

Influencing factors of virus duration and virus clearance in COVID-19 patients in Shenzhen: A retrospective study.

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Abstract

Abstract Background. We aimed to analyze the influencing factors of virus duration and virus clearance in coronavirus disease 2019 (COVID-19) in Shenzhen, China, and to provide our experience in the treatment and management of COVID-19. **Methods.** The clinical data and laboratory test results of COVID-19 inpatients admitted to the Third People's Hospital of Shenzhen, Guangdong Province from January 2020 to March 2020 were retrospectively collected. In COVID-19 rehabilitation patients, two consecutive negative RT-PCR results on nasopharyngeal swabs were defined as virus clearance. The time from onset of the disease to virus clearance was defined as the virus duration. We analyzed the virus clearance rate at different time points and the impact of clinical features and treatments on virus clearance. **Results.** A total of 201 patients with COVID-19, including 89 women (44.3%) and 112 men (55.7%), were included in our study. According to the severity of the disease, the patients were divided into no severe patients and severe patients. The overall median virus duration for all patients was 17 days. The overall virus clearance rates within 1, 2, 3, 4, 5, and 6 weeks after onset were 1.5%, 36.6%, 73.4%, 90.2%, 97.3%, and 100%, respectively. A multiple linear regression model was performed to analyze the factors influencing virus clearance. The factors influencing virus clearance within 2 weeks were treatment timing and glucocorticoid usage. The influencing factors for virus clearance within 4 weeks were treatment timing, glucocorticoid usage and age. **Conclusion.** Treatment timing was related to virus clearance. The earlier the treatment was initiated, the faster the virus clearance. For COVID-19 patients, early detection and early treatment strategies should be adopted. Glucocorticoid usage may be detrimental to virus clearance and should be more restricted. Age > 60 years may also be a detrimental factor for virus clearance.

Background

In December 2019, there were several cases of pneumonia of unknown etiology in Wuhan, China, which subsequently spread to Hubei Province and other parts of China. On January 7, 2020, the Chinese CDC identified a new coronavirus from patients' pharyngeal swab specimens. This virus was named the 2019 novel coronavirus (2019-nCoV) by the WHO (1). The disease caused by this virus is coronavirus disease 2019 (COVID-19). As of 24:00 on April 7, the Chinese Health Commission reported that there were 1190 new confirmed cases (including 189 severe cases) in China, 77279 cases were cured and discharged, 3333 cases died, and 81802 active cases were reported. At present, COVID-19 is epidemic in many countries and regions around the world. On April 7, 2020, according to WHO reports, the cumulative number of confirmed cases worldwide was 1279722 cases, and the number of deaths was 72614.

A negative viral nucleic acid test is an important laboratory result to define that patients will no longer discharge virus and the infectivity has declined. In China, the "Diagnosis and treatment of new coronavirus pneumonia, version 7" guideline recommends two consecutive negative RT-PCR results from sputum, nasopharyngeal swabs, or other respiratory specimens as an important indicator of patients' recovery and discharge standard. At present, virus clearance and its related influencing factors in COVID-19 patients are not yet clear. This study aimed to explore the virus duration in patients with COVID-19, to

analyze the influencing factors of the virus clearance rate at different time points and to provide a reference for clinical decision-making.

Methods

Patients and clinical definitions

All included COVID-19 patients were from the Third People's Hospital of Shenzhen City, Guangdong Province, including 89 females and 112 males. Two consecutive (at two different times) negative RT-PCR results from the nasopharyngeal swabs were defined as virus clearance. The time from the onset of the disease (symptomatic patients) or the first RT-PCR positive result (asymptomatic carriers) to virus clearance was defined as virus duration.

Viral RNA detection in patients with COVID-19: In this study, the detection of the 2019 new coronavirus was performed by the CDC of Shenzhen City, Guangdong Province, using RT-PCR. The interval between two tests was not less than 24 hours, generally 24–48 hours.

