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COVID-19 patients benefit from early antiviral treatment: A comparative, retrospective study

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Abstract

The outbreak of COVID-19, caused by severe acute respiratory syndrome coronavirus 2, started in December 2019, Wuhan, China. We aimed to figure out the time-point and duration of using antiviral drugs for receiving the maximal effects in patients with COVID-19. In this study, we enrolled 129 confirmed COVID-19 mild to moderate patients who had been treated with antiviral drugs during their hospitalization in Wuhan Union Hospital China. The patients were divided into an early antiviral treatment group and late antiviral treatment group. The demographic data, laboratory tests, the virus clearance time, chest computed tomography scans, and so forth were extracted, calculated, and compared between two groups. Our data showed that the median time from illness onset to initiation of antiviral treatment was 6 days in all patients. The group with early antiviral treatment demonstrated 7 days shorter in the virus clearance time when compared to the group with late antiviral treatment. After virus clearance, the group with early antiviral treatment showed milder illness than the group with late antiviral treatment. Early antiviral treatment could effectively shorten the virus clearance time, and prevent the rapid progression of COVID-19. Therefore, the COVID-19 patients should receive combined therapies with antiviral treatment at an early stage.

KEYWORDS
antiviral treatment, COVID-19, SARS-CoV-2 RNA, virus clearance

1 | INTRODUCTION

Since December 2019, coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) broke out in Wuhan, China.[1-4] There is growing evidence of strong human-to-human transmission of the virus.[5-7] Due to effective measures, the situation of COVID-19 in China has witnessed marked mitigation. However, morbidity and mortality surged abroad. As of 29 March 2020, a total number of 678 592 patients have been diagnosed in the world, and 31 752 have died. The global situation still remains grim.

So far, no specific drugs for COVID-19 have been proved.[8,9] The main treatment comprises life support and empirical medication, such as antivirals, antibiotics, antifungals, and glucocorticoids. Up to now, the reports on the optimal antiviral treatment strategies are absent. And the optimization of antiviral strategies is crucial for shortening virus clearance time and improving prognosis. Therefore, the use of antiviral drugs needs to be further optimized, including the timing and duration of antiviral treatment.

Based on this, we investigated confirmed COVID-19 mild to moderate inpatients who had taken antiviral drugs during hospitalization from Wuhan Union hospital. We aim to evaluate the appropriate intervention timing and duration of antiviral treatment and its impact on virus clearance and clinical manifestation.

Ting Yu, Chunxia Tian, Si Chu, Shanshan Luo, Desheng Hu, and Heng Fan contributed equally to this study.

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2 | METHODS

2.1 | Study design and participants

This single-center retrospective cohort study was conducted in Union Hospital, Tongji Medical College, Huazhong University of Science and Technology. Union Hospital is a designated hospital for the treatment of patients with SARS-CoV-2 infection. Between 13 February and 28 February 2020, we enrolled 129 mild to moderate patients with COVID-19 that were hospitalized at Union hospital and given standardized treatments according to the published guidance by Chinese National Health Commission.[10] The clinical typing of the patients were classified based on the COVID-19 Guideline version 7.[10] Mild to moderate patients who were enrolled in this study. Severe patients were excluded. "Mild" was defined as mild clinical symptoms and no signs of pneumonia on imaging; "Moderate" was defined as having fever, respiratory tract and other symptoms, and pneumonia can be observed on imaging. "Severe" was classified if one of the following occurred: (a) dyspnea with a respiratory rate exceeding 30 times per minute, (b) oxygen saturation was less than 93%, and (c) PaO2/FiO2 was less than 300 mm Hg. In severe influenza virus infection, late antiviral treatment was not conducive to the virus clearance. The longer the virus remained in the body, the viral load gradually increased, resulting in enhanced transmission ability. According to the median time from illness onset to initiation of antiviral treatment (6 days), 129 patients were divided into 66 patients with early antiviral treatment (within 6 days) and 63 patients with late antiviral treatment (more than 6 days). We defined virus clearance as two consecutive SARS-CoV-2-negative results by reverse transcription polymerase chain reaction (RT-PCR) in throat-swab samples (detection interval ≥24 hours) and the virus clearance time as the time from illness onset to SARS-CoV-2 negative. This study was approved by the Ethics Commission of the Wuhan Union Hospital of Tongji Medical College, Huazhong University of Science and Technology (No. [2020]93), and the requirement for informed consent was waived by the Ethics Commission for the emerging infectious disease.

