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LETTER TO THE EDITOR

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Early administration of Paxlovid reduces the viral elimination time in patients infected with SARS-CoV-2 Omicron variants

To the Editor,

Nirmatrelvir/ritonavir (Paxlovid) is an oral antiviral drug that has been shown to reduce the risk of hospitalization, severe COVID-19, and mortality among mild-to-moderate COVID-19 patients who are at risk of developing severe disease.[1,2] Paxlovid received emergency use authorization from the Chinese National Medical Products Administration on February 31, 2022. The efficacy and safety of Paxlovid in COVID-19 have been studied in clinical studies.[1–3] Further, Fangfang Sun et al.[4] recently reported that early administration of Paxlovid within 5 days since diagnosis is associated with a faster clearance of viral load and a shorter time to viral elimination compared with administration of Paxlovid beyond 5 days in high-risk COVID-19 patients who are immunocompromised. However, limited clinical studies have evaluated the effects of early Paxlovid use in the entire COVID-19 inpatient. In this retrospective cohort study, we analyzed the characteristics and outcomes of patient infected with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron variant and evaluated the effect of timing of Paxlovid treatment from patient's symptom onset on the time to viral elimination and hospital stay.

Data of 470 patients were obtained from the medical records of patients infected with the SARS-CoV-2 Omicron variant from April 12, 2022 to May 20, 2022. SARS-CoV-2 Omicron variant infection was confirmed by reverse-transcription polymerase chain reaction assay (RT-PCR). Inclusion criteria were mild-to-moderate COVID-19 patients who have at least one comorbidity or condition associated with high risk of progression to severe COVID-19: age ≥60 years, cigarette smoking, hypertension, diabetes, cardiovascular disease, chronic lung disease, chronic liver disease, chronic kidney disease, malignancy, immunosuppressive disease, neurological disease, and body mass index ≥30 kg/m.[21] The exclusion criteria were as follows: contraindications to use Paxlovid,[1] severe or critical COVID-19, transfer to another hospital, and lack of data. The diagnosis and severity of COVID-19 was in accord with the Diagnosis and Treatment Scheme for COVID-19 released by the National Health Commission of China (9th Edition). Viral clearance was defined as two consecutive negative results (cycle threshold ≥35 by RT-PCR) at least 24 h apart, according to the Diagnosis and Treatment Scheme for COVID-19 released by the National Health Commission of China (9th Edition).[5] Patients who were treated with Paxlovid were administered the drug (300 mg nirmatrelvir and 100 mg ritonavir) every 12 h for 5 days. This study was approved by the Medical Ethics Committee of Shidong Hospital, which is affiliated with the University of Shanghai for Science and Technology. The requirement for individual consent for this retrospective study was waived.

Data were shown as number (%) or median (interquartile range). Continuous variables with skewed distribution were analyzed by Kruskal–Wallis test, and categorical variables were analyzed by χ^2 test to compare the characteristics of three groups. The early Paxlovid group, late Paxlovid group, and no Paxlovid group were compared by Kruskal–Wallis test and Bonferroni post hoc correction. Statistical analyses were conducted with the IBM SPSS software (version 25.0).

Of the 470 patients, there were 209 patients did not receive treatment of Paxlovid (no Paxlovid group) and 261 patients treated with Paxlovid, among which 141 patients received Paxlovid early within 5 days of symptoms onset (early Paxlovid group) and 120 patients received Paxlovid late at 5 days or later following their symptom's onset (late Paxlovid group). The characteristics of three groups are presented in Table 1. The differences in the viral elimination time between the three groups were statistically significant ($p < 0.001$). Moreover, the difference in hospital stay between three groups was no significance. The median time of viral elimination was 11 versus 15 versus 16 days (early Paxlovid group vs. late Paxlovid group vs. no Paxlovid group). The viral elimination time was evidently shorter in the early Paxlovid group compared with the late Paxlovid group and no Paxlovid group, respectively (Figure 1), Kruskal–Wallis test and Bonferroni post hoc test indicated that the differences of viral elimination time in the early Paxlovid group and late Paxlovid group, the early Paxlovid group and no Paxlovid group were statistically significant, and there was no statistical difference between late Paxlovid group and no Paxlovid group in viral elimination time.