Clinical classification

Overall, patients were divided into no severe patients and severe patients. No severe patients included asymptomatic carriers and mild and common patients. Asymptomatic carriers were patients who were asymptomatic but positive on the nucleic acid test; mild type patients had mild clinical symptoms and no pneumonia manifestations on imaging; and common type patients had fever, respiratory symptoms, and pneumonia manifestations on imaging.

Severe patients included serious and critical patients. Serious patients met any of the following conditions: 1. shortness of breath, $RR \geq 30$ times/min; 2. at rest, the pulse oxygen saturation was $\leq 93\%$; 3. $PaO_2/FiO_2 \leq 300$ mmHg; or 4. lung imaging showed that, within 24–48 hours, the lesions significantly progressed by $> 50\%$. Critical patients met any of the following conditions: 1. respiratory failure occurred, and mechanical ventilation was required; 2. shock occurred; or 3. ICU monitoring treatment was required for the combined failure of other organs.

For the definition of asymptomatic carriers, mild, common, serious and critical patients, please refer to the Chinese(4)" Diagnosis and treatment of new coronavirus pneumonia, version 7" guideline.

Statistical analysis

Data are expressed as the median (25th–75th percentile) or number (percentage). The normality of variables was assessed. The Mann–Whitney U test was used to compare continuous variables. Pearson's χ^2 analysis or Fisher's exact test was used to compare categorical variables. Variables that achieved statistical significance ($P < .05$) by univariate analysis were subsequently included in the multivariate analysis, which was performed to identify the influencing factors for virus clearance. All statistical analyses were performed with IBM SPSS Statistics V20.

Results

Baseline characteristics of all patients

Table 1 shows the characteristics of 201 hospitalized patients with confirmed COVID-19. In all patients, the median age was 51 years (IQR, 33.5–62 years), and 89 (44.3%) were men. Of the 201 patients, 13 (6.5%) had underlying pulmonary diseases, including chronic bronchitis, emphysema, and previous tuberculosis. Fifty-eight (28.9%) of the confirmed patients had other underlying diseases, such as diabetes, hypertension, cardiovascular disease, HBsAg positivity, autoimmune diseases, fatty liver, acute cerebral infarction, arrhythmia, valvular disease, allergic cough, thyroid disease, chronic pharyngitis, tumor, or mental illness. Fourteen of the patients had a smoking history, and the median BMI was 22.81 (IQR, 20.72–24.94). A total of 168 (86.3%) patients had fever at the onset of the illness, 162 (80.6%) had respiratory symptoms (e.g., dry cough, expectoration, chest tightness and shortness of breath), and 77 (38.31%) had symptoms of other systems (e.g., abdominal pain, diarrhea, nausea, vomiting, myalgia, headache).

Table 1
Baseline Characteristics of Patients with COVID-19

	Overall (N = 201)	Nonsevere (N = 131)	Severe (N = 70)	P value^a
Age, median (IQR), y	51(33.5–62)	40(30–55)	62(51.75–66.25)	0.000
Male Sex	89(44.3%)	68(51.9%)	21(30%)	0.003
Underlying pulmonary diseases	13(6.5%)	11(8.4%)	2(2.9%)	0.128
Other underlying diseases	58(28.9%)	17(13.0%)	41(58.6%)	0.000
Smoking history	14(7.0%)	7(5.3%)	7(10.0%)	0.217
BMI, median (IQR)	22.81(20.72–24.94)	21.90(20.11–23.83)	24.43(22.25–26.82)	0.000
Symptoms				
Fever	168(83.6%)	99(75.6%)	69(98.6%)	0.000
Respiratory symptoms	162(80.6%)	98(74.8%)	64 (91.4%)	0.005
Other symptoms	77(38.3%)	38(29.0%)	39(55.7%)	0.000
Laboratory findings				
WBC count, median (IQR),×10 ⁹ /L	4.66(3.75–5.72)	4.68(3.64–5.61)	4.58(3.79–5.90)	0.788
Lymphocyte count, Median (IQR),×10 ⁹ /L	1.28(0.84–1.69)	1.39(1.09–1.76)	1.06(0.86–1.41)	0.000
CRP, median (IQR), mg/L	0.00(0.00–9.00)	0.00(0.00-5.82)	0.00(0.00-23.85)	0.308
hsCRP, median (IQR), mg/L	6.10(0.34–21.53)	3.08(0.13–14.05)	15.20(2.91–33.78)	0.000
IL-6, median (IQR), pg/ML	14.26(5.03–22.43)	8.36(3.42–15.82)	23.50(16.62–43.09)	0.000
PCT, median (IQR), ug/L	0.04(0.03–0.07)	0.04(0.02–0.06)	0.06(0.04–0.08)	0.000

