ORIGINAL RESEARCH

Disease Progression of Hospitalized Elderly Patients with Omicron BA.2 Treated with Molnupiravir

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ABSTRACT

Introduction: The efficacy of molnupiravir (MLN) on Omicron sublineages is limited. We investigated the effectiveness of MLN in older adults diagnosed with Omicron BA.2.

Methods: Data of elderly COVID-19 patients (over 60 years) admitted to Chinghai Hospital (Shanghai, China) from 26 March to 31 May 2022 were reviewed. Study outcomes were a composite of undetectable viral load (VL) and disease progression [all-cause mortality, initiation of oxygen supply through high-flow device or invasive mechanical ventilation (IMV), or intensive care unit (ICU) admission] and their individual outcomes.

Results: A total of 42 elderly patients were enrolled: 26 of them received MLN, 17 (40.5%) were males, the median age was 84 years, and 12 were fully vaccinated (31.0%). Among these elderly COVID-19 patients, five (11.90%) experienced obvious dyspnea or were transferred to ICU [three MLN users (11.5%) versus two non-MLN users (12.5%)]. Compared with no MLN use, MLN use was associated with rapid undetectable VL. At day 10, MLN users achieved

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significantly greater undetectable VL than non-MLN users. Adjusted analysis showed that elderly patients who received MLN were 7.584 times more likely to achieve undetectable VL at day 10 than non-MLN users. Overall, elderly patients experienced a median hospital stay of 13 days. Compared with patients receiving standard care (SC), the median hospital stay of MLN users was reduced by 2.5 days.

Conclusion: Early initiation of MLN in elderly COVID-19 was associated with fast undetectable VL and short hospital stay.

Key Summary Points

Why carry out the study?

As the probability of serious COVID-19 disease is higher in people aged ≥ 60 years, it is urgent to carry out research on the antiviral drugs for elderly patients with COVID-19.

The efficacy and safety of molnupiravir in a real-world setting against the Omicron variant is still lacking, especially for hospitalized elderly patients.

What was learned from the study?

We conducted a real-world, single-center, retrospective, observational study to evaluate if molnupiravir would be safe and decrease the time to undetectable viral load (VL) in nasopharyngeal swabs, as well as improve disease progression.

We found that early initiation of molnupiravir within 5 days of a first positive test or symptom onset in elderly COVID-19 patients was associated with fast viral clearance.

The efficacy of molnupiravir in fully vaccinated elderly patients requires further evaluation.

INTRODUCTION

Coronavirus disease 2019 (COVID-19), triggered by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has devastating impacts on human health and economic development. By 3 June 2022, the number of confirmed COVID-19 cases reported to the World Health Organization (WHO) had reached 528,816,317, including 6,294,969 deaths (https://covid19. who.int). COVID-19 manifests from fully asymptomatic to severe disease and death, and the risk for severe illness increases with age [1]. During the COVID-19 pandemic wave in Shanghai from 26 February to 25 April 2022, 190 deaths were recorded, with an average age of 82.52 years, among which 180 were over 60 years (accounting for 94.7%). During the 2022 COVID-19 outbreak in Hong Kong, 95.9% of deaths occurred in people ≥ 60 years old [2].

The Omicron variant (B.1.1.529) and its sublineages BA.1 and BA.2 have become the predominant variant across the globe. This variant has caused an increase in vaccine breakthrough infections and widespread escape from existing neutralizing antibodies due to high mutations in its spike protein, which is the target of most COVID-19 vaccines and therapeutic antibodies [3–8]. Previously published in vitro data have shown that antiviral agents such as remdesivir, molnupiravir (MLN), or nirmatralvir/ritonavir, which target the highly conserved protein of SARS-CoV-2 [RNA-dependent RNA polymerase (RdRp) or the conserved viral main protease], consistently retains in vitro data activity against the BA.1 and BA.2 sublineages [9–11]. However, in vivo data evaluation of the efficacy of these agents against the new variant is limited. Reports focusing on MLN activity against the currently circulating Omicron variant have primarily used data from the Hong Kong pandemic between January and May 2022. They found that MLN use is associated with a significantly low risk of all-cause mortality compared with non use, whereas hospitalizations are comparable to controls [8, 11, 12]. Data on the efficacy of MLN on hospitalized COVID-19 elderly adults infected with the Omicron variant are still lacking.

