Clinical characteristics of patients with SARS-CoV-2 Omicron variant and COVID-19 vaccination with clinical outcome findings in Shanghai, China: a single center, retrospective, observational study

Abstract

Background: In March 2022, a severe outbreak of the SARS-CoV-2 Omicron variant occurred in Shanghai. This study aimed to determine disease severity, clinical features, clinical outcome in hospitalized patients with the Omicron variant and evaluate the effectiveness of one-dose, two-dose, and three-dose inactivated vaccines in reducing viral loads, disease course, ICU admissions and severe diseases. **Methods:** Retrospective cohort analysis was performed on 5,170 adult patients (⩾18 years) identified as severe acute respiratory syndrome coronavirus 2 positive with Reverse Transcription Polymerase Chain Reaction admitted at Shanghai Medical Center for Gerontology between March 2022 and June 2022. Demographic information, laboratory data, immunization status, clinical characteristics and outcomes were extracted from electronic medical records. **Results:** Among 5,170 enrolled patients, the median age was 53 years, and 2,861 (55.3%) were male. 71.0% were mild COVID-19 cases, and cough (1,137 [22.0%]), fever (592 [11.5%]), sore throat (510 [9.9%]), and fatigue (334 [6.5%]) were the most common symptoms on the patient's first admission. The median length of hospital stay was 8.7±4.5 days. In multivariate logistic analysis, booster vaccination can significantly reduce ICU admissions and decrease the severity of COVID-19 outcome when compared with less doses of vaccine (OR=0.75, 95%CI, 0.62-0.91, P⩽ 0.005; OR=0.99, 95%CI, 0.99–1.00, p＜0.001). **Conclusions:** In summary, the most of patients who contracted SARSCoV-2 omicron variant had mild clinical features and patients with vaccination took less time to lower viral loads.

Keywords: COVID-19, Omicron, Recurrent, Clinical Characteristics, Vaccination, cycle threshold, Outcome

Introduction

Various variants of severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) continue to emerge during the COVID-19 pandemic. Since the SARS-CoV-2 omicron variant was considered as a variant of concern (VOC) by the WHO on November, 2021, the omicron variant has spread worldwide including China, which is posing a high risk of infection surges with serious repercussions in some areas, reducing the effect of COVID-19 vaccines and exerting a huge impact on the global economic and social development[1-4]. An outbreak of pandemic caused by the SARS-CoV-2 Omicron variant has occurred in Shanghai[5], between February and June 2022. The entire city was forced to enter a phased stage of lockdowns starting by the end of March and the total number of reported infections and deaths were 626,811 and 588 respectively until June[6]. Compared to Western countries, the population in Shanghai was mostly vaccinated with inactivated vaccines and the COVID-19 vaccination coverage was highest in the young and lowest in the elderly[7].

Highly effective vaccination is an important tool to prevent infectious diseases and decrease the impact of the pandemic[8-11]. In some countries, Vaccination has reduced the disease burden of COVID-19, with most severe COVID-19 illnesses and deaths occurring among unvaccinated patients[3, 12-15]. By 6 September 2022, more than 3.4 billion doses have been administrated in China, most of which were domestically-developed inactivated COVID-19 vaccines[14]. Although the vaccination programs had been effective in containing pre-Omicron outbreaks, peer reviewed data describing its effectiveness against Omicron in China is thus far limited. The aim of this study was to describe the clinical characteristics and outcomes of patients who contracted the SARS-CoV-2 Omicron variant and evaluate the effectiveness of one-dose, two-dose, and three-dose inactivated vaccines in reducing viral loads, disease course, ICU admissions and severe diseases.

Methods

Ethical approval

This study is supported by National Natural Science Foundation of China (82170110), Fujian Province Department of Science and Technology (2022D014), Shanghai Pujiang Program (20PJ1402400), Science and Technology Commission of Shanghai Municipality (20DZ2254400, 21DZ2200600, 20DZ2261200), Shanghai Municipal Science and Technology Major Project (ZD2021CY001) and Shanghai Municipal Key Clinical Specialty (shslczdzk02201).