Abbreviations: BMI, body mass index; WBC, white blood cell; CRP, C-reaction protein; hsCRP, high-sensitivity C-reaction protein; PCT, procalcitonin; IL-6, interleukin 6; FER, ferritin; ESR, erythrocyte sedimentation rate; IQR, interquartile range; 2019-nCoV, 2019 novel coronavirus.

The ^a*p* values indicate differences between nonsevere patients and severe patients. *P* < 0.05 was considered statistically significant.

	Overall (N = 201)	Nonsevere (N = 131)	Severe (N = 70)	<i>P</i> value ^a
FER, median (IQR), µg/L	710.5(115.75–106.5)	458(88.5–828)	882(449–1371)	0.036
ESR, median (IQR), mm/h	30(14–50)	25(12–45)	37(17.5–52.5)	0.029
Abnormalities on chest CT	182(90.5%)	114(87%)	68(97.1%)	0.002
Treatment				
Antibiotic therapy	36(17.9%)	27(20.6%)	9(12.9%)	0.172
Glucocorticoids usage	53(26.4%)	8(6.1%)	45(64.3%)	0.000
Combination of Anti-Virus	107(53.2%)	63(48.1%)	44(62.9%)	0.168
Treatment timing median (IQR), d	3(2–6)	3(1–5)	4(2.75-7)	0.000
Average virus duration , median (IQR), d	17(13–22)	15(12–19)	20(15.5–27)	0.000
Abbreviations: BMI, body mass index; WBC, white blood cell; CRP, C-reaction protein; hsCRP, high-sensitivity C-reaction protein; PCT, procalcitonin; IL-6, interleukin 6; FER, ferritin; ESR, erythrocyte sedimentation rate; IQR, interquartile range; 2019-nCoV, 2019 novel coronavirus.				
The ^a <i>p</i> values indicate differences between nonsevere patients and severe patients. <i>P</i> < 0.05 was considered statistically significant.				

The white blood cell and lymphocyte counts were normal in the study population, but they were close to the lower limit of normal value (WBC, $4.66 \times 10^9/L$ [IQR, $3.75-5.72 \times 10^9/L$]; [lymphocyte count, $1.28 \times 10^9/L$ ($0.94-1.69 \times 10^9/L$)]. In terms of inflammatory factors, the overall CRP, HSCRP, IL-6, PCT, and ESR values did not change significantly, but the FER increased significantly. A total of 182 (90.5%) patients had abnormal CT imaging.

All patients received antiviral treatment, and 107 patients (53.2%) received two or more combined antiviral treatments. Thirty-six patients (17.9%) received antibiotic treatment. Fifty-three people (26.4%) received glucocorticoid therapy.

The median time from onset or positive nucleic acid test to admission in the overall patient population was 3 days, and the median virus duration was 17 days.

Baseline characteristics between severe patients and no severe patients

According to the severity of the disease, the patients were divided into severe patients and no severe patients (70 vs 131).

As shown in Table 1. Severe patients were significantly older than no severe patients (median age, 62 years [IQR, 51.75–66.25] vs 40 years [IQR, 30–55]; $P < 0.001$), and the sex composition ratio was also significantly different (male, 51.9% vs 30%). There was no significant difference in the prevalence of underlying lung diseases between the two groups. However, other underlying diseases were more common among patients with severe disease than among patients with no severe disease (58.6% vs 13.0%). Smoking history was similar between the two groups. Compared with the no severe patients, fever, respiratory symptoms, and other symptoms were more likely to be reported in severe patients.