The present real-world study focused on evaluating the clinical and virological outcomes associated with MLN use in elderly COVID-19 patients during a community epidemic dominated by the Omicron BA.2 variant in Shanghai, China.

METHODS

Study Design, Participants, and Data Collection

This single-center, retrospective, observational study was approved by the local ethical committee (CHEC2022-111). This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments. Written consent was not required because anonymized data were used and because of the extraordinary nature of the COVID-19 pandemic.

Elderly hospitalized COVID-19 patients with Omicron BA.2 diagnosis were considered for this study if they were admitted to Changhai Hospital (Shanghai, China) between 26 March 2022 and 31 May 2022. There were no other lineages detected in our hospital population during this period. Eligible patients were required to be over 60 years old with SARS-CoV-2 infection confirmed by real-time PCR. The exclusion criteria were as follows: (1) patient was diagnosed as COVID-19 recurrence by PCR test, (2) patient had ever received convalescent plasma for COVID-19 and monoclonal antibodies to SARS-CoV-2 prior to MLN treatment or before admission, (3) patient had ever taken antiviral drugs against SARS-CoV-2 other than MLN, (4) patient was enrolled in other investigational drugs for COVID-19 treatment, and (5) hospital electronic information system data were missing.

Clinical electronic medical records were reviewed for all patients who tested positive for SARS-CoV-2 RNA. Basic demographic and clinical data were collected, including age, sex, weight, height, oxygen saturation (with or without oxygen supply), medical history and basic medications, vital signs (temperature, pulse, respiratory rate, and blood pressure), and

symptom onset (fever, fatigue, cough, sputum, dyspnea, sore throat, or diarrhea). We also determined the interval between symptom onset and first positive SARS-CoV-2 RNA test (nasopharyngeal swab), as well as the treatment strategy (antiviral agent, standard care, glucocorticoid, anticoagulation therapy, and tocilizumab) and clinical outcome [recovery, initiative of oxygen supply through high-flow device, invasive mechanical ventilation (IMV), or registered death]. Laboratory (blood, biochemical, inflammation, and coagulation) tests and pulmonary computed tomography (CT) scans were conducted. Pulmonary CT showed ground-glass opacity, consolidation, lymphadenopathy, and pleural effusion, which were confirmed to be due to SARS-CoV-2 infection. Results of SARS-CoV-2 RNA RT-PCR test (nasopharyngeal swab) for monitoring viral-replication level were collected. These data were stored independently and limited to this analysis.

Treatment Exposure and Follow-Up Period

MLN has only been available in our center since 20 April 2022. Prior to this, all admitted patients received only standard care (SC) recommended by the Chinese COVID-19 prevention and treatment program, including nonsteroidal antiinflammatory drugs, paracetamol (if body temperature $\geq 38\,^{\circ}C$), and cough mixture (licorice mixture, a traditional Chinese medicine). Subsequently, all the elderly patients were prescribed with MLN except one patient who had a definite history of food and multiple drug allergies. MLN therapy was initiated within 5 days of symptom onset or first positive nucleic acid test, whichever was earlier. Patients receiving MLN (Lot number 0,000,033,094, provided by National Engineering Research Center for the Emergency Drug, Beijing, China) 800 mg twice daily for 5 days were defined as MLN users. Patients with only SC during the observation period were defined as SC users.

All patients were hospitalized for precaution, and were observed from hospital admission date until registered death, the occurrence of outcome events, or the end of the observation

period (30 days from admission date), whichever came first.

