Clinical Characteristics of Mild/moderate COVID-19 Patients with a Prolonged Negative Conversion Time of SARS-CoV-2 Nucleic Acid Detection

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Abstract

Background: The impact of COVID-19 has been devastating on a global scale. Our study aimed to identify factors in predicting prolonged negative conversion time (NCT) of SARS-CoV-2 RNA in mild/moderate COVID-19 patients.

Methods: The clinical features and treatment outcomes were retrospectively analyzed from 32 hospitalized mild/moderate COVID-19 patients. Then univariate and multivariate analysis were used to predict in the factors of prolonged NCT of SARS-CoV-2 RNA.

Results: The general clinical symptoms were cough (78.1%), fever (75%), diarrhea (68.8%), expectoration (56.3%), and nausea (37.5%). More than 40% of the patients had decreased erythrocyte, hemoglobin and leucocyte and 93.8% patients were detected in abnormalities of chest CT. The median NCT of SARS-CoV-2 RNA was 19.5 days (IQR: 14.25–25). Univariate analysis found fever, nausea, diarrhea and abnormalities in chest CTs were positively associated with prolonged NCT of viral RNA (P<0.05). The multivariate Cox proportional hazard model revealed that fever [Exp (B), 0.284; 95% CI, 0.114-0.707; P⬚0.05] and nausea [Exp (B), 0.257; 95%CI, 0.096-0.689; P⬚0.05] were two significant independent factors.

Conclusions: Fever, nausea, diarrhea and abnormalities in chest CT are potential factors for predicting prolonged NCT of viral RNA. Moreover, Fever and nausea were two significant independent factors in prolonged NCT of viral RNA in mild/moderate COVID-19 patients.

Background

In December 2019, novel pneumonia of unknown causes was reported in Wuhan, Hubei province in China. On February 11, 2020, the World Health Organization (WHO) officially named the disease as Coronavirus Disease 2019 (COVID-19), which caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). Following the initial outbreak, COVID-19 has become a global public health emergency of international concern [1]. There had been 23 million confirmed cases, and 800,000 confirmed deaths by 23 August 2020 spreaded across 216 countries and territories[2]. The number of COVID-19 patients has increased exponentially, causing devastation on a global scale [3].

Many studies have focused on the epidemiological, clinical symptoms, laboratory tests, and radiological characteristics of patients since the COVID-19 outbreak. Current epidemiological investigations show that the incubation period of COVID-19 ranges from one to fourteen days, with the majority of cases being three to seven days. The SARS-CoV-2 is mainly transmitted through respiratory droplets and by fomites [4]. Moreover, SARS-CoV-2 has also been isolated from anal/rectal swabs, stool specimens, and urine, suggesting fecal-oral transmission [5]. The main clinical symptoms of COVID-19 include fever, myalgia, dry cough, dyspnea, fatigue and diarrhea. Laboratory tests have shown that most patients had decreased white blood cell counts, increased C-reactive protein, and increased serum sedimentation rates. Computed tomograms (CT) examination showed multiple plaque shadows and interstitial changes in the early stage, which had then developed into various ground glass shadows and infiltration shadows in both

lungs in the later stage. COVID-19 patients also could be asymptomatic with no associated clinical manifestations, but the SARS-CoV-2 RNA test was positive.

According to the severity of the disease, COVID-19 patients were were divided into asymptomatic, mild/moderate and severe cases. Without timely treatment, mild/moderate patients will develop into severe cases, increasing the fatality rate. It is very important to control the disease progression of mild/moderate patients. The standard of cure is the relief of symptoms and two successive negative viral nucleic acid in the "Diagnosis and Treatment Scheme of New Coronavirus Infected Pneumonia" (trial version 7)[6]. The negative conversion of SARS-CoV-2 RNA was essential in the discharge criteria during hospitalization [7, 8]. The negative conversion time (NCT) of SARS-CoV-2 RNA is closely related to clinical manifestation and disease progression in COVID-19 patients. Hu et al. reported that NCT of SARS-CoV-2 RNA occurred in 14 days (IQR: 10–18). Older age and chest tightness were independently associated with delayed clearance of SARS-CoV-2 RNA in hospitalized patients [9]. The COVID-19 patients with digestive symptoms are more likely to test positive for viral RNA in a stool sample and have a longer delay before viral clearance than patients with only respiratory symptoms [10]. Preliminary clinical treatment showed that some drugs, such as chloroquine, effectively potentiated virus clearance in COVID-19 patients [11]. However, there is limited data regarding the potential predictors of NCT in mild/moderate COVID-19 patients.