Further comparison between severe and no severe patients showed that lymphocyte count, hsCRP, IL-6, PCT, FER, and ESR were higher in the severe patients than in the no severe patients. There were more CT abnormalities in the severe patients than in the no severe patients.

Regarding treatment schemes, glucocorticoid usage was more common in the severe patients, but there was no significant difference between the two groups in the use of a combination of antiviral drugs and antibiotic therapy.

The time from symptoms or first positive viral RNA test to admission was longer in the severe patients than in the no severe patients. The virus duration of the severe patients was longer than that of the no severe patients.

Virus Clearance rates at Different Time Points

For all included patients, the virus clearance rates within 1, 2, 3, 4, 5, and 6 weeks were 1.5%, 36.6%, 73.4%, 90.2%, 97.3%, and 100%, respectively. The virus clearance rates of the no severe patients were 1.5%, 45%, 83.9%, 96.9%, 100%, and 100%, respectively. The virus clearance rates of the severe patients were 1.5%, 20%, 52.3%, 76.9%, 92.3%, and 100%, respectively. Within 2, 3, 4, and 5 weeks, the viral clearance rate of the severe patients was less than that of the no severe patients (see Table 2 and Fig. 1).

Table 2
Virus Clearance Rates at Different Time Points

Time*	Cumulative virus clearance rate for all patients (%)	Cumulative virus clearance rate for nonsevere patients (%)	Cumulative virus clearance rate for severe patients (%)	<i>P</i> value ^a
≤ 1 W	1.5	1.5	1.5	1.000
≤ 2 W	36.6	45	20	0.001
≤ 3 W	73.4	83.9	52.3	0.000
≤ 4 W	90.2	96.9	76.9	0.000
≤ 5 W	97.3	100	92.3	0.004
≤ 6 W	100	100	100	

*From symptom/2019 nCoV-RNA positive (asymptomatic carriers) ^a*p* value indicates differences between nonsevere patients and severe patients; *p* < 0.05 was considered statistically significant.

Analyses of Factors Influencing Virus Clearance in All Patients

To clarify the influencing factors of early and late virus clearance in patients with COVID-19, we performed univariate analysis and multivariate regression analysis on the influencing factors for viral clearance within 2 and 4 weeks.

Univariate analysis of the factors virus clearance within 2 weeks showed that there were differences in respiratory symptoms and other symptoms at onset, glucocorticoid usage, treatment timing < 7 days, and CT abnormalities between the virus clearance group and the nonclearance group. Multivariate regression analysis showed that glucocorticoid usage was a disadvantageous factor for virus clearance (OR = 4.041, *P* < 0.05), and earlier treatment was an advantageous factor for virus clearance (OR = 0.093, *p* < 0.05) (see Table 3).

Variables	Univariate			Multivariate	
	Virus clearance within 2 weeks	No virus clearance within 2 weeks	P value ^a	OR	P value
WBC count, median (IQR), ×10 ⁹ /L	4.74(3.86-5.85)	4.55(3.53-5.58)	0.350		
Lymphocyte count, Median (IQR), ×10 ⁹ /L	1.29(1.02-1.62)	1.23(0.91-1.23)	0.496		
Sex, Male	28(48.3%)	69(61.1%)	0.110		
Smoking history			0.539		
No	56 (96.6%)	105 (92.9%)			
Yes	2 (3.4%)	8 (7.1%)			
Underlying pulmonary diseases			0.077		
No	52(89.7%)	110(97.3%)			
Yes	6(10.3%)	3(2.7%)			
Other underlying diseases			0.909		
No	39(67.2%)	75(66.4%)			
Yes	19(32.8%)	38(33.6%)			
Respiratory symptoms at onset			0.026		NS
No	15(25.9%)	14(12.4%)			
Yes	43(74.1%)	99(87.6%)			
Other symptoms at onset			0.020		NS
No	41(70.7%)	59(52.2%)			
Yes	17(29.3%)	54(47.8%)			
Antibiotic therapy#			0.850		
No	46(79.3%)	91(80.5%)			
Yes	12(20.7%)	22(19.5%)			
Glucocorticoids usage*			0.000		
No	52(89.7%)	71(62.8%)			
Yes	6(10.3%)	42(37.2%)		4.041	0.005
Combination of two or more antiviral drugs			0.107		
No	29(50%)	42(37.2%)			