2.2 | Procedures

The basic demographic data, symptoms and signs, comorbidities, treatments, disease onset process, laboratory data, viral RNA detections, chest computed tomography (CT) images were obtained from electronic medical records. The date of illness onset was defined as the day when the first symptom showed up. Clinical outcomes were followed up to 10 March 2020. Laboratory validation of SARS-CoV-2 was performed at the Union Hospital. Throat-swab specimens obtained from the upper respiratory tract of patients during hospitalization were stored in the viral-transport medium. Total RNA was extracted within 2 hours using the respiratory sample RNA isolation kit (Huirui, China). SARS-CoV-2 was examined by RT-PCR as described previously.[3] Antiviral drugs of arbidol, interferon, oseltamivir, ribavirin, and ganciclovir were used for the treatment of these patients. All the data were reviewed carefully by a trained team.

2.3 | Statistical analysis

We presented continuous variables as median (interquartile range [IQR]), and categorical variables as number (%). For all data, we used independent group *t*-tests, the Mann-Whitney U test, χ^2 test, or the Fisher's exact test to compare differences between patients with early antiviral treatment and those treated late as appropriate. To explore the impacts of timing and duration of antiviral treatment on the virus clearance time, univariable and multivariable regression models were used. $P < .05$ was considered statistically significant. SPSS software (version 23.0) was used for all analyses.

3 | RESULTS

3.1 | Demographic and clinical characteristics

To figure out the time-point and duration of using antiviral drugs for receiving the maximal effects in patients with COVID-19, 129 enrolled mild to moderate inpatients were divided into early antiviral treatment and late antiviral treatment as above mentioned, including 66 patients and 63 patients respectively. All patients were residents of Wuhan City, some of them were first admitted to the union hospital and some were transferred from other hospitals.

The median age of the 129 patients was 64 years (IQR 56.00-69.00), ranging from 20 to 93 years (Table 1). Among them, there were more females (56.59%) than males (43.41%), which was the exact opposite of patients with severe illness reported earlier (Table 1). All patients had no history of exposure to the Huanan seafood market. 12 (9.30%) had contact with confirmed or highly suspected SARS-CoV-2 infection individuals (Table 1). For all patients, the median time from illness onset to admission was 15 days (IQR 8-12) (Table 1). The most common first symptoms are fever (66.67%), cough (54.26%), and chest tightness (34.88%), followed by fatigue (30.23%), expectoration (19.38%), and myalgia (19.38%). For patients with fever, their axillary temperature was mostly between 37.3 to 38°C (Table 1). Nearly half of the patients had comorbidities, the most comorbidities were hypertension (35.66%), diabetes (11.63%), and heart disease (10.85%) (Table 1). Except for the time from illness onset to hospital admission, there were no significant differences in age, sex, exposure history, comorbidities, signs, and symptoms between the two groups (Table 1).

3.2 | Treatment strategies

In terms of treatment, all the (100%) patients received antiviral treatment. The main antiviral drugs included arbidol (97.67%), interferon (24.03%), ribavirin (13.95%), and oseltamivir (8.53%);