Therefore, it was necessary to identify systematically factors associated with prolonged NCT in mild/moderate COVID-19 patients. This study analyzed clinical characteristics of mild/moderate COVID-19 patients with prolonged NCT of SARS-CoV-2 RNA, which provide a useful references for disease progression and treatment of COVID-19.

Methods

Subjects and data collection

The clinical data and laboratory test results were analyzed retrospectively from 32 mild/moderate COVID-19 patients admitted to the Public Health Medical Center and Prevention of Chongqing from January 31 to February 28, 2020. All patients were identified to be nucleic acid positive for SARS-CoV-2 and were convalescent before hospital discharge.

Data was collected and recorded from each patient, which included demographic and clinical information (gender, age, smoking history, and comorbidities), clinical manifestations (fever, coughing, expectoration, anhelation, myalgia, nausea and vomiting, diarrhea, osphyalgia, etc.), and laboratory test results (standard blood counts, procalcitonin, C-reactive protein, blood biochemistry, coagulation function, and myocardial enzyme spectrum, etc). The normal range of laboratory examination is the standard of Reference Range Values for National Practice for Clinical Testing (4th Edition) published by People's Medical Publishing House[12]. Chest CT and therapeutic drug use were also documented. Then, the factors associated with NCT of SARS-CoV-2 RNA in upper respiratory specimens were analyzed.

Therapeutic strategies

Strategies of treatment for COVID-19 patients included antiviral treatment and symptomatic treatment. The primary treatment strategy for COVID-19 is combined antiviral therapy, which mainly comprises interferon-α2b（IFN-α2b） and lopinavir / ritonavir, or IFN-α2b and ribavirin. When SARS-CoV-2 RNA was still detectable after 19 days of drug combination therapy, chloroquine phosphate was added to the antiviral treatment.

Definitions of basic concepts

Sputum and throat swab specimens were collected from patients. RT-PCR assay was used to detect genes of SARS-CoV-2, which were performed twice in every 24 h period. Patients with consecutive positive nucleic acid tests were confirmed as SARS-CoV-2 infection. The standard of negative conversion is two successive negative viral nucleic acid detection tests in 24 h minimum sampling intervals. The term convalescent patients refer to recovered afebrile patients without respiratory symptoms who had two successive (minimum 24 h sampling interval) negative results for SARS-CoV-2 RNA from oropharyngeal swabs by RT-PCR.

Statistical analysis

Normally distributed continuous variables are summarized as the mean mean (standard deviation, SD), otherwise, median (interquartile range, IQR) was used to describe. Categorical variables are expressed using numbers and percentages. Cox regression analysis was used to analyze the factors. First, univariate analysis was performed, and the indicators with statistical significance were analyzed for Kaplan-Meier survival analysis. The Log Rank method was used to compare the differences between groups. A Cox proportional hazard model was used for multivariate analysis. IBM SPSS Statistics 26 was used for statistical analysis and survival image rendering. $P<0.05$ was considered to indicate a statistically significant difference.

Results

The relationship between demographic and clinical information and NCT of SARS-CoV-2 RNA

Of these patients, males accounted for 43.8% (14) of confirmed cases, and 56.3% (18) were females. The median age of males and females was 34.00 (29.00, 47.00) years and 43.00 (37.75, 57.25) years respectively, suggesting that middle-aged people were more susceptible to infection than other age groups. A total of 12.5% of patients were smokers. More than a quarter of patients (34%) had underlying diseases, including cardiovascular and cerebrovascular diseases (25%), gastrointestinal disease (15.6%),

respiratory disease (12.5%), endocrine disease (9.3%), a neurological disorder (3.1%) and urinary disease (3.1%). All patient data were analyzed using the Cox regression analysis for univariate analysis. However, we found that no demographic or clinical information had a significant positive association with NCT of viral RNA in patients (P > 0.05, Table 1).