Study Population and Design

This retrospective study analyzed data that were consecutively collected from patients treated at Shanghai Medical Center for Gerontology, an officially-designated hospital that treats patients with SARS-CoV-2. A total of 5,170 adult patients (⩾18 years) who were tested positive for SARS-CoV-2 Omicron variant before being hospitalized between March 23, 2022 and June 16, 2022 were consecutively recruited. Virological diagnosis was established by a positive result of transcription-polymerase chain reaction (RT-PCR) assay from the nasal and pharyngeal swab specimens. Negative results from two consecutive SARS-CoV-2 RNA tests were significant part of the discharge criteria, a patient with one negative and one recurrent-positive test results was defined as a Hospital-recurrent positive patient. These patients remained at the hospital for further medical observation until they met the discharge criteria again. Criteria for admission, diagnoses, therapy, and discharge were made based on the Clinical Guidance for COVID-19 Pneumonia diagnosis and treatment protocol (8th version in 2021 and 9th in 2022) for COVID-19 in China. This study was approved by the Ethics Committee of Zhongshan Hospital, and informed consent was obtained from all patients involved before data were collected.

Data collection

We retrospectively collected the data from patients' electronic medical records, including age, sex, marital status, comorbidities, clinical severity, clinical symptoms, vaccination (dose of vaccine and manufacturer), the cycle threshold (Ct) value of RT-PCR, treatment and clinical outcomes. The detection limit value of cycle threshold (Ct) was set to be 35.0. Samples with Ct of less than 35.0 and 20.0 were considered positive and positive with a high viral load respectively.

Statistical analysis

Descriptive statistics were used to summarize characteristics and outcomes from the study population. Continuous variables were presented as means ± standard deviations (SD) and categorical variables were described as frequencies and percentages. Univariate and multivariate logistic regression analyses were used to assess the association between risk of clinical outcomes and COVID-19 vaccination status. A possible nonlinear relationship between the continuous variables and clinical outcomes was examined by a restricted cubic spline regression model. Results are expressed as odds ratios (ORs) and 95 % confidence intervals (95 % CIs). Data using restricted cubic splines were displayed graphically. P values < 0.05 were considered statistically significant. Statistical analyses were performed with R Statistical Software 3.6.3 with default parameters.

Results

Patient Characteristics

Of 5,170 confirmed COVID-19 patients, the median age was 53.0 (SD,19.5), 44.7% (2,309) were female, and 55.3% (2,861) were male. The most common comorbidities were hypertension (21.2%), followed by diabetes (9.3%), Solid malignancies (2.8%), coronary heart disease (2.4%), nerve system disease (1.9%), and Chronic lung disease (1.2%). 71.0% were mild COVID-19 cases, while 22.6% were Asymptomatic. Among the patients, most of those had symptoms (77.4%), while 22.6% cases had no symptoms. Cough (1,137 [22.0%]), Fever (592 [11.5%]), Sore throat (510 [9.9%]) and fatigue (334 [6.5%]) were the most common symptoms, and digestive symptoms such as loss of taste (52 [1.0%]) and loss of smell (36 [0.7%]) were also reported. There were 389 (7.5%) patients receiving Paxlovid, 401 (7.8%) receiving ordinary oxygen therapy, 72 (1.4%) receiving high-flow oxygen, 63 (1.2%) receiving prone ventilation, 27(0.5%) receiving invasive ventilation, and 22 (0.4%) receiving noninvasive ventilation (Table 1).

Table 1 Characteristics of patients tested positive for SARS-CoV-2 Omicron variant (n=5170)

Demographic and Clinical Characteristics		Frequency（%）
Age		52.94 ± 19.54
Gender		
	Male	2,861 (55.3)
	Female	2,309 (44.7)
Marital status		
	Married	3,365 (88.5)
	Single	397 (10.4)
	Other（Including divorce, widowhood）	41 (1.1)
	Missing	1,367(26.4)
Comorbidities		
	Hypertension	1,092 (21.2)
	Diabetes	477 (9.3)
	Solid malignancies	146 (2.8)
	Coronary heart disease	124 (2.4)
	Nerve nerve system disease	99 (1.9)
	Chronic lung disease	60 (1.2)
	Atrial fibrillation	51 (1.0)
	Renal insufficiency	44 (0.9)
	Cardiac insufficiency	36 (0.7)
	Autoimmune disease	15 (0.3)
	Hematologic malignancy	12 (0.2)

