/Critical	1 (1.18 %)	1 (0.29 %)	2 (0.47 %)	
Signs and symptoms	- (		_ ()	
Cough	28 (32.94 %)	130 (37.68 %)	158 (36.74 %)	0.417
Fever	27 (31.76 %)	105 (30.43 %)	132 (30.70 %)	0.812
Sore throat	16 (18.82 %)	66 (19.13 %)	82 (19.07 %)	0.949
Fatigue	15 (17.65 %)	38 (11.01 %)	53 (12.33 %)	0.096
Stuffy nose	9 (10.59 %)	39 (11.30 %)	48 (11.16 %)	0.851
Runny nose	14 (16.47 %)	39 (11.30 %)	53 (12.33 %)	0.194
Dysgeusia	2 (2.35 %)	3 (0.87 %)	5 (12.55 %)	0.258
Diarrhea	0 (0 %)	4 (1.16 %)	4 (0.93 %)	1.000
Abnormal sense of smell	0 (0 %)	1 (0.29 %)	1 (0.23 % %)	1.000
Rash	0 (0%)	1 (0.29 %)	1 (0.23 %)	1.000
Conjunctivitis	9 (10.59 %)	11 (3.19 %)	20 (4.65 %)	0.008 *
Mucosal inflammation	9 (10.59 %)	10 (2.90 %)	19 (4.42 % %)	0.008
Low blood pressure	9 (10.59%)	10 (2.90 %)	19 (4.42 % %)	0.005 *
Coexisting disorder	5 (10.35%)	10 (2.50 %)	15 (4.42 %)	0.005
Yes	44 (51.8 %)	134 (38.8 %)	178 (41.4 %)	0.030
No	44 (51.8 %) 41 (48.2 %)	211 (61.2 %)	252 (58.6 %)	
Coexisting disorder	41 (40.2 %)	211 (01.2 %)	232 (30.0 %)	
Cardiovascular System	45 (52.94 %)	59 (17.10 %)	104 (24.19 %)	< 0.001
Digestive system diseases	45 (52.94 %) 36 (42.35 %)	59 (17.10 %) 76 (22.03 %)	104 (24.19 %)	< 0.001
8	, ,	. ,	. ,	< 0.001
Endocrine System	34 (40.00 %)	59 (17.10 %) 10 (2.00 %)	93 (21.63 %)	
Respiratory system	13 (15.29 %)	10 (2.90 %)	23 (5.35 %) 11 (2.56 %)	< 0.001
Nervous system	5 (5.88 %)	6 (1.74 %) 9 (0 %)	11 (2.56 %)	0.046 *
Genitourinary system	4 (4.71 %)	0 (0 %)	4 (0.93 %)	0.001 *
Blood system	7 (8.24 %)	12 (3.48 %)	19 (4.42 %)	0.074
Skin disease	1 (1.18 %)	2 (0.58 %)	3 (0.70 %)	0.484
Other	1 (1.18 %)	13 (3.77 %)	14 (3.26 %)	0.320

## Logistic regression analysis of characteristics of the trial results

Logistic regression equation was used to explore the factors affecting the positive nucleic acid test in the rehabilitation period. Compared with unvaccinated patients, the re-positivity rate was significantly lower in those who received two doses of the vaccine [OR 0.388 (0.165, 0.915), P = 0.031], and in those who received three doses of the vaccine [OR 0.405 (0.167, 0.982), P = 0.046]. For each unit of IL-6 increase, the risk of re-positivity increases by 10.8 % [OR 1.108 (1.025, 1.198), P = 0.010]. The risk in the adolescent population was lower than in the elderly group. In addition, two or three doses of vaccine could effectively reduce the probability of recurrence. Table 3.