Table 1
The relationship between demographic and clinical information and NCT of SARS-CoV-2 RNA in 32
patients with COVID-19

Factors	Count n (%)	p value	Exp(B)	95.0% CI for Exp(B)	
				lower limit	detection limits
Total	32(100)				
Age in years, median (IQR)					
Male	34.00 (29.00, 47.00)				
Female	43.00 (37.75, 57.25)				
Age breakdown					
≤45	21(65.6)	0.636	1.190	0.579	2.446
>45	12(37.5)				
Sex					
Male	14(43.8)	0.689	1.325	0.398	4.411
Female	18(56.3)				
Smoking	4(12.5)	0.988	0.992	0.343	2.868
Underlying diseases					
Hypertension	3(9.4)	0.710	1.257	0.376	4.197
Diabetes	1(3.1)	0.110	5.750	0.671	49.244
Coronary heart disease	1(3.1)	0.252	3.373	0.421	26.993
Viral hepatitis type B	2(6.3)	0.399	0.536	0.126	2.282
Kidney stone	1(3.1)	0.880	1.169	0.155	8.786
Hyperlipemia	2(6.3)	0.199	0.550	0.221	1.370
Gout	1(3.1)	0.593	0.578	0.078	4.305
Cerebral hemorrhage	1(3.1)	0.593	0.578	0.078	4.305
Obstructive sleep apnea syndrome(OSAS)	2(6.3)	0.593	0.578	0.078	4.305

Data are shown as n (%) or IQR unless specified otherwise.

The Log Rank method was used to compare the differences between groups, $p < 0.05$ was considered to indicate a statistically significant difference (indicated by *).

Factors	Count n (%)	p value	Exp(B)	95.0% CI for Exp(B)	
				lower limit	detection limits
Appendicectomy	2(6.3)	0.545	1.874	0.245	14.352
Head trauma	1(3.1)	0.545	1.874	0.245	14.352
Thyroid adenoma	1(3.1)	0.110	5.750	0.671	49.244
Chronic bronchitis	1(3.1)	0.110	5.750	0.671	49.244
Depression	1(3.1)	0.075	7.340	0.820	65.691
Pneumonia	1(3.1)	0.258	0.312	0.042	2.342
Appendicitis	1(3.1)	0.258	0.312	0.042	2.342
Data are shown as n (%) or IQR unless specified otherwise.					
The Log Rank method was used to compare the differences between groups, p < 0.05 was considered to indicate a statistically significant difference (indicated by *).					

The relationship between clinical manifestation and NCT of SARS-CoV-2 RNA

The median duration from disease onset to hospital admission was 3.5 (IQR: 2–6) days, with a median of 20 days from illness onset to hospital discharge (IQR: 15.25–26) and the median time from positive to negative conversion of SARS-CoV-2 RNA was 19.5 days (IQR: 14.25–25). The majority of the patients showed an initial symptom of fever (75%), but a quarter of the patients were afebrile, alerting the need for the caution of atypical cases. In addition to fever, other clinical symptoms mainly included fatigue (78.1%), expectoration (56.3%), diarrhea (68.8%), nausea (37.5%), anhelation (34.4%), and throat discomfort (34.4%). Clinical manifestations of the study population are summarized in Table 2.

Table 2
The relationship between clinical manifestation and NCT of SARS-CoV-2 RNA in 32 patients with COVID-19

Factors	Count n (%)	p value	Exp(B)	95.0% CI for Exp(B)	
				lower limit	detection limits
Total	32(100)				
Fever	24(75.0)	0.050*	0.431	0.186	1.000
Cough	25(78.1)	0.564	0.779	0.334	1.818
Expectoration	18(56.3)	0.335	0.707	0.349	1.431
Anhelation	11(34.4)	0.714	0.871	0.416	1.822
Throat discomfort	11(34.4)	0.669	0.852	0.409	1.775
Headache and dizziness	7(21.9)	0.323	0.650	0.277	1.526
Myodynia	7(21.9)	0.123	0.491	0.199	1.213
Osphyalgia	2(6.3)	0.341	0.495	0.117	2.103
Diarrhea	22(68.8)	0.007*	0.318	0.138	0.733
Ventosity	2(6.3)	0.524	0.622	0.145	2.677
Nausea	12(37.5)	0.002*	0.262	0.112	0.613
Vomiting	3(9.4)	0.314	2.161	0.482	9.686
Muscular stiffness	5(15.6)	0.235	0.559	0.214	1.460
Chills	2(6.3)	0.126	3.288	0.716	15.105
Fatigue	9(28.1)	0.509	0.768	0.350	1.683
Snot	3(9.4)	0.123	0.387	0.113	1.329
Insomnia	5(15.6)	0.444	0.678	0.250	1.836
Chest tightness	5(15.6)	0.978	1.014	0.385	2.670
Bitter taste and thirst	4(12.5)	0.703	1.231	0.422	3.588
Data are shown as n (%) unless specified otherwise.					
The Log Rank method was used to compare the differences between groups, p < 0.05 was considered to indicate a statistically significant difference (indicated by *).					