Rheumatism	5 (0.1)
Myocardial infarction	8 (0.2)
Missing	24(0.5)
Classification of admission	
Asymptomatic	1,090 (22.6)
Mild	3,423 (71.0)
Moderate	248 (5.1)
Severe	41 (0.9)
Critical	16 (0.3)
Missing	342(6.8)
Symptoms	
Cough	1,137 (22.0)
Fever	592 (11.5)
Sore throat	510 (9.9)
Expectoration	279 (5.4)
Fatigue	334 (6.5)
Loss of taste	52 (1.0)
Loss of smell	36 (0.7)
Treatment	
Paxlovid	389 (7.5)
Ordinary oxygen therapy	401 (7.8)
High-flow oxygen	72 (1.4)
Prone Ventilation	63 (1.2)
Noninvasive ventilation	22 (0.4)
Invasive ventilation	27 (0.5)

RT-PCR Test Results and Clinical outcome

Table 2 show the increases of Ct values generally over time. Viral loads in nasopharyngeal swabs were estimated with Ct values by RT-PCR. At the third day, fifth day, seventh day, fourteenth day after admission, Ct values were 26.7±6.5, 30.4±6.2, 33.0±5.3 and 35.1±3.4 respectively(Table 2). About one-quarter of the patients had a high viral load (Ct value< 20), while they were hospitalized. There were some differences between different control periods or different vaccination doses in RT-PCR detection frequency, which showed that patients admitted after May 15th or with 0 dose of vaccine had longer detection frequency or hospital stay (Figure 1).

Table 2 Distribution of Ct values in patients tested positive for SARS-CoV-2 Omicron variant（n=2170）

Nucleic acid test for novel coronavirus	Ct value	Frequency（%）
Ct value at 3 days after admission		**26.7±6.5**
	<35	1,646 (75.9)
	>=35	219 (10.1)
	Discharged	305 (14.1)
Ct value at 5 days after admission		**30.4±6.2**
	<35	1,300 (59.9)

	>=35	514 (23.7)
	Discharged	356 (16.4)
Ct value at 7 days after admission		**33.0±5.3**
	<35	903 (41.6)
	>=35	583 (26.9)
	Discharged	684 (31.5)
Ct value at 14 days after admission		**35.1±3.4**
	<35	99 (4.6)
	>=35	109 (5.0)
	Discharged	1,962 (90.4)
Ct minimum value after admission	<20	589 (27.1)
	>=20	1,581 (72.9)

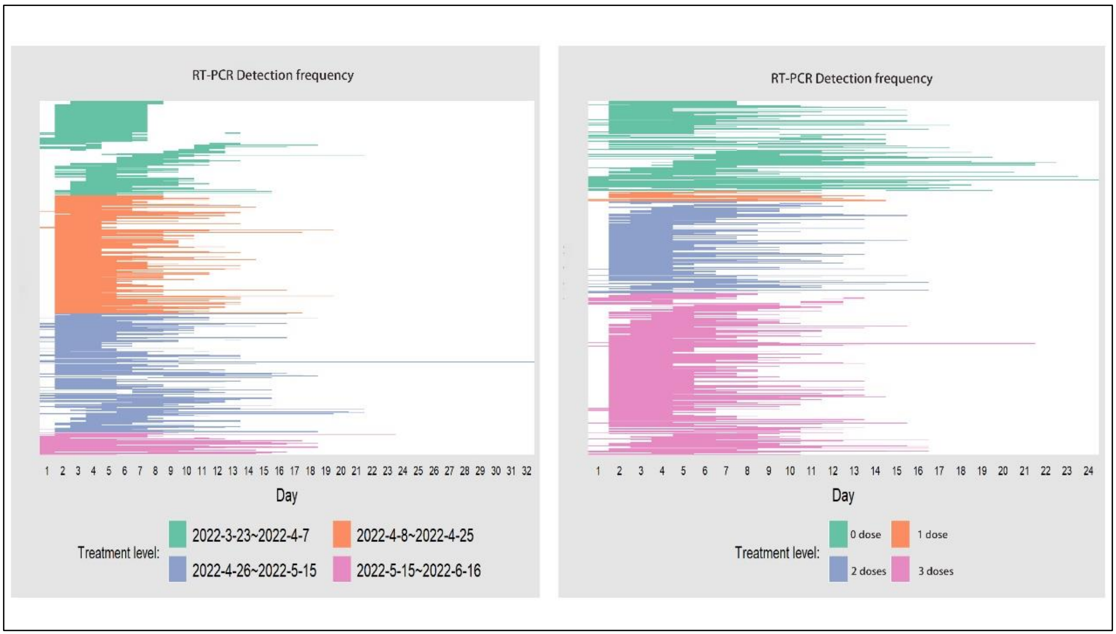

Figure 1 RT-PCR detection frequency of patients tested positive for SARS-CoV-2 Omicron variant