TABLE 1 Clinical characteristics of patients with COVID-19

	No.(%)			
	Total (n = 129)	Early treatment (n = 66)	Late treatment (n = 63)	*P* value*
Age, median (IQR), y	64 (56-69)	62.5 (55.25-68.75)	64 (56.5-68.5)	.634
Sex				
Male	56 (43.41%)	32 (48.48%)	24 (38.10%)	.234
Female	73 (56.59%)	34 (51.52%)	39 (61.90%)	.234
Clear suspected and confirmed patient exposure	12 (9.30%)	6 (9.10%)	6 (9.52%)	.9326
Comorbidities				
Cardiovascular disease	60 (46.51%)	28 (42.42%)	27 (42.86%)	.9604
Hypertension	46 (35.66%)	22 (33.33%)	24 (38.10%)	.5725
Heart disease	14 (10.85%)	10 (15.15%)	4 (6.35%)	.1081
Cerebrovascular disease	2 (1.55%)	0	2 (3.17%)	.1446
Pulmonary disease	4 (3.10%)	3 (4.55%)	1 (1.59%)	.3326
Endocrine disease	24 (18.60%)	14 (21.21%)	10 (15.87%)	.4360
Diabetes	15 (11.63%)	9 (13.64%)	6 (9.52%)	.4664
Hyperlipidemia	7 (5.43%)	6 (9.09%)	1 (1.59%)	0.06
Digestive system disease	10 (7.75%)	5 (7.58%)	5 (7.94%)	.9389
Urinary system disease	7 (5.43%)	4 (6.06%)	3 (4.76%)	.7448
Malignancy	8 (6.20%)	4 (6.06%)	4 (6.35%)	.9458
Signs and symptoms at onset				
Fever	86 (66.67%)	49 (74.24%)	37 (58.73%)	.0617
Range of temperature				
<37.3°C	43 (33.33%)	17 (25.76%)	26 (41.27%)	.0617
37.3-38.0°C	48 (37.21%)	25 (37.88%)	23 (36.51%)	.8721
38.1-39.0°C	34 (26.36%)	22 (33.33%)	12 (19.05%)	.0656
>39.0°C	4 (3.10%)	2 (3.03%)	2 (3.17%)	.9623
Cough	70 (54.26%)	41 (62.12%)	29 (46.03%)	.0667
Chest congestion	45 (34.88%)	23 (34.85%)	22 (34.92%)	.9931
Fatigue	39 (30.23%)	22 (33.33%)	17 (26.98%)	.4325
Expectoration	25 (19.38%)	15 (22.73%)	10 (15.87%)	.3249
Myalgia	25 (19.38%)	13 (19.70%)	12 (19.05%)	.9257
Dyspnea	23 (17.83%)	12 (18.18%)	11 (17.46%)	.9148
Chill	22 (17.05%)	10 (15.15%)	12 (19.05%)	.5565
Anorexia	13 (10.08%)	10 (15.15%)	3 (4.76%)	.0501
Diarrhea	12 (9.30%)	8 (12.12%)	4 (6.35%)	.2592
Nausea	9 (6.98%)	5 (7.58%)	4 (6.35%)	.7846
Pharyngalgia	8 (6.20%)	5 (7.58%)	3 (4.76%)	.5077
Time from illness oneset to, median (IQR), d				
Hospital admission	15 (8-21)	11.5 (7-16)	16 (11-22)	.000

Abbreviation: IQR, interquartile range.
*P values indicate differences between early treatment and late treatment patients. $P < .05$ was considered statistically significant.

105 (81.40%) patients received antibiotic treatment; 3 (2.33%) patients received antifungal treatment; 28 (21.71%) patients received glucocorticoids; 95 (73.64%) patients received oxygen therapy; 8 (6.20%) patients received immunotherapy (Table 2). A significant difference was only observed in glucocorticoids (28.79% vs 14.29%) between patients with early antiviral treatment and late (Table 2).

3.3 | Effects of different antiviral treatment strategies on the SARS-CoV-2 clearance time

Among all patients, the median time from illness onset to positive SARS-CoV-2 RNA detection was 10 days (IQR 3-16). As some inpatients were transferred from other hospitals, viral RNA detection has been accomplished before admission. The median time from