The Cox regression analysis was used for univariate analysis; we found that fever, nausea, and diarrhea were a significant positive association with NCT of viral RNA in patients (P < 0.005, Table 2). The KaplanMeier curves revealed that fever, nausea, and diarrhea had a significantly prolonged NCT of SARS-CoV-2 RNA compared with the normality's group (P < 0.05; Fig. 1A, B, C).

The relationship between laboratory findings and NCT of SARS-CoV-2 RNA

As shown in Table 1, the laboratory inspection section showed that 43.8% of the patients developed leucopenia, and 28.1% of patients had lymphocytopenia. The hemoglobin, platelets, and albumin levels were lower in 53.1%, 37.5%, and 34.4% of patients, respectively. The levels of procalcitonin, C-reactive protein, total bilirubin, direct bilirubin, creatinine, lactic dehydrogenase were increased in 9.4%, 40.6%, 40.6%, 46.9%, 25%, and 21.9% of patienst, respectively. All patient data were analyzed using the Cox regression analysis for univariate analysis. Still, there were no significant findings with a positive association with NCT of viral RNA in patients (P > 0.005, Table 3).

Table 3
The relationship between laboratory findings and NCT of SARS-CoV-2 RNA in 32 patients with COVID-19

Factors	Count n (%)	p value	Exp(B)	95.0% CI for Exp(B)	
				lower limit	detection limits
Total	32(100)				
Leukocyte count decrease (↓)	14(43.8)	0.176	0.612	0.301	1.246
Neutrophil count decrease (↓)	8(25)	0.661	0.836	0.375	1.864
Neutrophil percentage decrease (↓)	9(28.1)	0.171	0.581	0.267	1.263
Lymphocyte count decrease (↓)	12(37.5)	0.959	1.019	0.494	2.102
Lymphocyte percentage decrease (↓)	9(28.1)	0.529	1.275	0.598	2.718
Erythrocyte count decrease (↓)	24(75)	0.942	1.031	0.453	2.349
Hemoglobin decrease (↓)	17(53.1)	0.678	0.858	0.417	1.765
packcd cell volume (↓)	20(62.5)	0.722	1.140	0.554	2.344
Platelet count decrease (↓)	12(37.5)	0.140	1.823	0.820	4.052
Procalcitonin increase (↑)	3(9.4)	0.536	1.477	0.429	5.091
C-Reactive Protein increase (↑)	13(40.6)	0.492	1.302	0.614	2.761
Total Protein (↓)	21(65.6)	0.934	1.032	0.494	2.155
Albumin decrease (↓)	11(34.4)	0.824	0.920	0.442	1.917
Total bilirubin increase (↑)	13(40.6)	0.297	1.465	0.715	3.000
Direct bilirubin increase (↑)	15(46.9)	0.339	1.411	0.697	2.859
Creatinine increase (↑)	8(25)	0.936	0.968	0.433	2.163
Lactic dehydrogenase increase (↑)	7(21.9)	0.993	1.004	0.433	2.327
D-Dimer increase (↑)	2(6.3)	0.783	1.227	0.286	5.260
Data are shown as n (%) unless specified otherwise.					
The Log Rank method was used to compare the differences between groups, p < 0.05 was considered to indicate a statistically significant difference (indicated by *).					

The relationship between radiological findings and NCT of SARS-CoV-2 RNA

Ground-glass opacity (GGO) and high-density shadow were the typical radiological findings on chest CT scan. Abnormalities in chest CT were detected in 93.8% of patients. A total of 87.5% of patients had ground-grass opacities over bilateral lungs, which was the most common pattern of CT changes and corresponded to pathological diffuse alveolar damage [13].

We analyzed the univariate analysis using the Cox regression and found that abnormalities in chest CT were a significant positive association with NCT of viral RNA in patients (P < 0.005, Table 4). The Kaplan Meier curves revealed that abnormalities in chest CT had a significantly prolonged NCT of SARS-CoV-2 RNA compared with normality's group (P < 0.05; Fig. 1D).