Paxlovid treatment should be initiated within 5 days after symptom onset,[6] however, limited studies have investigated the efficacy of Paxlovid based on symptom onset to Paxlovid treatment (early vs. late initiation). In this study, early administration of Paxlovid within 5 days of symptom onset significantly reduced the time to viral elimination, and administration of Paxlovid 5 days after symptom onset didn't show obvious effect on viral elimination time compared with untreated patients. These results suggested that Paxlovid works well and only works if it is given within 5 days of infection, which highlighted the importance of treatment timing of Paxlovid on high-risk COVID-19 patients.

AUTHOR CONTRIBUTIONS

Yu Wang, Xinbing Liu, Xubo Chen, Danyang Zhao, Wenying Xiao, and Liuliu Feng planned the study, wrote and revised the paper. Yu Wang,

TABLE 1 Characteristics of the overall study population

Variables	No Paxlovid (*n* = 209, 44.47%)	Late Paxlovid (*n* = 120, 25.53%)	Early Paxlovid (*n* = 141, 30.00%)	*p* Value
Age (years)	75 (67–86)	78 (66–86)	80 (70–88)	0.056
Time to negative conversion of viral RNA (days)	16 (12–21)	15 (13–19)	11 (9–14)	<0.001
Hospital stay (days)	12 (10–16)	12 (9–15)	12 (10–14)	0.241
Sex				0.776
Female	115 (46.0%)	62 (24.8%)	73 (29.2%)	
Male	94 (42.7%)	58 (26.4%)	68 (30.9%)	
COVID-19 vaccine received				0.289
0	143 (42.3%)	88 (26.0%)	107 (31.7%)	
1	66 (50.0%)	32 (24.2%)	34 (25.8%)	
Hypertension				0.628
No	87 (46.0%)	50 (26.5%)	52 (27.5%)	
Yes	122 (43.4%)	70 (24.9%)	89 (31.7%)	
Diabetes				0.216
No	154 (42.9%)	90 (25.1%)	115 (32.0%)	
Yes	55 (49.5%)	30 (27.0%)	26 (23.4%)	
Coronary artery disease				0.176
No	162 (44.3%)	100 (27.3%)	104 (28.4%)	
Yes	47 (45.2%)	20 (19.2%)	37 (36.6%)	
Cerebrovascular disease				0382
No	170 (45.9%)	94 (25.4%)	106 (28.6%)	
Yes	39 (39.0%)	26 (26.0%)	35 (35.0%)	
Chronic obstructive pulmonary disease				0.872
No	192 (44.1%)	112 (25.7%)	131 (30.1%)	
Yes	17 (48.6%)	8 (22.9%)	10 (28.6%)	
Chronic kidney disease				0.063
No	195 (43.3%)	117 (26.0%)	138 (30.7%)	
Yes	14 (70.0%)	3 (15.0%)	3 (15.0%)	
Severity status of COVID-19				0.612
Mild	97 (42.4%)	59 (25.8%)	73 (31.9%)	
Moderate	112 (46.5%)	61 (25.3%)	68 (28.2%)	
Fever				0.422
No	163 (43.2%)	96 (25.5%)	118 (31.3%)	
Yes	46 (49.5%)	24 (25.8%)	23 (24.7%)	
Cough				0.125
No	52 (40.9%)	28 (22.0%)	47 (37.0%)	
Yes	157 (45.8%)	92 (26.8%)	94 (27.4%)	
Sputum				0.087
No	80 (41.2%)	45 (23.2%)	69 (35.6%)	
Yes	129 (46.7%)	75 (27.2%)	72 (26.1%)	

TABLE 1 (Continued)