## Discussion

Several previous studies have reported clinical features of patients with RP who suffered from SARS-CoV-2 [4–6]; however, no clinical features have been reported for patients infected with the Omicron variant. In this study, we retrospectively analyzed 425 patients infected with the SARS-CoV-2 Omicron variant during recovery, with a follow-up period of 28 days. Among these patients, 85 suffered from recurrence until March 20, 2022. We also found that patients who received two or three doses of the vaccine and patients with low IL-6 levels had a lower risk of recurrence. The incidence of RP (19.77 %) was slightly higher compared to previous reports, which reported a 12 %- 17.7 % recurrence rate in COVID-19 patients [3]. This outbreak was characterized by a clear family clustering, which was mainly due to the presence of surface proteins such as S-trimer on the surface of the Omicron variant, making it more stable and allowing it to persist for a longer period after exposure to the

#### Table 2

Differences in laboratory indicators between RP patients and NRP patients.

	RP(n = 85)	NRP $(n = 345)$	All (n = 430)	P-value	
White-cell count (×10 <sup>9</sup> /liter)	6.31 (5.30,7.53)	6.23 (5.28,7.44)	6.74 (5.54,7.74)	0.182	
Lymphocyte count (×10 <sup>9</sup> /liter)	2.18 (1.74,2.70)	2.19 (1.77,2.71)	2.13 (1.55,2.66)	0.373	
Monocyte count (×10 <sup>9</sup> /liter)	0.42 (0.34,0.52)	0.42 (0.34,0.51)	0.43 (0.36,0.52)	0.386	
Neutrophil count (×10 <sup>9</sup> /liter)	3.42 (2.67,4.25)	3.34 (2.65,4.23)	3.67 (2.77,4.64)	0.159	
Platelet count (×10 <sup>9</sup> /liter)	279 (235,324)	279 (233,322,50)	273 (236,326.50)	0.739	
Eosinophil (×10 <sup>9</sup> /liter)	0.14 (0.09,0.21)	0.14 (0.09,0.21)	0.14 (0.1,0.21)	0.613	
Basophil (×10 <sup>9</sup> /liter)	0.03 (0.02,0.04)	0.03 (0.02,0.04)	0.03 (0.02,0.04)	0.847	
Alanine aminotransferase (U/L)	28.25 (23.24,36.34)	28.08 (23.26,35.73)	30.07 (23.10,37.95)	0.699	
Aspartate aminotransferase (U/L)	26.93 (15.55,57.32)	27.12 (15.38,59.96)	26.18 (16.21,44.79)	0.591	
ALT/AST	1.03 (0.64,1.56)	0.98 (0.63,1.55)	1.11 (0.71,1.59)	0.195	
CRP	0.7 (0.26,1.65)	0.66 (0.26,1.44)	1.07 (0.29,2.94)	< 0.001 *	
IL-6	1.5 (1.5,1.97)	1.5 (1.5,1.5)	1.5 (1.5,4.56)	< 0.001 *	
Anti-SARS-CoV-2 IgM	0.46 (0.25,0.83)	0.47 (0.26,0.88)	0.46 (0.22,0.82)	0.627	
Anti-SARS-CoV-2 IgG	200.33(168.64,230.03)	200.36 (170.86,229.73)	195.85 (159.41,231.85)	0.679	
CD3 +T cell	73.38 (66.67,78.7325)	73.11 (68.22,77.19)	73.11 (67.83,77.34)	0.747	
CD3 +CD4 +Th cell	40.385 (35.0625,45.9)	40.24 (35.21,46.73)	40.37 (35.17,46.66)	0.552	
CD3 +CD8 +Ts cell	25.565 (20.508,29.48)	24.72 (20.22,29.65)	25 (20.3,29.65)	0.515	
CD4/CD8	1.675 (1.285,2.05)	1.68 (1.25,2.22)	1.68 (1.25,2.2)	0.619	

### Table 3

Logistic regression analysis of potential features in RP patients.