Table 4

The relationship between radiological findings[a] and NCT of SARS-CoV-2 RNA in 32 patients with COVID-19

Factors	Count n (%)	p value	Exp(B)	95.0% CI for Exp(B)	
				lower limit	detection limits
Total	32(100)				
Abnormal	30(93.8)	0.044*	0.209	0.046	0.957
Involved lung field					
Unilateral	8(25)	0.202	0.570	0.241	1.350
Bilateral	22(68.8)	0.503	1.314	0.591	2.920
Radiological characteristics					
Ground-grass opacities	28(87.5)	0.940	0.960	0.331	2,782
High-density shadow	17(53.1)	0.083	0.536	0.265	1.086
Data are shown as n (%) unless specified otherwise.					
The Log Rank method was used to compare the differences between groups, p < 0.05 was considered to indicate a statistically significant difference (indicated by *).					
[a]How many patients have the following lesion location.					

Taking antiviral medications during hospitalization

All patients received antiviral therapy during hospitalization. All 32 patients were treated with IFN-α2b. Utilization rates of opinavir/ritonavir, ribavirin, and chloroquine phosphate were treated in 84.4%, 46.9%, and 40.6% of patients, respectively. The proportion of patients receiving combined treatment using IFN-α2b plus lopinavir/ritonavir, IFN-α2b plus ribavirin, IFN-α2b plus lopinavir/ritonavir plus ribavirin, and IFN-α2b plus chloroquine phosphate were 75%, 12.5%, 12.5%, 40.6%, respectively (Fig. 2).

Predictors of NCT

We had summarized the results of the univariate analysis that fever, nausea, diarrhea, and abnormalities in chest CT had a significantly prolonged NCT of SARS-CoV-2 RNA. To analyze factors on NCT of SARS-CoV-2 RNA systematically, the multivariate Cox's proportional hazard model was used to analyze the multivariate analyses. We revealed that fever [Exp (B), 0.284; 95% CI, 0.1140.707; P < 0.005] and nausea [Exp (B), 0.257; 95%CI, 0.0960.689; P < 0.005] were independent factors in prolonged NCT of SARS-CoV-2 RNA in patients with COVID-19 (Table 5).

Table 5
Independent factors of negative conversion time by the multivariate Cox's proportional hazard model

Factors	p value	Exp(B)	95.0% CI for Exp(B)	
			lower limit	detection limits
Fever	0.007*	0.284	0.114	0.707
Nausea	0.007*	0.257	0.096	0.689
Diarrhea	0.376	0.648	0.248	1.692
CT imaging	0.150	0.299	0.058	1.550

A Cox proportional hazard model was used for multivariate analysis, p < 0.05 was considered to indicate a statistically significant difference (indicated by *).

Discussion

COVID-19 is a global pandemic that has rapidly spread worldwide since reported in December 2019. A negative nucleic acid test of SARS-CoV-2 is the standard for a cure of COVID-19. To investigate the timeline of RNA negative conversion of COVID-19 patients, this study retrospectively analyzed clinical characteristics in a cohort of mild/moderate hospitalized patients in Chongqing, China. We found that fever, nausea, diarrhea, and abnormalities in chest CT were correlated to a prolonged NCT of SARS-CoV-2 RNA. More importantly, fever and nausea were the independent factors predicting NCT of mild/moderate COVID-19 patients.

Fever, a respiratory manifestation, is the most commonly reported symptom in patients infected with SARS-CoV-2 [14, 15]. Accordingly, fever may be a clinical sign of poor prognosis in patients and response to the release of inflammatory mediators such as cytokines and chemokines [16] [17]. These inflammatory mediators cause tissue damage and organ dysfunction by stimulating toxic oxygen derivatives suggesting that the NCT of SARS-CoV-2 RNA may be prolonged in patients [18, 19].

Chest CT has a high sensitivity to detect lung abnormalities, which is quite helpful in the early diagnosis of the disease. The "Diagnosis and Treatment Scheme for Coronavirus Disease (Trial Version 7)" recommended that a CT examination serves as the diagnostic basis for COVID-19. For chest imaging in

patients with COVID-19, the early manifestation was multiple plaque shadows and interstitial changes. The later development was multiple ground glass shadows and infiltration shadows in both lungs. In severe cases, lung consolidation can occur, presenting as "white lung," which may be related to the immunopathology. Most studies have suggested that a dysregulated/exuberant innate responses are the primary cause of coronavirus-mediated pathology [20]. Many cytokines or chemokines are involved in the immune storm after the infection of coronavirus,which eventually leads to lung injury and acute respiratory distress syndrome [21]. The improvement of chest CT was after that of body temperature. Still, it preceded the negative conversion of nucleic acid tests, suggesting that abnormalities in chest CT could indirectly reflect the persistence of SARS-CoV-2 RNA in patients with COVID-19. Our study found that abnormalities in chest CT could prolong the NCT of patients with COVID-19. Therefore, the improvement of chest CT as soon as possible has an essential effect on shortening NCT in patients with COVID-19 and promoting patients to be discharged more rapidly.