Outcomes

Clinical outcomes were a composite of viral shedding in nasopharyngeal swabs and disease progression [all-cause mortality, initiation of oxygen supply through high-flow device or IMV, or intensive care unit (ICU) admission] and the individual outcomes. SARS-CoV-2 viral load (VL) in nasopharyngeal swabs on alternate days since hospital admission was quantified by a commercially available RT-PCR test [Novel Coronavirus (2019-nCoV) Real Time RT-PCR Kit, cat. no. RR-0479–02, Liferiver Bio-Tech(China) Corp. Shanghai]. PCR-positive throat swab samples from the patients were used to isolate SARS-CoV-2 virus via Vero-E6 cell. The virus isolation was sequenced and submitted to GenBank (ON965380; ON965371; ON965362; ON965361). A cycle threshold (Ct) value ≥ 35 for both *ORF1ab* and *N* genes was considered as negative. Two consecutive negative tests at least 24 h apart were defined as a negative nucleic acid test or undetectable VL. The undetectable VL time was defined as the first positive nucleic acid test date to the first negative test date (two consecutive times).

Statistical Analysis

The VL test result was expressed as Log2 (Ct value). Continuous data are expressed as mean ± standard deviation(SD) or median [interquartile range(IQR)], and the Mann–Whitney *U* test was used for univariate comparisons between two groups. Categorical variables were expressed as number (percentage) and tested by chi-square or Fisher's exact tests. Cumulative incidences of virological outcomes were estimated and plotted by the Kaplan–Meier method with right censoring. The logistic regression model was used to identify predictors of early viral shedding. *P*-value < 0.05 was considered statistically significant. All analyses were performed using SPSS software (version 21.0.0; Chicago, IL, USA). The graph was made with GraphPad Prism 9 (San Diego, CA, USA).

RESULTS

Patients' Basic Characteristics

A total of 42 elderly COVID-19 patients were enrolled into this study: 26 of them were MLN users, 17 were male, the median age was 84 (69.5–91.25) years, and they had a median body mass index (BMI) of 24.32 kg/m². A high proportion of these elderly patients had preexisting medical comorbidities, of which the top three were hypertension (71.4%), diabetes (19.0%), and coronary heart disease (26.2%). About 35.7% of these patients had multiple underlying medical conditions, and 40.5% has an age-adjusted Charlson Index over 6. Vaccination rates were relatively low (31.0%), especially in patients over 80 years old (9.1%) (Table 1).

The median administration time since the first RNA test positive or symptom onset was 2 days, and the initial VL at admission was high with a low mean Ct value (*ORF1ab* 4.16 Log2 and *N* 4.06 Log2). The majority (88.5%) of MLN users were treated within 5 days of the first positive test for SARS-CoV-2, with a median of 2 days. All MLN users finished the intended 5-day therapy. No adverse events were documented for patients receiving MLN. Moreover, all patients received symptom-remission treatment according to clinical manifestations and laboratory examinations, including nonsteroidal antiinflammatory drugs and cough mixtures.

The patients were stratified into two groups according to whether they had been prescribed MLN. Good comparability was found between the two groups in terms of demographic variables, including age, sex, and BMI, as well as medical history, including vaccination history (Table 1).

Clinical Characteristics of Elderly COVID-19 Patients with Omicron BA.2 Infection

A total of five (11.90%) patients experienced in-hospital disease exacerbation, manifested as pronounced dyspnea and oxygen saturation on room air below 93%, of whom three patients received MLN. Four of these five patients