Yes	29(50%)	71(62.8%)		
Treatment timing			0.002	
>7 days	1(4.5%)	21(18.6%)		
≤7 days	57(98.3%)	92(81.4%)	0.093	0.024
Age			0.087	
<18 years	6(10.3%)	3(2.7%)		
18-60 years	33(30.6%)	75(69.4%)		
>60 years	19(32.8%)	35(31%)		
BMI			0.233	
<28	55(94.8%)	101(89.4%)		
≥28	3(5.2%)	12(10.6%)		
Temperature			0.937	
<37.3°C	39(67.2%)	73(64.6%)		
37.3-38°C	15(25.9%)	28(24.8%)		
38.1-39°C	4(6.9%)	11(9.7%)		
>39°C	0(0%)	0(0%)		
Abnormalities on chest CT			0.045	NS
None	8(13.8%)	5(4.4%)		
Unilateral	14(24.1%)	21(18.6%)		
Bilateral	36(62.1%)	87(77%)		
Abbreviations: BMI, body mass index; WBC, white blood cell; NS, not significant.				
^a p value indicates differences between two groups, and p<0.05 was considered statistically significant.				
# Antibiotics used in this study include moxifloxacin, levofloxacin, azithromycin, and cefpodoxime.				
* The glucocorticoid used in this study was methylprednisolone with a dose of 40-80 mg for a period of 1 week or less.				

Table 3

Univariate and Multivariate Analyses of Factors Influencing Virus Clearance Within 2 Weeks in All Patients
 Univariate analysis of the factors influencing virus clearance within 4 weeks showed that there were differences in sex, other underlying diseases, other symptoms at onset, glucocorticoid usage, treatment timing < 7 days, and age > 60 years between the virus clearance group and the nonclearance group.

Multivariate regression analysis showed that glucocorticoid usage was a disadvantageous factor for virus clearance (OR = 11.273, $P < 0.05$), age > 60 years was a disadvantageous factor for virus clearance (OR = 7.890, $P < 0.05$), and earlier treatment was an advantageous factor for virus clearance (OR = 0.0115, $p < 0.05$) (see table 4).

Variables	Univariate			Multivariate		
	Virus clearance within 4 weeks	No virus clearance within 2 weeks	P value ^a	OR	95% CI	P value
WBC count, median (IQR), ×10 ⁹ /L	4.59 (3.55-5.62)	4.94 (4.08-5.99)	0.264			
Lymphocyte count, Median (IQR), ×10 ⁹ /L	1.27 (0.93-1.70)	1.21 (0.97-5.99)	0.443			
Sex, Male	83 (53.9%)	14 (82.4%)	0.025			NS
Smoking history			1.000			
No	145 (94.2%)	16 (94.1%)				
Yes	9 (5.8%)	1 (5.9%)				
Pulmonary underlying diseases			1.000			
No	146(94.8%)	16(94.1%)				
Yes	8(5.2%)	1(5.9%)				
Other underlying diseases			0.019			NS
No	107(69.5%)	7(41.2%)				
Yes	47(30.5%)	10(58.8%)				
Respiratory symptoms at onset			0.346			
No	28 (18.2%)	1(5.9%)				
Yes	126(81.8%)	16(94.1%)				
Other symptoms at onset			0.041			NS
No	94 (61%)	6 (35.3%)				
Yes	60 (39%)	11 (64.7%)				
Antibiotic therapy#			0.573			
No	122 (79.2%)	15 (88.2%)				
Yes	32 (20.8%)	2 (11.8%)				
Glucocorticoids usage*			0.000			
No	120 (77.9%)	3 (17.6%)				
Yes	34 (22.1%)	14 (82.4%)		11.273	2.142-	0.004