Although COVID-19 most commonly presents with respiratory symptoms, such as cough and shortness of breath [14, 22, 23], there is evidence that the illness can also present with nonrespiratory symptoms, most notably digestive symptoms such as diarrhea, diminished appetite, nausea, and vomiting [24–26]. Diarrhea appeared to be the most common GI complaint [27], followed by nausea and vomiting [22]. SARS-CoV-2 RNA was detected in stool samples from COVID-19 patients for the first time, first reported in the United States [28]. Viral RNA was still positive in gastrointestinal specimens even after levels could not be detected in respiratory samples [27], implying direct infectivity of the virus on the intestinal tract. Current research shows that the primary target organ of COVID-19 is the lung, but clinical evidence suggests that the gastrointestinal tract may be another viral target organ.

The SARS-CoV-2 receptor angiotensin-converting enzyme 2 (ACE2) has been found in both upper and lower gastrointestinal tract where its expression level was nearly 100 times higher than that of respiratory organs [29, 30]. Patients with symptoms of the digestive system have more viruses in their gut [10], and maybe more likely to cause direct damage to the intestinal mucosa. Our research found that digestive symptoms, including nausea and diarrhea, are the factors of NCT of COVID-19 patients, suggesting that patients with gastrointestinal symptoms should seek medical care to avoid delayed diagnosis and prolong treatment time.

Chinese experts recommend that patients diagnosed as mild, moderate, and severe cases of COVID-19 pneumonia and without contraindications to chloroquine, be treated with 500 mg of chloroquine twice a day for ten days[31]. In our study, when SARS-CoV-2 RNA was still detectable after 19 days of drug combination therapy, chloroquine was added to the antiviral treatment. Thirteen patients were treated with chloroquine and a median duration of viral shedding of 6.0 (IQR: 5.0–7.0) days. Therefore, these results suggest that chloroquine may play a role in reducing viral load and shortening the time of virus negative transition. Other studies have also confirmed the role of chloroquine in promoting virus negative conversion and shortening the disease course. Other studies have also confirmed the role of chloroquine in promoting virus negative conversion, shortening the course of the disease [11] and reducing/eliminating viral load in COVID-19 patients [32]. However, we did not conduct a randomized

controlled study to evaluate the efficacy of chloroquine and most infections with COVID-19 were self-limited, about 15% of infected adults developed severe pneumonia that required treatment [22, 33], the numerical reduction in time to clinical improvement in those treated with chloroquine requires confirmation in more extensive studies.

There are several limitations to our study. First, the sample size of this study is not large enough. Second, we have not conducted randomized controlled trials, so we cannot determine the therapeutic effect of chloroquine on COVID-19 and its impact on shortening the time of negative viral conversion.

Conclusion

In conclusion, our study suggests that fever, nausea, diarrhea and abnormalities in chest CT hve a significantly prolonged NCT of SARS-CoV-2 RNA in mild/moderate COVID-19 patients. More importantly, fever and nausea are the independent factors in predicting NCT of SARS-CoV-2 RNA. Meanwhile, we should pay attention to gastrointestinal symptoms and provide timely treatment. This study provide a useful references for disease progression and treatment of COVID-19.

Abbreviations

COVID-19: Coronavirus disease 2019; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2; NCT: Negative conversion time; RT-PCR: Reverse Transcription-polymerase Chain Reaction; CT: Computerized tomography; IFN-α2b: Interferon-α2b; IQR: Interquartile range; GGO: Ground-glass opacities.

Declarations

Ethics approval and consent to participate

This study was conducted following the Declaration of Helsinki. It was approved by the Ethics Commission of Chongqing Public Health Medical Center (ethics approval registration number:2020-043-01-KY) and written informed consent was waived in consideration of the emergency of infectious disease.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

Funding

Authors' contributions

FS, LZ, YY and XH conceived and designed the project and had roles in the data analysis, data interpretation, literature search, and writing of the manuscript. LX, PF, WF and WL had roles in data collection, data interpretation, iterature search, and writing of the manuscript. LZ had roles in clinical management and data collection, and had full access to all of the data in the study and take responsibility for the integrity of the data. The authors read and approved the final manuscript.