The clinical outcomes of the 5,170 patients infected with Omicron are shown in Table 3. 105(2.0%) of these patients were transferred to the intensive care unit after admission. Among 2,713 patients, 27.0% of them were Hospital-recurrent positive patients, and the length for the negative to positive (NTP) interval was 5.7 ± 3.4 days. 97.1% patients were cured or showed an improvement in symptoms and 0.9% died (Table 3). Patients who died in the hospital were mainly the elderly and the median age was 84 ± 12 years. The median length of hospital stay was 8.7±4.5 days.

Table 3 Clinical efficacy of patients tested positive for SARS-CoV-2 Omicron variant（n=5170）

Clinical efficacy	Classification	Frequency（%）
Transfer to intensive care unit		
	No	5,065 (98.0)
	Yes	105 (2.0)
Rebound in hospital		

	No Rebound	1,980 (73.0)
	Rebound	733 (27.0)
	Missing	2,997(47.5)
	Length for NTP interval, days	5.7 ± 3.4
Clinical outcome		
	cure	4,444 (93.2)
	improve	187 (3.9)
	death	43 (0.9)
	other	94 (2.0)
	Missing	402(7.8)
Hospital stay, days		8.7 ± 4.5

* NTP: negative to positive, Length for NTP interval: Length from admission to the NTP's positive time

COVID-19 vaccination characteristics and multivariate analysis

Among all 5,170 patients, 73.0% had gotten at least one dose of the COVID-19 vaccine and 27.0% were unvaccinated. A total of 3,211 (69.7%) cases received vaccine with 1 dose (3.0%), 2 doses (24.0%) and 3 doses (42.7%). These vaccine manufacturers included Sinopharm Beijing Biotech Co., Ltd. (30.4%), Sinovac Biotech Co., Ltd. (26.9%) and so on (Table 4). As is shown in the Figure 2, Ct values of patients vaccinated remained higher than patients unvaccinated most of the time, and vaccination, especially 2 or 3 doses of vaccination, was clear in reaching the limit value of cycle threshold (Ct=35) earlier, which showed that Vaccine has a positive effect on the prognosis of patients and discharge management.

Table 4 Distribution of vaccine doses in patients with novel coronavirus pneumonia（n=5170）

Vaccination status		Frequency（%）
Vaccination status		
	No	1,396 (27.0)
	Yes	3,774 (73.0)
Vaccination dose		
	Not vaccinated	1,396 (30.3)
	One dose	137 (3.0)
	Two doses	1,106 (24.0)
	Three doses	1,968 (42.7)
	Missing	563(10.9)
Vaccine manufacturers		
	Sinopharm Beijing Biotech	535 (30.4)
	Sinovac	474 (26.9)
	Other	96 (5.4)
	Unknown	657 (37.3)
	Missing	3,408(65.9)