				59.332	
Combination of two or more antiviral drugs			0.113		
No	67 (43.5%)	4 (23.5%)			
Yes	87 (56.5%)	13 (76.5%)			
Treatment timing			0.000		
>7 days	15 (9.7%)	7(41.2%)			
≤7 days	139 (90.3%)	10(58.8%)	0.115	0.024-0.550	0.007
Age			0.000		
<18 years	9 (5.8%)	0(0%)			
18-60 years	104 (67.5%)	4(23.5%)			
>60 years	41(26.6%)	13(76.5%)	7.890	1.489-41.810	0.015
BMI			0.994		
<28	141(91.6%)	15(88.2%)			
≥28	13(8.4%)	2(11.8%)			
Temperature			1.000		
<37.3°C	100(64.9%)	12(70.6%)			
37.3-38°C	39(25.3%)	4(23.5%)			
38.1-39°C	14(9.1%)	1(5.9%)			
>39°C	1(0.6%)	0(0%)			
Abnormalities on chest CT			0.117		
No	13(8.4%)	0(0%)			
Unilateral	34 (22.1%)	1(5.9%)			
Bilateral	107(69.5%)	16(94.1%)			
Abbreviations: BMI, body mass index; WBC, white blood cell; NS, not significant.					
^a p value indicates differences between two groups, and p<0.05 was considered statistically significant.					
[#] Antibiotics used in this study include moxifloxacin, levofloxacin, azithromycin, and cefpodoxime.					
[*] The glucocorticoid used in this study was methylprednisolone with a dose of 40-80 mg for a period of 1 week or less.					

Table 4

Discussion

Airway droplet transmission is the most important route of COVID-19 transmission. In the case of long-term exposure to high-concentration aerosols, there is also the possibility of aerosol transmission (5). Therefore, by detecting the novel respiratory coronavirus, we can determine whether patients with COVID-19 can excrete novel coronavirus and whether they are infectious. In China, a positive nasopharyngeal swab nucleic acid test is an important indicator for the diagnosis of COVID-19. Two consecutive negative nasopharyngeal swab RT-PCR tests is one of the conditions for patients to meet the discharge standards.

As shown in Table 1, for the overall patient group, the median virus duration was 17 days (IQR 13–22); for no severe patients, it was 15 days (IQR 12–19), and for severe patients, it was 20 days (IQR 15.5–27). There was a significant difference between the two groups, suggesting that it took longer for the severe patients to clear the novel coronavirus from the body. Clinical classification was an important factor for virus duration.

As shown in Table 2 and Fig. 1, it took 6 weeks for the overall patient group to reach 100% virus clearance; it took 5 weeks for the no severe patients and 6 weeks for the severe patients. To minimize the transmission of pathogens from the respiratory tract, the transmission route was cut off. For no severe patients who are not admitted to the hospital, the time of home isolation should be more than 5 weeks. The discharge standards should include two consecutive negative RT-PCR results to ensure that patients no longer discharge 2019 coronavirus. Due to various reasons, such as a shortage of medical resources, if COVID-19 patients are discharged without two consecutive negative RT-PCR results, we recommend that no severe patients continue to be home-isolated after discharge. The time from onset to the end of home isolation should be more than 5 weeks for no severe patients and more than 6 weeks for severe patients. Our view is similar to that of some epidemiologists(6)..

To clarify the factors influencing virus clearance, we performed a univariate analysis and multiple linear regression analysis on the baseline characteristics and treatment schemes in the overall patient group. As shown in Table 3 and 4, the factors influencing virus clearance within 2 weeks were treatment timing and glucocorticoid usage. The factors influencing virus clearance within 4 weeks were treatment timing, glucocorticoid usage and age.

This study showed that earlier treatment was a favorable factor for virus clearance. For patients with COVID-19, treatment should be started as soon as possible. Even if the patient's symptoms are mild or asymptomatic, early treatment is also meaningful. Because active treatment strategies are conducive to virus clearance, early treatment means successful management of the source of infection and fewer new infections. Similarly, for people with a history of exposure, rigorous monitoring is necessary, and early detection and initiation of treatment are conducive to the control of the epidemic. An article reported that COVID-19 can be treated as soon as possible to obtain a better clinical prognosis(7), and faster virus clearance may be the reason.