Factor	Category	В	S.E.	OR (95 %CI)	P-value
Age range (years)	≥ 60				0.366
	0-17	0.694	0.535	0.500 (0.175, 1.426)	0.195
	18-44	-0.066	0.422	0.936 (0.410, 2.138)	0.875
	45-59	0.168	0.414	1.183 (0.525, 2.665)	0.684
COVID-19 vaccine	None				0.149
	One dose	-0.352	0.827	0.703 (0.139, 3.557)	0.670
	Two dose	-0.946	0.438	0.388 (0.165, 0.915)	0.031
	Three dose	-0.903	0.452	0.405 (0.167, 0.982)	0.046
Coexisting disorder	Yes/No	-0.013	0.317	0.987 (0.530, 1.838)	0.967
CRP		0.028	0.020	1.029 (0.989, 1.070)	0.161
IL-6		0.102	0.040	1.108 (1.025, 1.198)	0.010

environment [7], thus increasing the risk of infection among family members.

The univariate analysis of RP patients revealed differences in age, vaccination status, clinical typing, presence of underlying disease, and levels of CRP and IL-6 indicators between the two groups, while the multifactorial logistic regression analysis showed that abnormal vaccination status, presence of underlying disease, and levels of CRP and IL-6 indicators increased the risk of relapse in patients. These results suggested that the recurrence of Omicron may be a multifactorial and complex disease process.

As the antigen structure of the Omicron variant is substantially altered [8], allowing it to escape most existing SARS-CoV-2 neutralizing antibodies (NAb) and humoral immune responses induced by natural infection or vaccination [7], breakthrough infection occurred in 91.63 % of the vaccinated population in this study. Yet, the results indicate that the probability of recurrence after vaccination was lower than that of the unvaccinated population. However, there was no difference between the two groups in terms of the effect of the booster vaccine on the recurrence outcomes.

Based on previous studies, differences in recurrence across different ages remain controversial [9]. In An's study, 94.7 % of RP patients were < 60 years old [10], while Wu et al. similarly reported a lower percentage of elderly people in RP patients [11]. This is not consistent with our results, which showed a higher recurrence rate (30.88 %) in elderly patients. In contrast, the recurrence rate in children was only 12.28 %, which is most likely one of the characteristics of the Omicron variant.

High levels of serum CRP have been consistently associated with mortality in critical patients who suffered from COVID-19. Du et al.

found a low CRP threshold of 10 mg/L as a predictor of in-hospital mortality [12], while CRP levels in the RP group were slightly higher than those in the NRP group during the recovery period, and although most of the CRP values in the RP group remained within the normal reference interval. In addition to CRP, IL-6 is an important marker for predicting recurrence in COVID-19 patients. IL-6 can act as a pro-inflammatory cytokine, activate the intracellular cascade of Jak/STAT (Janus kinase/signal transducer and activator of transcription), and can create a positive feedback loop in non-immune cells through the inflammatory cascade of STAT3, the IL-6 amplifier (IL-6 AMP). When excessive activation of NF- $\kappa$ B occurs [13], it may result in a cytokine storm [14]. Therefore, it is often considered an independent prognostic factor for COVID-19 severity and mortality [15]. In the present study, we found that patients with high IL-6 had a higher probability of recurrence, suggesting we should focus on this group in our clinical practice.

In their study, Aljabr et al. demonstrated that lymphocytopenia was correlated with the degree of infection in patients during different stages of SARS-CoV-2 infection [16]. In another study, a mouse model of SARS-CoV-2 infection was constructed, revealing that depletion of CD4<sup>+</sup> helper T cells delayed the clearance of the virus from the lungs [17], while dynamic changes in CD8<sup>+</sup> T cells did not affect virus replication or clearance. In the present study, we found no significant difference in the counts of lymphocyte subpopulations in the RP group compared to the NRP group, suggesting that the immune system was stable during the recovery even though in RP groups, the changes in lymphocyte subpopulations were not significant due to the milder degree of infection.