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Figures
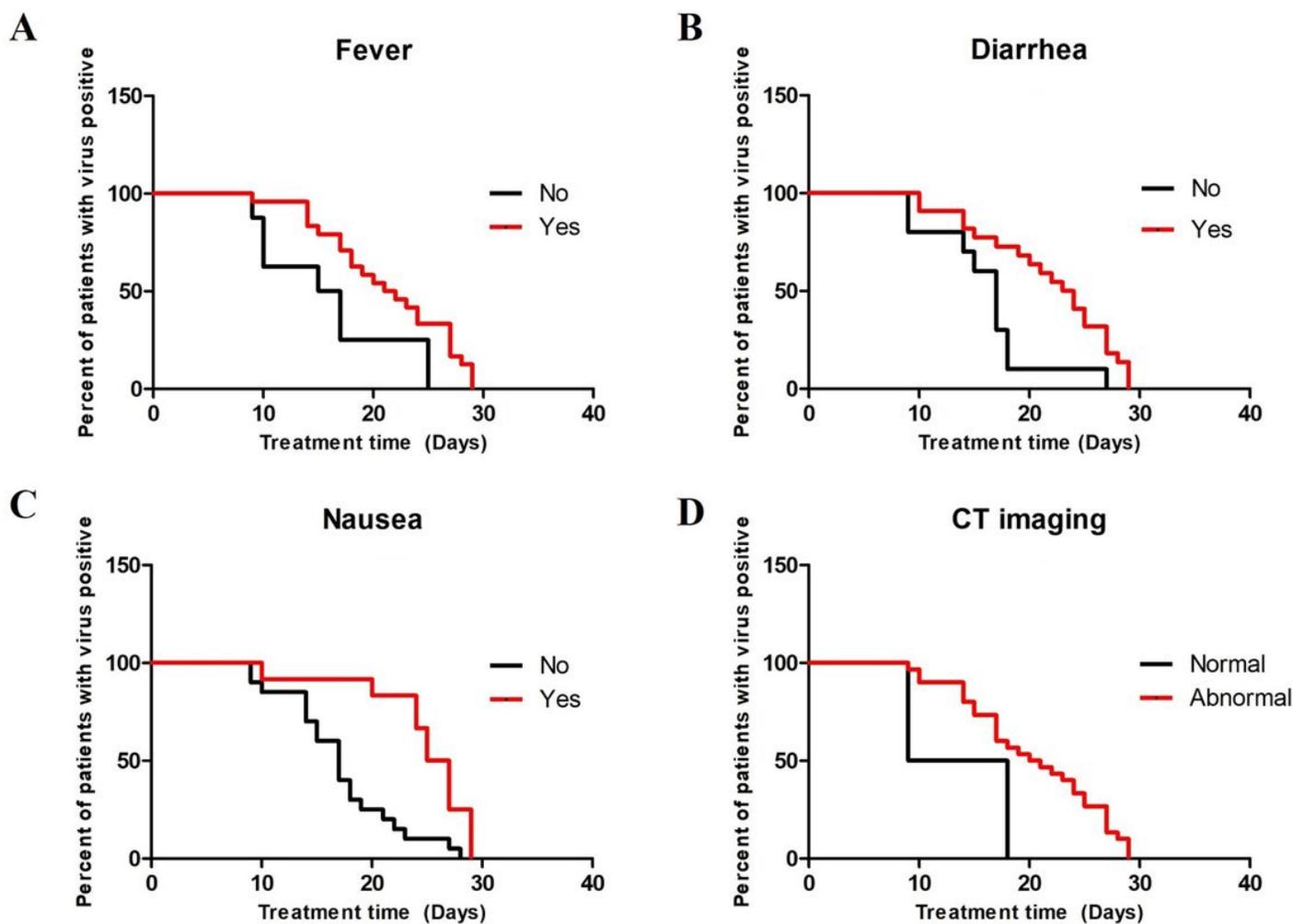
Figure 1