Our study showed that age was an important influencing factor of virus clearance. In all patients, age > 60 years was an unfavorable factor for virus clearance. This may be related to the decline of cellular and humoral immune functions in elderly people. Multiple studies have reported that the prognosis of COVID-19 was worse in elderly patients(8, 9), which may be related to the poor virus clearance of these patients. An article also reported that RNA virus detection testing in children's fecal samples took more time to turn negative than in adult samples(10), but our results showed no difference in virus clearance between patients aged < 18 years and 18–60 years. Since there were few patients aged < 18 years included in our study, the small sample size may be the reason.

Glucocorticoid usage can reduce inflammatory factors and chemokines, thereby reducing the excessive inflammatory response and reducing lung tissue damage, which is why glucocorticoids are often used in acute lung injury and ARDS(11). However, glucocorticoid usage in coronavirus pneumonia is controversial. Studies have supported the use of low to moderate doses of glucocorticoids in patients with coronavirus infection. A retrospective study(12) of 401 patients suggested that the correct use of glucocorticoids can reduce SARS mortality and shorten hospital stays. Recently, an article retrospectively analyzed a variety of viral infectious diseases, such as SARS, MERS, influenza, and respiratory syncytial virus infection, and found that the use of glucocorticoids had no significantly benefit. Therefore, the use of glucocorticoids in patients with COVID-19 is not recommended(13). A study also showed that glucocorticoid usage may lead to longer virus duration in COVID-19 patients (14). Our results show that glucocorticoid usage may be an adverse factor in viral clearance. From the perspective of virus clearance, glucocorticoid usage in new coronavirus pneumonia is not supported. However, viral clearance does not represent an improvement in clinical symptoms or lung function. The effects of glucocorticoids on clinical outcomes such as symptom improvement, length of hospital stay, and mortality should be further studied to assess the pros and cons of using glucocorticoids as a whole.

The antiviral drugs used in this study were lopinavir/ritonavir, ribavirin, arborol and different combinations of them. There were different kinds of antiviral schemes used in this study, but there were few patients in any specific scheme, so the impact of different antiviral schemes on virus clearance was difficult to assess. Therefore, we only compared the group using more than two antiviral drugs with the group using a single drug. Studies have shown that the combination of antiviral drugs has no stronger effect on virus clearance. The comparison of antiviral therapy and combined antiviral effects needs to be revealed by large, prospective controlled studies. The other clinical characteristics, including sex, underlying disease, BMI, smoking history, clinical symptoms, white blood cells, lymphocytes, common inflammatory factors, pneumonia severity, and antibiotics, according to this study, were not influencing factors for virus clearance.

Our research has some limitations. First, the detection of virus RNA in this study was only a qualitative test, not a quantitative test, so our study failed to analyze the changing process of viral load and its influencing factors. Second, our study only discussed the effect of glucocorticoids usage on virus clearance. Due to the small sample size, it was not possible to discuss whether the type, duration, daily

dose, and total amount of glucocorticoids can affect virus clearance. There may be a method of using glucocorticoids that does not delay the virus clearance, but also helps control inflammation in the lungs.

Conclusion

In summary, severe patients require more time for virus clearance than no severe patients. Earlier treatment was conducive to virus clearance. The use of glucocorticoids may be an unfavorable factor for viral clearance, and glucocorticoid usage should be strictly limited. Ages > 60 years and < 18 years were detrimental to virus clearance. The combination of multiple antiviral drugs does not increase virus clearance.

Abbreviation

coronavirus disease 2019 (COVID-19), acute respiratory distress syndrome (ARDS), interquartile range (IQR), odds ratio (OR), confidence interval (CI)

Declarations

Ethical Approval and Consent to participate

This study procedures adhered to the tenets of the Declaration of Helsinki, and informed consent was obtained from all patients. The study was approved by the Human Ethics Committee of The Third Hospital of Shenzhen(No.2020-127).