Table 1 Demographic and baseline clinical characteristics

Characteristics	Therapy strategy categories			
	Total ($n = 42$)	Molnupiravir ($n = 26$)	SC ($n = 16$)	*P*-value
Age, median (IQR), years	84 (69.5,91.25)	84.0 (71.0, 92.0)	84.0 (66.0,88.0)	0.476
Male, n (%)	17 (40.5)	12 (46.2)	5 (31.3)	0.339
Overweight, n (%)	23 (54.8)	17 (65.4)	6 (37.5)	0.078
Medical history, n (%)				
Hypertension	30 (71.4)	20 (76.9)	10 (62.5)	0.514
Diabetes	8 (19.0)	6 (23.1)	2 (12.5)	0.658
Coronary heart disease	11 (26.2)	7 (26.9)	4 (25)	1.000
COPD	4 (9.5)	3 (11.5)	1 (6.3)	0.979
CKD	5 (11.9)	2 (7.7)	3 (18.8)	0.559
Cancer	1 (2.38)	0 (0)	1 (6.25)	–
Alzheimer's disease	4 (7.1)	3 (11.5)	1 (6.3)	0.979
Liver cirrhosis	3 (7.1)	1 (3.8)	2 (12.5)	0.659
> 1 comorbidities	15 (35.7)	7 (26.9)	8 (50.0)	0.130
Charlson Index (≥ 6)	17 (40.5)	11 (42.3)	6 (37.5)	0.758
Vaccination status, n (%)				
Unvaccinated	29 (69.0)	16 (61.5)	13 (81.3)	0.318
[a]Fully vaccinated	12 (31.0)	9 (34.6)	3 (18.8)	0.451
Initial SARS-CoV-2 RNA level (Log2 Ct value)				
ORF1ab, mean $\pm$ SD	4.16 $\pm$ 0.27	4.14 $\pm$ 0.29	4.18 $\pm$ 0.25	0.621
N, mean $\pm$ SD	4.06 $\pm$ 0.24	4.01 $\pm$ 0.25	4.16 $\pm$ 0.19	0.053
Administration time since the first positive test				
Median (IQR), days	2 (2–4.0)	2 (1–3.25)	2.5 (2.0–6.75)	0.019
≤ 5 days, n (%)	37 (89.0)	23 (88.5)	14 (87.5)	0.271

SC standard care, *SD* standard deviation, *IQR* interquartile range, *SARS-CoV-2* severe acute respiratory syndrome coronavirus 2, *COPD* chronic obstructive pulmonary disease, *CKD* chronic kidney disease

P-value refers to the comparison between molnupiravir and SC group

$P < 0.05$ means significant difference

[a]Fully vaccinated patients were defined as those with at least two doses of Comirnaty or three doses of CoronaVac

required oxygen through a high-flow oxygen device. One required IMV and was admitted to the ICU due to COVID-19. No difference in the disease-progression rate was found between MLN users and non-users (11.5% versus 12.5%; $P = 1.00$) (Table 2).

Overall, elderly COVID-19 patients experienced a long median hospital stay of 13 days. Most had at least one symptom associated with

Table 2 Clinical features and outcomes of patients by antiviral strategy

Variables	Therapy strategy categories			
	Total ($N = 42$)	MLN ($N = 26$)	SC ($N = 16$)	*P*-value
Clinical type, *n* (%)				
Mild	20 (47.6)	12 (46.2)	8 (50.0)	0.808
Moderate	17 (40.5)	11 (42.3)	6 (37.5)	0.758
Severe/critical	5 (11.9)	3 (11.5)	2 (12.5)	1.000
Symptoms, *n* (%)				
Fever	23 (54.8)	17 (65.4)	6 (37.5)	0.078
Cough	12 (28.6)	5 (19.2)	7 (43.8)	0.175
Sore throat	11 (26.2)	7 (26.9)	4 (25%)	1.000
Sputum production	21 (50.0)	16 (61.5)	5 (31.3)	0.057
Dyspnea	5 (11.9)	4 (14.8)	1 (6.7)	0.776
Fatigue	14 (33.3)	11 (42.3)	3 (18.8)	0.116
Others	17 (40.5)	13 (50.0)	4 (25.0)	0.109
> 1 symptom	36 (85.71)	25 (96.17)	11 (68.75)	0.044
In-hospital disease exacerbation, *n* (%)				
In-hospital death	0 (0)	0 (0)	0 (0)	–
Oxygen through high-flow device or IMV	4 (9.52)	2 (7.69)	2 (12.5)	1.000
ICU transfer	1 (2.38)	1 (3.85)	0 (0)	1.000
Virological outcomes				
Viral shedding time (days), median (IQR)	13 (9–15)	11 (8–14.5)	14 (12.25–16.5)	0.101
D5 undetectable VL, *n* (%)	3 (7.1)	3 (11.5)	0 (0)	0.428
D7 undetectable VL, *n* (%)	7 (16.7)	6 (23.1)	1 (6.3)	0.320
D10 undetectable VL, *n* (%)	14 (33.3)	12 (46.2)	2 (12.5)	0.025
D14 undetectable VL, *n* (%)	29 (69)	19 (73.1)	10 (62.5)	0.428
D21 undetectable VL, *n* (%)	39 (92.9)	24 (92.3)	15 (93.8)	1.000
Clinical outcomes				
Hospital stay (days), median (IQR)	13 (9–16)	11.5 (8.5–15.25)	14 (12.25–16.75)	0.135
28-day all-cause death rate, *n* (%)	0 (0)	0 (0)	0 (0)	–