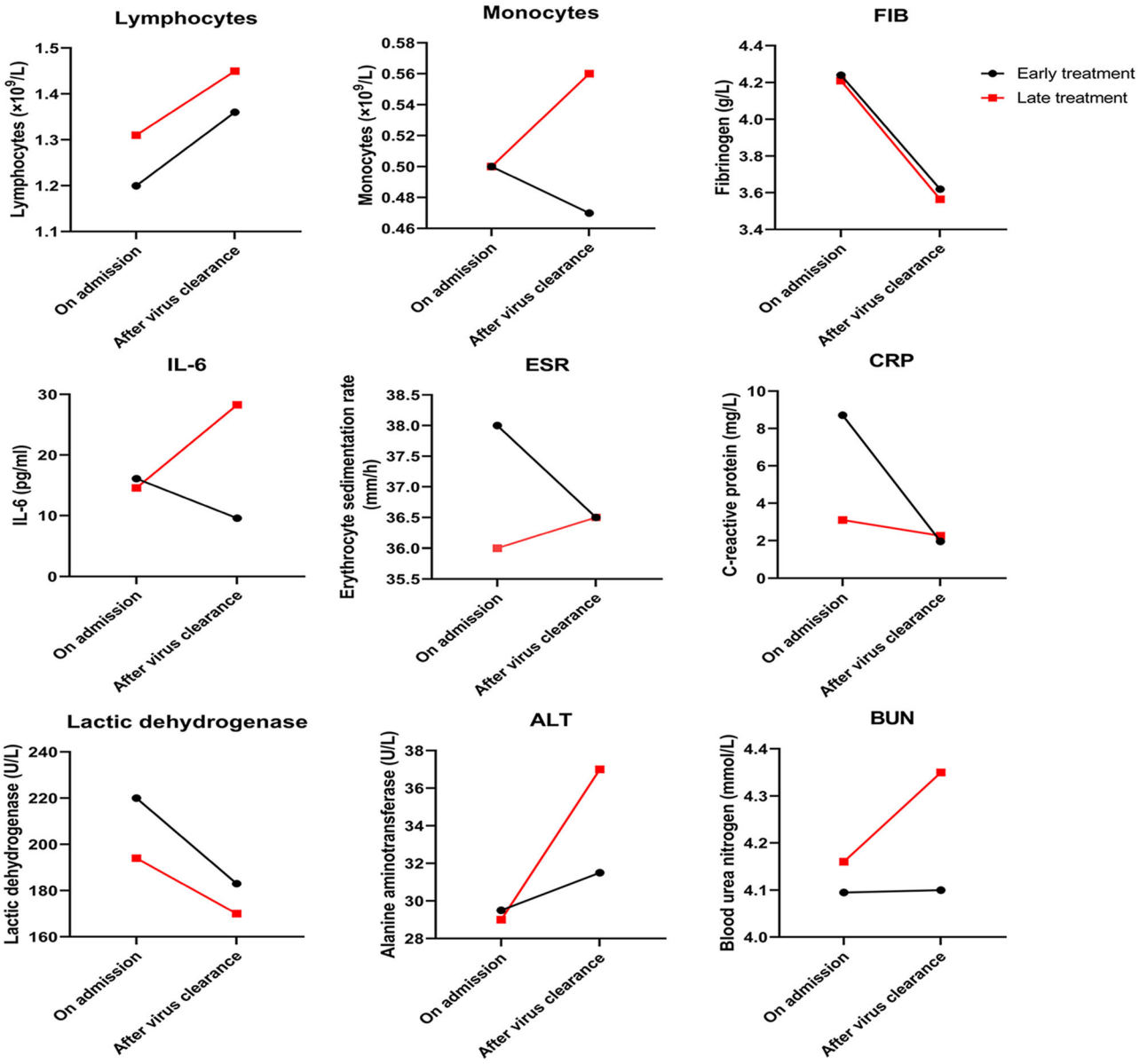

FIGURE 1 Dynamic analysis of laboratory examinations in patients with COVID-19 under different antiviral treatment strategies. The black and red lines represent the early antiviral treatment group and late antiviral treatment group, respectively. ALT, alanine aminotransferase; BUN, blood urea nitrogen; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FIB, fibrinogen; IL-6, interleukin-6

illness onset to initiation of antiviral treatment was 6 days (IQR 3-12). In addition, the median duration of antiviral medication during illness was 19 days (IQR 15-24). And the median time of virus clearance was 25 days (IQR 19-32) (Table 2). Of note, the data revealed a significant difference in virus clearance time between the two treatment groups. The patients with early antiviral treatment had a shorter virus clearance time than the patients with late antiviral treatment (22 [IQR, 17-29.75] vs 29 [IQR 23-36]) (Table 2). This results revealed that the virus clearance was significantly accelerated in patients with early antiviral treatment, early antiviral treatment accelerated virus clearance by 7 days. What's more, the duration of antiviral medication during illness was 21 days (IQR 17.25-26) for the patient treated early and 17 days (IQR 14-24) for those treated late. Then, patients in early and late treatment were further categorized into different subgroups based on the median duration of antiviral medication (19 days). The median virus clearance time was 17 days (IQR 13.5-22) in the early treated patients who had taken antivirals for 19 days or less, whereas the time was 25 days (IQR 20-31) in those who had taken antivirals more than 19 days. Likewise, the median time from illness onset to virus clearance was 26 days (IQR 19.5-32.5) in the late treated patients who had taken antivirals for 19 days or less, whereas the median time was 34.5 days (IQR 28.5-39) in those who had taken antivirals more than 19 days (Figure 3). To identify the optimal duration of antiviral medication, patients