Kaplan-Meier curves for NCT of SARS-CoV-2 RNA according to clinical characteristics of COVID-19 patients. A: Fever was positively associated with NCT of viral RNA in patients [Exp (B), 0.431; 95% CI, 0.186 1.000; P=0.035]; B: Diarrhea was positively associated with NCT of viral RNA in patients [Exp (B), 0.262; 95% CI, 0.112 0.613; P=0.002]; C: Diarrhea was positively associated with NCT of viral RNA in

patients [Exp (B), 0.318; 95% CI, 0.138 0.733; P=0.007]; D: Abnormalities in chest CTs were positively associated with NCT of viral RNA in patients [Exp (B), 0.209; 95% CI, 0.046 0.957; P=0.044].
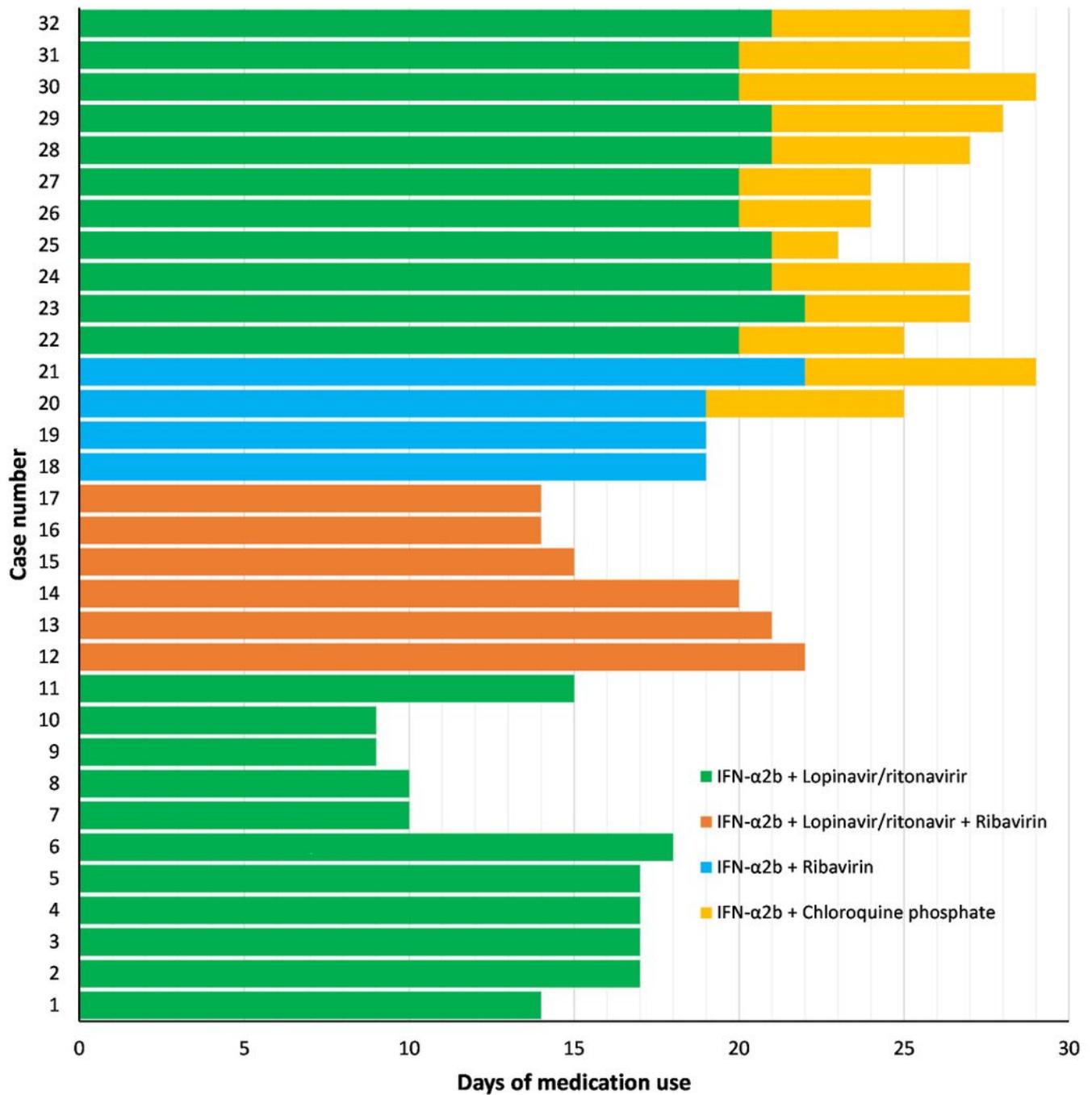

Figure 2

Using of antiviral medications during hospitalization in 32 patients with COVID-19