MLN molnupiravir, *SC* standard care, *IMV* invasive mechanic ventilation, *ICU* intensive care unit, *VL* viral load, *IQR* interquartile range, *D5* day 5, *D7* day 7, *D10* day 10, *D14* day 14

P-value refers to the comparison between the molnupiravir and SC groups

$P < 0.05$ means significant difference

viral infection (95.24%), and 85.71% patients experienced multiple symptoms, with the most frequently reported symptoms being fever (54.8%), cough and sputum production (50.0%), and fatigue (33.3%) (Table 2). In terms of pulmonary CT scan, all patients with moderate clinical process had at least one appearance of viral infection-related manifestations, such as ground-glass opacity, consolidation, lymphadenopathy, and pleural effusion.

Clinical Outcomes

All of these elderly patients recovered and were discharged from the hospital, with a median hospital stay of 13 days. Compared with SC users, the median hospital stay time of the MLN users was reduced by 2.5 days. However, no significant difference was found in the in-hospital disease exacerbation rate between MLN users and non-users (Table 2). However, for those over 85 years old, a Charlson Comorbidity Index ≥ 6 and a lymphocyte count less than 1×10^9/L was associated with disease exacerbation (Table 3).

Virological Outcomes

The median SARS-CoV-2 RNA shedding time of elderly COVID-19 patients was 13 days (IQR 9–15 days) from therapy time. The rate of undetectable VL in MLN users at days 5, 7, and 10 were 3/26 (11.56%), 6/26 (23.1%), and 12/26 (46.2%), respectively. Compared with non-users, MLN users achieved a significantly higher undetectable VL rate at day 10 (46.2% versus 12.5%, respectively; $P = 0.025$) (Table 2; Fig. 1). Multivariate adjusted analysis showed that elderly patients who received early MLN treatment were 7.584 times more likely to achieve undetectable VL at day 10 than non-users (Table 4).

DISCUSSION

In this real-world retrospective observational study, the clinical features of elderly patients infected with SARS-CoV-2 Omicron variant

BA.2 and the efficacy of MLN in these patients were described and evaluated. We found that elderly COVID-19 patients with Omicron BA.2 experienced a relatively long hospital stay, and early initiation of MLN at a median of 2 days from the first positive test or symptom onset was associated with fast VL shedding by 3 days compared with not using any oral antivirals. Overall, our experience confirmed the role of early MLN therapy and remission therapy in SARS-CoV-2 VL shedding and reducing the morbidity and mortality of COVID-19 in elderly patients.