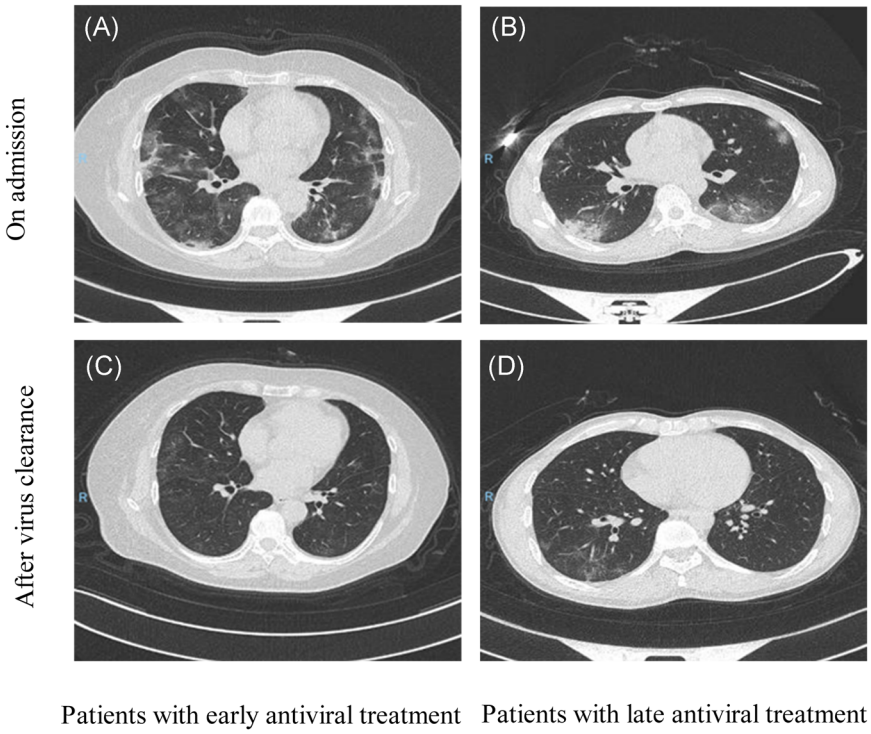

FIGURE 2 Comparison of the chest CT images in patients with COVID-19 under different antiviral treatment strategies. A and C, were the contrast chest CT images of early treatment patients on admission and after virus clearance. This patient, 58 years old, female, was a representative of patients with early antiviral treatment, whoes time of initiation of antiviral treatment, duration of antiviral medication and virus clearance time were 3, 15, and 6 d respectively. B and D, were the contrast chest CT images of late treatment patients on admission and after virus clearance. This patient, 45 years old, male, was a representative of patients with late antiviral treatment, whoes time of initiation of antiviral treatment, duration of antivirals medication and virus clearance time were 13, 20, and 30 d respectively. CT, computed tomography

were divided into 6 groups by duration: 0-7, 8-14, 15-21, 22-28, 29-35, 36-42 d. In the "0-7 day" group, the virus clearance time was significantly shortened compared to other group. Besides, virus clearance time gradually increased in a time-dependent manner (Figure 3). Therefore, our study suggested that the applied antiviral medication within 7 days was the optimal period to get a best virus clearance time. In addition, linear regression analysis showed that time of initiation of antiviral treatment and duration of medication correlated with virus clearance time (both $P < .001$) (Figure 4). Furthermore, we also compared age and sex factors, and found that the effect of age and sex on the time of virus clearance was not obvious (Table S1; Figure S1). Due to the significant difference in glucocorticoids treatment between the two groups, we further analyzed the correlation of glucocorticoids treatment and virus clearance time.