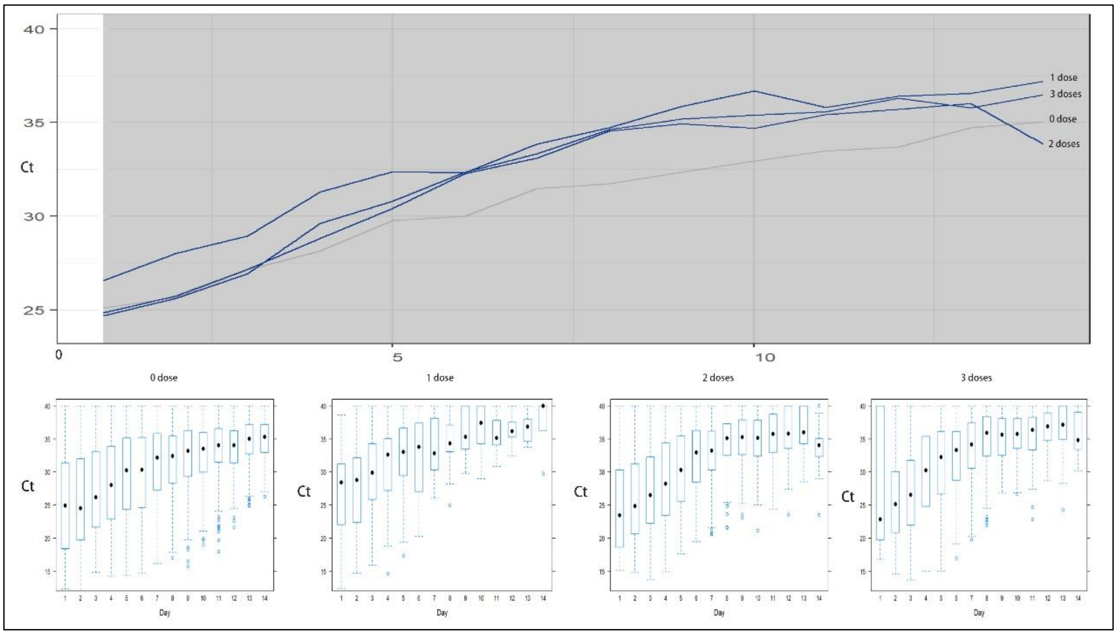

Figure 2　The trend of Ct value between different vaccination doses

Based on the trend of vaccine efficacy, the multivariable logistic regression model is constructed and demonstrates that COVID-19 vaccination was a statistically significant factor of reducing ICU admission (OR=0.75, 95%CI 0.62-0.91, P⩽0.005)(Table 5). Multivariable-adjusted restricted cubic spline analyses suggested a “U-shaped” association between age and ICU admission without significant difference (Figure 3).

Table 5　Multivariate analysis of Vaccination associated with transfer to ICU admission

Models	OR(odds ratio)	95%CI	P value
Unadjusted	0.67	0.57, 0.78	p＜0.001
Adjusted	0.75	0.62, 0.91	p＜0.005

*Model adjusted for sex, age, hypertension, diabetes, solid malignancies, coronary heart disease and chronic lung disease.

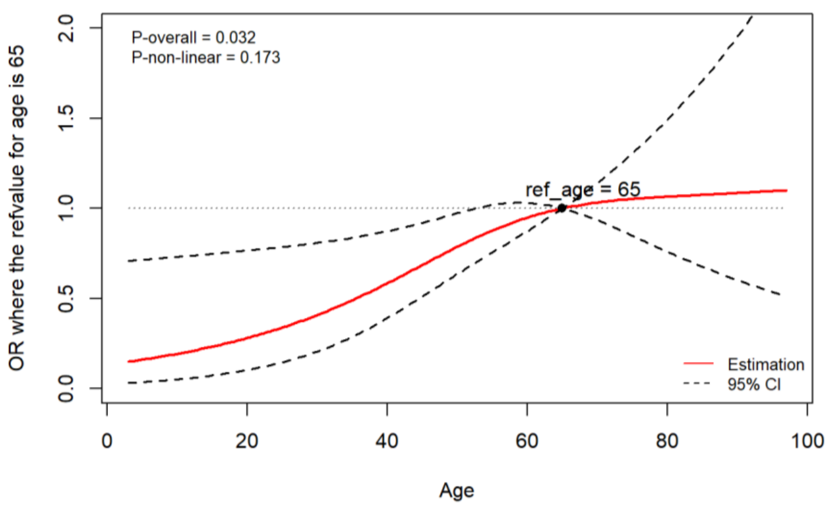

Figure 3 Relationship between age and the risk of being transferred to intensive care

* Model adjusted for vaccination status, sex, hypertension, diabetes, solid malignancies, coronary heart disease and chronic lung disease.

Another logistic regression models were used to measure the association of COVID-19 vaccination with outcomes of COVID-19. After adjustment for some variables, COVID-19 vaccination was still found to be associated with clinical outcomes, with multivariable-adjusted ORs of 0.99 (95% CI, 0.98–0.99) for medical improvement and 0.99 (95%CI, 0.99–1.00) for in-hospital mortality, respectively, in comparison with individuals with fewer doses of COVID-19 vaccine (Table 6).