In theory, the high mutations in the spike protein and RdRp of the Omicron variant enable it to reduce the potency of existing RdRp inhibitors, such as MLN, along with successfully evading neutralizing antibodies [1, 6, 10]. Laboratory studies have demonstrated that the inhibitory concentration (IC)$_{50}$ of the Omicron strain for RdRp inhibitors is similar to that of early strains (i.e., IC$_{50}$ values for remdesivir and MLN differing by factors of 1.2 and 0.8, respectively) [9–11]. Real-world studies among community-dwelling COVID-19 in both in- and outpatients during the Hong Kong pandemic dominated by the Omicron variant have shown that early initiation of MLN is associated with lower risks of disease progression and all-cause mortality, in addition to achieving low VL faster than non-use [8, 11]. However, in patients not fully vaccinated and elderly patients (> 65 years old), the effectiveness of MLN is not consistent [11]. In the current study, the patients were a group of hospitalized elderly COVID-19 patients amid a pandemic wave of Omicron BA.2 variant in Shanghai, China. We obtained similar results in that the early initiation of MLN was associated with fast shedding of VL compared with non use, but MLN was not associated with low risk of disease progression. The inferior efficacy in elderly patients may be closely related to the higher rate of patients who were not fully vaccinated and their hypoimmune state. These results suggested that, although MLN retained its efficacy toward the Omicron variant, it may not be the optimum choice in some special cases, such as patients aged > 65 years and who are not fully vaccinated. Additionally, current information on MLN efficacy in elderly COVID-

Table 3 Subgroup analysis of the differences in the rate of progression to severe disease

	No oxygen n (%)	Oxygen through high-flow device or IMV, or ICU transfer, n (%)	P-value
Age			
$\geq$ 85 years ($N = 20$)	15 (75)	5 (25.0)	0.043
$<$ 85 years ($N = 22$)	22 (100)	0 (0)	
Gender			
Female ($N = 25$)	23 (92.0)	2 (8.0)	0.644
Male ($N = 17$)	14 (82.4)	3 (17.6)	
BMI, kg/m^2			
$\geq$ 24 ($N = 23$)	20 (87.0)	3 (13.0)	1.00
$<$ 24 ($N = 19$)	17 (89.5)	2 (10.5)	
COPD			
Yes ($N = 4$)	2 (50)	2 (50)	0.097
No ($N = 38$)	35 (92.1)	3 (7.9)	
Charlson Index			
$\geq$ 6 ($N = 11$)	6 (54.4)	5 (45.5)	0.001
$<$ 6 ($N = 31$)	31 (100)	0 (0)	
Therapy strategy			
MLN use ($N = 26$)	23 (88.5)	3 (11.5)	1.000
SC only ($N = 16$)	14 (87.5)	2 (12.5)	
Lymphocyte count ($\times$ 10^9/L)			
$<$ 1.0 ($N = 13$)	9 (69.2)	4 (30.8)	0.044
$\geq$ 1.0 ($N = 29$)	28 (96.6)	1 (3.4)	
CRP (mg/L)			
$\geq$ 10 ($N = 12$)	9 (75)	3 (25)	0.258
$<$ 10 ($N = 30$)	28 (93.3)	2 (6.7)	
IL-6 (pg/ml)			
$\geq$ 10 ($N = 23$)	18 (78.3)	5 (21.7)	0.092
$<$ 10 ($N = 19$)	19 (100)	0	
D-dimer level (mg/L)			
$\geq$ 0.5 ($N = 22$)	17 (77.3)	5 (22.7)	0.073
$<$ 0.5 ($N = 20$)	20 (100)	0	

IMV invasive mechanic ventilation, *ICU* intensive care unit, *BMI* body mass index, *COPD* chronic obstructive pulmonary disease, *MLN* molnupiravir, *SC* standard care, *CRP* C-reactive protein, *IL-6* interleukin 6
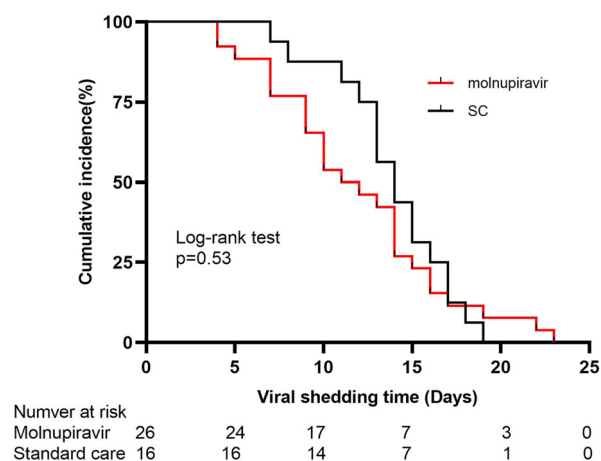
$P < 0.05$ means significant difference

Fig. 1 Cumulative incidence of lower viral load (Ct $\geq$ 35) for molnupiravir users and standard care users. *SC* standard care, *Ct* cycle threshold

19 patients with the Omicron variant was targeted at non-fully vaccinated elderly people, so the efficacy of MLN on fully vaccinated elderly patients requires further evaluation.