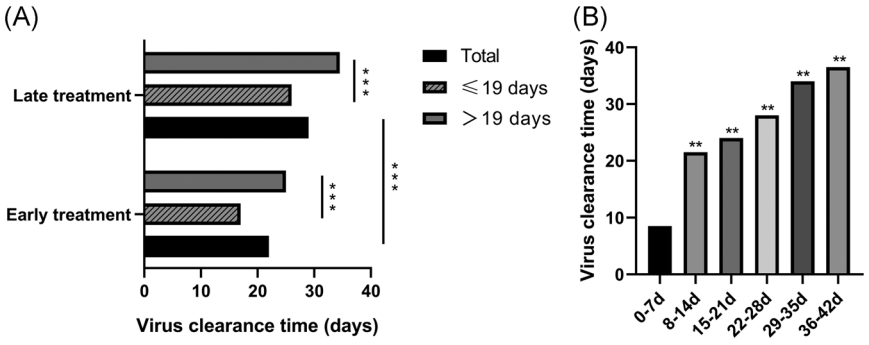

FIGURE 3 Comparison of the virus clearance time in patients with COVID-19 under different antiviral treatment strategies. A, The differences in virus clearance time between early and late treatment groups. B, The relationship between different duration of antiviral medication and virus clearance time in all patients. The virus clearance time were presented as median. $P < .05$ was considered statistically significant. $^{**}P < .01$ vs "0-7 d" group, $^{***}P < .001$

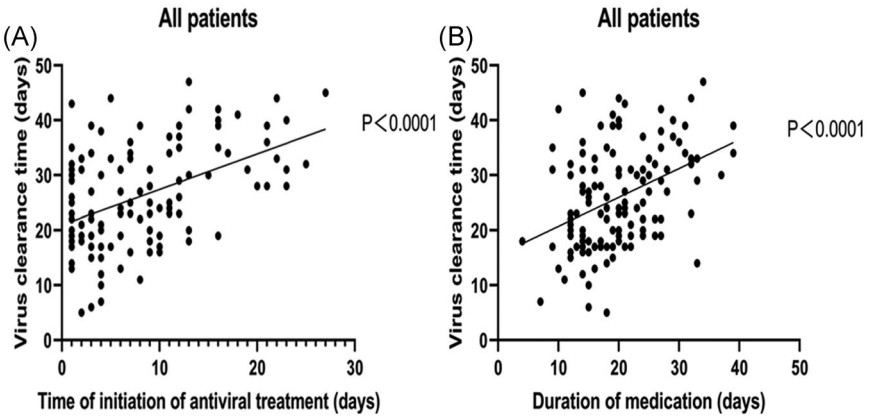

FIGURE 4 Univariate linear regression analysis of time of initiation of antiviral treatment and duration of antiviral medication with virus clearance time. A, The correlation of time of initiation of antiviral treatment and virus clearance time in all patients ($P < .0001$). B, The correlation of duration of antiviral medication and virus clearance time in all patients ($P < .0001$). $P < .05$ was considered statistically significant

Univariate analysis demonstrated that glucocorticoids treatment was slightly negatively correlated with virus clearance time (Figure S1). With the elimination of confounding factors such as glucocorticoids treatment, sex, and age, multivariate regression analysis further revealed that time of initiation of antiviral treatment and duration of antivirals medication were independent impact factors for virus clearance time. Especially, time of initiation of antiviral treatment was highly correlated with the time of virus clearance (Table S2). Our data indicated early use of antiviral drugs and medication duration within 7 days could effectively shorten the virus clearance time.

TABLE 2 Treatments and outcomes of patients with COVID-19

	No.(%) or median (IQR)			
	Total (n = 129)	Early treatment (n = 66)	Late treatment (n = 63)	*P* Value*
Treatment, number (%)				
Antiviral treatment	129 (100.00%)	66 (100.00%)	63 (100.00%)	
Arbidol	126 (97.67%)	64 (96.97%)	62 (98.41%)	.5867
Interferon	31 (24.03%)	20 (30.30%)	11 (17.46%)	.0879
Oseltamivir	11 (8.53%)	5 (7.58%)	6 (9.52%)	.6921
Ribavirin	18 (13.95%)	12 (18.18%)	6 (9.52%)	.1560
Ganciclovir	1 (0.78%)	0	1 (1.59%)	.3042
Antibiotic treatment	105 (81.40%)	56 (84.85%)	49 (77.78%)	.3023
Antifungal treatment	3 (2.33%)	2 (3.03%)	1 (1.59%)	.5867
Oxygen therapy	95 (73.64%)	53 (80.30%)	42 (66.67%)	.0789
Glucocorticoids	28 (21.71%)	19 (28.79%)	9 (14.29%)	.0458
Immunotherapy	8 (6.20%)	4 (6.06%)	4 (6.35%)	.9458
Outcomes, median (IQR)				
Time from illness onset to be confirmed by SARS-Cov-2 RNA detection, days	10 (3-16)	7 (3-13)	12 (9-17)	.000
Time from illness onset to initiation of antiviral treatment, days	6 (3-12)	3 (1-4)	12 (9-16)	.000
Duration of total antiviral medication during the illness, days	19 (15-24)	21 (17.25-26)	17 (14-24)	.013
Time from illness onset to SARS-CoV-2 negative, days	25 (19-32)	22 (17-29.75)	29 (23-36)	.000

Abbreviations: IQR, interquartile range; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
*P values indicate differences between early treatment and late treatment patients. P < 0.05 was considered statistically significant.