Although the causes and mechanisms of SARS-CoV-2 recurrence in recovering patients are unclear, virus reactivation, viral shedding in persistent infection, re-infection with the same variant, and falsepositive laboratory results are currently considered responsible for the recurrence [18]. RT-PCR, a common detection technique for identifying SARS-CoV-2, varies greatly in sensitivity and primer specificity due to the selection of different kits. In order to improve the detection rate of the virus, we selected three kits from different manufacturers as a cross-comparison. However, while improving the detection rate, new challenges appeared. As RT-PCR functions on the principle of detecting the virus's genetic material, it is impossible to distinguish whether the detected virus is alive or dead [19].

In a relapse study involving 285 Korean patients who recovered from COVID-19, no live viruses were detected in samples from these patients. Viral culture tests were all negative [20], and it was suggested that the positive RT-PCR results were likely the result of the detection of inactivated viral RNA rather than reactivation or re-infection. In addition, the low viral load in some patients does not

reach the detection limit of the kit, which may also lead to false negative results.

It remains controversial whether patients with recurrence are infectious [21]. Viral infectivity is derived from viral replication, so when the viral load is at a low level, and the amount of viral genetic material is also low, its replication ability is inhibited. However, a survey from Korea showed that although all 296 patients with recurrence tested negative for the virus, three family members became infected [22]. This suggests that family members of patients with COVID-19 should also be regularly tested for SARS-CoV-2. Epidemiological investigation of re-positive patients is of utmost importance, especially for those with high viral load, to monitor their health status and assess their infectivity. Previous studies have shown that Omicron has a high risk of re-infection, which might increase social spread[23,24]. Therefore, it is necessary to identify patients at potential risk of testing positive again when first diagnosed.

Evidence suggests that re-infections may be significantly less severe than primary infections with SARS-CoV-2 [25]. Despite that, a small cohort of 12 cases of re-infection with SARS-CoV-2, including one death, was reported in a long-term care facility in South Korea [26]. This suggested that when re-infection occurs in recovering patients, some necessary measures should be taken based on their current clinical signs and symptoms. Pulliam et al. have demonstrated that compared with Belta or Delta variant, people who suffered from the Omicron variant infection were more likely to be reinfected with the Omicron variant [27]. In addition, these results highlighted that it is very important to develop methods to establish reinfection risk when the pathogen emerges. Our findings showed that people with high levels of CRP and/or IL-6 were more likely to be re-infected. Thus, more attention should be paid to the disease status of those patients, which may bring meaningful clinical implications to the Omicron epidemiological study.

There are some limitations in the present study. Firstly, this is a single medical center retrospective study with a relatively small sample size, but it is the first large-scale epidemic with the SARS-CoV-2 Omicron variant in China. Secondly, this study addressed the clinical characteristics of Omicron patients during recovery with a relatively short follow-up period. Thirdly, this study lacked quantitative analysis of viral RNA and neutralizing antibodies, and dynamic detection of viral characteristics. We were unable to assess the association of viral load and antibody concentration with RP RNA testing. Finally, we could not analyze the impact of treatment strategies on patients with RP due to the lack of sufficient treatment information.

### Conclusion

Our results showed that age, vaccination status, the number of doses, and the presence of underlying disease and accompanying symptoms could affect re-positive events. After the patient completed the vaccination, even if breakthrough infection occurs, the probability of re-positivity during the recovery period is low. In addition, in terms of laboratory examinations, the CRP and IL-6 of the patients in the retest positive group were slightly elevated, and there was no significant difference in other laboratory indicators, which suggests that even if the re-detectable positive RNA test occurs during the recovery period, its clinical symptoms are relatively mild, and there is no need for excessive medical interventions.

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## **CRediT authorship contribution statement**

Tianning Li, and Meng Han are co-first authors on this paper. Tianning Li designed the study, collected and analyzed the data, and drafted the manuscript. Meng Han collected and analyzed the manuscript the data, and helped draft the manuscript. Jingyu Wang and Chunlei Zhou helped collect and analyze the data. Hong Mu designed and supervised the study, revised the manuscript.

## **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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## **Ethics statement**

The study protocol was approved by the Medical Ethics Committee of our medical center (No. 2022N054KY) and conformed to the principles outlined in the Declaration of Helsinki.

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