Although our research fills some gaps in the application of MLN, several limitations remain.

First, our small dataset, retrospective approach, and single-center nature limited our ability to fully characterize the efficacy difference between subgroups of patients with different vaccination statuses and age. Evaluating the difference in severity of preexisting comorbidities among elderly patients was also impossible. In addition, owing to the small sample size and overall low number of events, the possibility of performing a powerful multivariable analysis to detect a difference between treatment strategy groups is limited. Second, we reported a limited follow-up time, and long-term outcomes related to COVID-19 diseases (e.g., long sequelae beyond 30 days) were not captured in the present study. Finally, our study was also subject to selection bias because the treatment options for patients were contingent to our center's treatment strategy. In the early stage of the pandemic, antiviral agents and certain treatments (e.g., nirmatrelvir and ritonavir) were unavailable in our center. Consequently, we cannot make suggestions on the optimization of oral antiviral agents for elderly patients.

Table 4 Day 10 undetectable viral load predictors (logistic analysis)

Variables	Univariate			Multivariate		
	OR	**95% CI**	*P*-value	**OR**	**95% CI**	*P*-value
Male	1.35	0.359–5.078	0.657			
Age < 80 years	4.50	1.117–18.132	0.034	6.949	1.295–37.295	0.024
BMI < 24 kg/m^2	0.205	0.047–0.898	0.036	0.237	0.043–1.303	0.098
Fully vaccinated	2.03	0.493–8.408	0.325			
Charlson Comorbidity Index < 6	2.842	0.522–15.465	0.227			
COPD	0.462	0.058–3.679	0.465			
Lymphocyte count $\geq 1.0 \times 10^9$/L	1.184	0.291–4.825	0.814			
D-dimer < 0.5 mg/L	2.782	0.735–10.524	0.132			
CRP $\geq$ 10 mg/L	1.737	0.386–7.807	0.472			
Interleukin-6 $\geq$ 10 pg/ml	2.061	0.56–7.577	0.276			
Molnpiravir therapy	6.00	1.129–31.880	0.036	7.584	1.094–52.562	0.04

OR odds ratio, *CI* confidence interval, *BMI* body mass index, *COPD* chronic obstructive pulmonary disease, *CRP* C-reactive protein
$P < 0.05$ means significant difference

CONCLUSIONS

Our experience suggests that, during a pandemic wave of the Omicron variant BA.2, elderly COVID-19 patients experienced a difficult clinical process. Early initiation of MLN within 5 days of the first positive test or symptom onset among hospitalized elderly patients was associated with rapidly achieving low VL and shorter hospital stay.

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Author Contributions. Yayun Liu recruited the patients and collected specimens, edited the clinical data and performed the data analysis; Lingling Ge edited the clinical data of enrolled patients; Shiyong Fan drafted the manuscript; Aijing Xu recruited the patients and treated the patients; Wang, Xu Dong, Mingxiao Xu and Wenhan Fan treated the patients; Wu Zhong conceived and designed the study; Xuesong Liang conceived and designed the study; checked the data analysis and drafted the manuscript; All authors have read and approved the final manuscript.

Disclosures. Yayun Liu, Lingling Ge, Shiyong Fan, Aijing Xu, Xinyu Wang, XuDong, Mingxiao Xu, Wenhan Fan, Wu Zhong and Xuesong Liang declare that they have no competing interests.

Compliance with Ethics Guidelines. This study was approved by the Ethics Committee of Changhai Hospital. (CHEC2022-111).Written informed consent was exempted from all the study participants. This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments.

Data Availability. All data and analysis results are included in this article. The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request. All authors have read and approved the final manuscript.

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