3.4 | Patients have a good prognosis after SARS-CoV-2 RNA clearance, especially in patients treated early

All laboratory tests were traced from patients on admission. After virus clearance, lymphocytes absolute counts in all patients increased. The level of monocytes decreased in patients with early antiviral treatment, but it still increased in patients treated late (Figure 1; Table S4). In terms of blood coagulation function, the median level of fibrinogen (FIB) of the two groups on admission was above the normal range, whereas the value returned to within normal range after the virus clearance (Figure 1; Tables S3, S4). After virus clearance, we observed a clear distinction of the levels of serum inflammation markers between early and late antiviral treatment groups. More specifically, the level of C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and interleukin-6 (IL-6) decreased significantly after virus clearance in patients with the early antiviral treatment. However, IL-6 and ESR in patients treated late were clearly higher than baseline (Figure 1; Table S3, S4). In addition, we also noted the abnormal frequency of white blood cells and neutrophils in patients with late treatment was higher than that of patients with early treatment (Table S3, S4). Moreover, for blood biochemistry markers, the heart, liver and kidney function markers fluctuated within the normal range after virus clearance (Figure 1; Table S4). And the median value of lactic dehydrogenase (LDH) was lower than baseline in all patients (Figure 1). However, compared with patients treated early, the alanine aminotransferase (ALT), aspartate aminotransferase (AST) and blood urea nitrogen (BUN) in patients treated late were higher after virus clearance (Figure 1; Table S4). These may be due to the potential injury in liver and kidney in patients treated late. On chest CT images, lung infections in both groups were effectively relieved after virus clearance. CT images showed bilateral distribution of patchy shadows and ground glass opacity were occurred in most patients on admission while there was significant lesions absorption after virus clearance (Figure 2). It can be seen that after virus clearance, the patients did not have obvious multiple organs damage, and the coagulation disorder and inflammatory response were gradually controlled. Besides, patients treated early had a milder inflammatory response than those treated late after virus clearance.

4 | DISCUSSION

The level and duration of virus replication determine the capacity of transmission and provides instructive information on the isolation of patients. Since coronavirus RNA detection is more sensitive, most guidelines involve qualitative or quantitative viral RNA detection as an informative test in standards of discharge and terminating isolation.[11] In previous studies, it was found that for survivors, the median duration of virus shedding from the onset of disease was 20 days, but the virus continued to be detectable until death in non-survivors.[12] The long-term presence of the virus in the body was not conducive to the prognosis of the disease. In severe influenza virus infection, late antiviral treatment was associated with prolonged virus detection, and prolonged viral shedding was an independent risk factor for disease progression.[13] Effective antiviral treatment might improve outcome in COVID-19. But no shortening in the duration of viral shedding after lopinavir/ritonavir treatment was observed in previous studies.[14] In addition, optimized regimen of using antiviral drugs to curtail the virus clearance time had not been well described.

In this study, we depicted the intervention timing and total duration of antiviral medication, and evaluated its impact on virus clearance time and disease prognosis. Based on the median time from illness onset to initiation of antiviral treatment (6 days), we divided 129 mild to moderate COVID-19 patients into early antiviral treatment group and late antiviral treatment group to investigate the impact of timing of antiviral treatment on virus clearance time. The characteristics of the patients at baseline were generally consistent across the two groups. At the illness onset, patients mainly exhibited fever, cough, chest congestion and other symptoms. These symptoms gradually subsided as the virus was cleared away. Although we observed that there were slightly more obvious initial symptoms in patients with early treatment of antivirals, there was no significant difference between the two groups. It might be because patients with obvious early symptoms were more likely to pay attention to their disease. Thus, they took antiviral drugs earlier. Meanwhile, we found that the frequency of use of glucocorticoids had differences between two groups. As we known the use of glucocorticoids is controversial, this might related with the heterogeneity of treatment regimens and also was a confounder. Univariate regression analysis demonstrated that glucocorticoids treatment was slightly negatively correlated with virus clearance time. Thus, this confounder was excluded due to the weak correlation. With the virus clearance, the blood biochemistry, coagulation function, and inflammation markers of most early treated patients gradually returned to normal range, and chest CT showed that lung infections gradually were controlled. Also, there was no clearly multiple organs damage. However, the improvement of abnormal markers in patients with late treatment was not as good as that in patients treated early, and the inflammatory storm still existed. It might be related to the fact that the virus in patients with late antiviral treatment were not well contained. Thus, the virus might replicate in the body for a longer time, attack the body further, and cause a relatively durable inflammatory response. Taken together, our results showed that patients with early treatment was more likely to recover after virus clearance.