Table 6 Multivariate analysis of Vaccination associated with COVID-19 outcomes

Models	OR(odds ratio)	95%CI	P value
Model 1			
Unadjusted	0.98	0.97, 0.98	p＜0.001
Adjusted	0.99	0.98, 0.99	p＜0.001
Model 2			
Unadjusted	0.99	0.99, 0.99	p＜0.001
Adjusted	0.99	0.99, 1.00	p＜0.001

*Model 1: cured patients vs improved patients, Model 2: cured and improved patients vs death

*Model adjusted for sex, age, hypertension, diabetes, solid malignancies, coronary heart disease and chronic lung disease

Discussion

On admission, almost 71.0% were mild COVID-19 cases, while 22.6% were asymptomatic. Our results showed compared with SARS-CoV-2 Delta variant, patients with Omicron infection had a much lower incidence of symptoms and extent of disease. According to a study in Guangzhou, 419 patients infected with the Delta variant, fever (75%), cough (74%), expectoration (43%), and fatigue (25%) were predominant[16], which values were significantly higher than that in our study. There are two possible reasons accounting for this difference. First, the vaccination coverage was high in China when the Omicron outbreak occurred. In our study, vaccination rates of up to 73.0% were achieved, with 66.7% of the patients receiving more than two doses. Second, this study population was mainly about mild COVID-19 cases, which may explain the lower incidence of symptoms in Omicron than in Delta variant.

The estimate of the incidence of hospital-recurrent SARS-CoV-2 positivity was 27.0%, which is higher than most previous reports about recurrent patients after leaving the hospital (15%–21%)[17]. One study clearly reported that there were no family members infected from the patients with recurrent positivity[18]. However, Patients with repeat positivity may still be infectious because most patients are likely to have strictly obeyed self-isolation protocols[19], especially in China. Besides, our results show these hospital-recurrent positive results occurred from 2 to 9 days after admission, which were completely different from previous studies on positive RT-PCR results in patients who had recovered from COVID-19 due to the different definitions of recurrent positive results. And it's worth noting that if recurrent positive RT-PCR test results occur in hospital, a quick re-test in the short term will benefit to reduce the misjudgment caused by technology.

We observed low rates of ICU admission and death in patients infected with the Omicron variant and patients who died in the hospital were mainly the elderly, in line with other studies[20-22]. Compared to Delta variant during the same period of time, the clinical outcomes of COVID-19 in patients infected with the Omicron variant appeared less severe[4]. Many countries have implemented the COVID-19 vaccination programmes, but it is still not clear whether vaccination is effective in reducing the transmission and severity of Omicron infection. Our study presented that the vaccination can't avoid the occurrence of breakthrough infections and more than 40% of patients received a third booster vaccine and more than 65% of patients received two, which is consistent with previous studies[23, 24]. It is noteworthy that the number of vaccinations, however, was significantly negatively correlated with ICU admission and severity of outcome, suggesting that vaccination can prevent the COVID-19 disease from exacerbation. Moreover, Ct values is an important proxy for infectivity and significant part of the discharge criteria. The result found that Ct values increased generally over time and patients with vaccination had shorter time to reach the required value of cycle threshold, which is similar to a retrospective study about SARS-CoV-2 Omicron variant[25].

Since the pandemic, vaccination has gained great attention long among the elderly population, who are more vulnerable to underlying conditions and thus resultant reduced immunity. In the current study, further analyses found that ICU admission and severity of COVID-19 outcome were positively correlated with advanced age, but negatively with vaccination, which is the same in some studies[23]. This finding is result of potential significance for the elderly, who may benefit enormously from active vaccination[26].

Our study differed from many previous studies because it collected data from the period of the Omicron variant, which demonstrated the benefits of a booster vaccine for patients with Omicron variant precisely. There are some limitations in the present study. Firstly, this study presented the clinical characteristics of Omicron patients with a relatively short follow-up period. Secondly, Coronavirus test was not uniform throughout the entire pandemic therefore Ct values may have been influenced by different test types. Additionally, the study was unable to describe time interval after vaccination to infection, to determine the underlying mechanism of waning immunity.

Conclusions

In summary, the most of patients who contracted SARSCoV-2 omicron variant had mild clinical features and patients with vaccination took less time to lower viral loads. vaccination still provided strong protection against ICU admission and death caused by Omicron infection. Booster immunization was still critically significant as the waning immunity over time.

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