Variables	No Paxlovid (n = 209, 44.47%)	Late Paxlovid (n = 120, 25.53%)	Early Paxlovid (n = 141, 30.00%)	p Value
Myalgia				0.058
No	189 (43.1%)	116 (26.4%)	134 (30.5%)	
Yes	20 (64.5%)	4 (12.9%)	7 (22.6%)	
Headache				0.882
No	207 (44.5%)	119 (25.6%)	139 (29.9%)	
Yes	2 (40.0%)	1 (20.0%)	2 (40.0%)	
Dyspnea				0.987
No	195 (44.5%)	112 (25.6%)	131 (29.9%)	
Yes	14 (43.8%)	8 (25.0%)	10 (31.3%)	
Diarrhea				0.193
No	206 (44.4%)	117 (25.2%)	141 (30.4%)	
Yes	3 (50%)	3 (50%)	0 (0%)	
Treatment with glucocorticoid				0.591
No	203 (44.9%)	115 (25.4%)	134 (29.6%)	
Yes	6 (33.3%)	5 (27.8%)	7 (38.9%)	

Note: Data are presented as number (%), or median (interquartile range). Continuous variables use Kruskal–Wallis test and categorical variables use χ^2 test for comparing the characteristics of three groups.

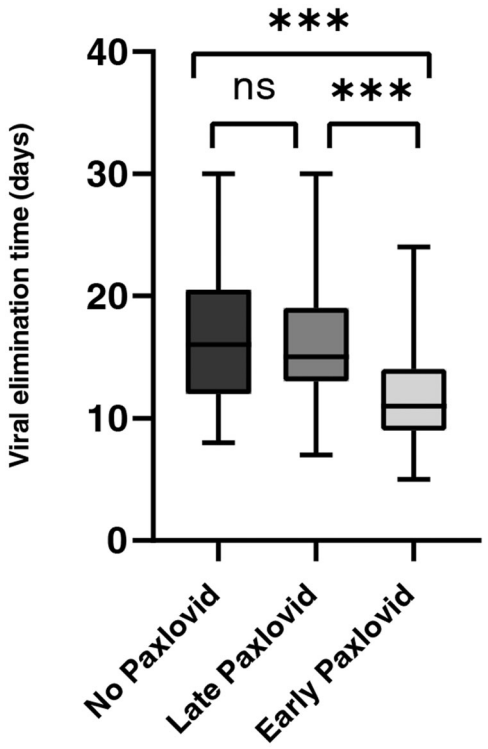

FIGURE 1 The timing to Paxlovid prescription and the duration of viral elimination. Three groups were analyzed by the Kruskal–Wallis test and Bonferroni post hoc correction, ***$p < 0.001$.
ns, nonsignificance.

Xubo Chen, and Wenying Xiao collected data. Danyang Zhao worked on data revision and methodology. Yu Wang analyzed and interpreted data. All authors analyzed the data, revised the manuscript, and approved it for publication.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data supporting reported results will be provided on reasonable request.

Yu Wang[1]
Danyang Zhao[2]
Xinbing Liu[1]
Xubo Chen[3]
Wenying Xiao[1]
Liuliu Feng[1]

[1]*Department of Cardiology, Shidong Hospital, Shidong Hospital Affiliated to University of Shanghai for Science and Technology, Shanghai, China*

[2]*Department of Plastic and Reconstructive Surgery, Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China*
[3]*Department of Rehabilitation Medicine, Shidong Hospital, Shidong Hospital Affiliated to University of Shanghai for Science and Technology, Shanghai, China*

Correspondence
Wenying Xiao and Liuliu Feng, Department of Cardiology, Shidong Hospital, Shidong Hospital Affiliated to University of Shanghai for Science and Technology, 999 Shiguang Rd, Yangpu District, Shanghai 200438, China.
Email: 13917804027@163.com and Llf20170101@usst.edu.cn

Xubo Chen, Department of Rehabilitation Medicine, Shidong Hospital, Shidong Hospital Affiliated to University of Shanghai for Science and Technology, 999 Shiguang Rd, Yangpu District, Shanghai 200438, China.
Email: examcode@163.com

Yu Wang and Danyang Zhao contributed equally to this work.

ORCID

Liuliu Feng http://orcid.org/0000-0001-6811-5646

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