Consent for publication

Not applicable.

Availability of supporting data

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Authors' contributions

LZ, XY, KZ, and QH contributed to the experimental design, data analysis and interpretation, manuscript writing, and manuscript revision. XL, YJ and FH contributed to the data collection and processing. All authors approved the final version of the manuscript.

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Figures

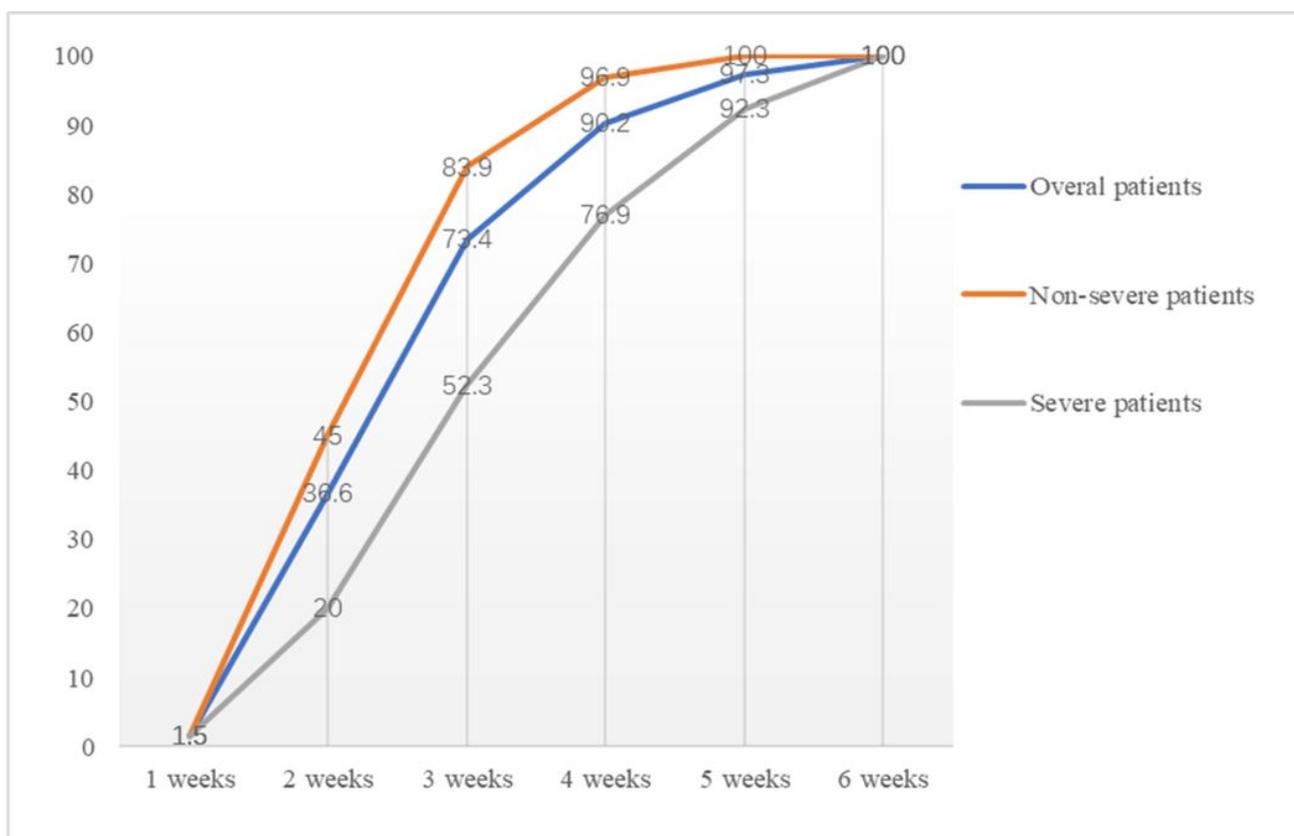


Figure 1

Virus Clearance Rates of No-severe patients and Severe patients at Different Time Points.

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