In this cohort, arbidol was the most widely used antiviral drug. Its usage rate is as high as 97.6%. Arbidol has been demonstrated to be a broad spectrum antiviral drug for prophylaxis and treatment of influenza.[15] It can not only interfere with virus-induced membrane fusion, but also degrade viral RNA (messenger RNA) to inhibit protein synthesis and thereby block the early replication of the virus.[16] This mode of action is mainly due to the disruption of key steps in virus-cell interactions.[17] In previous studies, its inhibitory activity has been extended to other human viruses, including respiratory syncytial virus, SARS and herpes simplex virus type I.[18,19] Up to now, there were no licensed vaccines or antiviral medicines

for SARS-CoV-2 infection. Broad-spectrum antiviral drugs, including arbidol, could be a useful alternative therapy. It might be beneficial for patients with COVID-19.

As showed in our study, the median virus clearance time in patients with early antiviral treatment was significantly lower by 7 days than that in patients who were treated late, and the time was further shortened after optimizing the duration of antivirals medication. Hence, we suggest that antiviral drugs should be administered to patients with COVID-19 as early as possible, because late antiviral drugs application could delay the clearance of virus and increase severe inflammatory response risk. Based on these findings, we further subdivided the duration of medication into 6 time intervals to ascertain the optimal duration of antiviral medication. We found that the virus clearance time was the shortest in patients taking antiviral medication within 7 days, which was consistent with the medication duration recommended in the guidelines. The virus clearance time increased sharply when the duration of antiviral medication more than 7 days and elevated in a time-dependent manner. Our study indicated that controlling the duration of antiviral medication within 7 days could effectively clear virus, and slow down the replication of the virus in the body. On the other hand, antiviral drugs also have some side effects, and virus-infected patients were able to develop resistance to antiviral drugs after long time administration. Thus, antiviral drugs should not be used for a long time for safety which was consistent with our findings. This study supported the idea that patients receiving antiviral drugs within 7 days benefit more. Last but not least, virus RNA detection should be done as early as possible. These have important implications for both virus clearance and disease progression. Taken together, early use of antiviral drugs and the reasonable control of duration of antiviral medication within 7 days might effectively shorten the virus clearance time, reduce the possibility of further aggravation of COVID-19, weaken the capacity of SARS-CoV-2 transmission, and save more time for the treatment and prevention of COVID-19.

This study has also several limitations. First, confounding factors exited. Due to the heterogeneity of treatment regimens among patients, the effects of antiviral drugs might be affected by other drugs. Second, the positive rate of SARS-CoV-2 RNA detection in throat swabs was relatively low, and inconsistent frequency of respiratory specimen collection affected virus clearance time.[20,21] Further research on virus clearance in other samples is needed. Third, since this is a retrospective study, laboratory tests were not uniformly launched among patients.

In conclusion, early (no more than 6 days) and short duration of antiviral medication (no more than 7 days) can effectively curtail the virus clearance time and improve the patient's prognosis. It would be beneficial in clinical management of patients with COVID-19 and provide a theoretical basis for optimizing the strategy of using antiviral drugs.

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CONFLICT OF INTERESTS

The authors do not have any professional and financial affiliations that may be perceived to have biased the presentation. Prior Publication: None of the material in this manuscript has been published or is under consideration for publication elsewhere, including the Internet and conferences.

AUTHOR CONTRIBUTIONS

DH and HF designed this study. TY, CT, SC, HZ, and ZZ collected the epidemiological and clinical data. TY and CT processed statistical data. TY, and SL drafted the manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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