The duration of viral shedding of discharged patients with severe COVID-19

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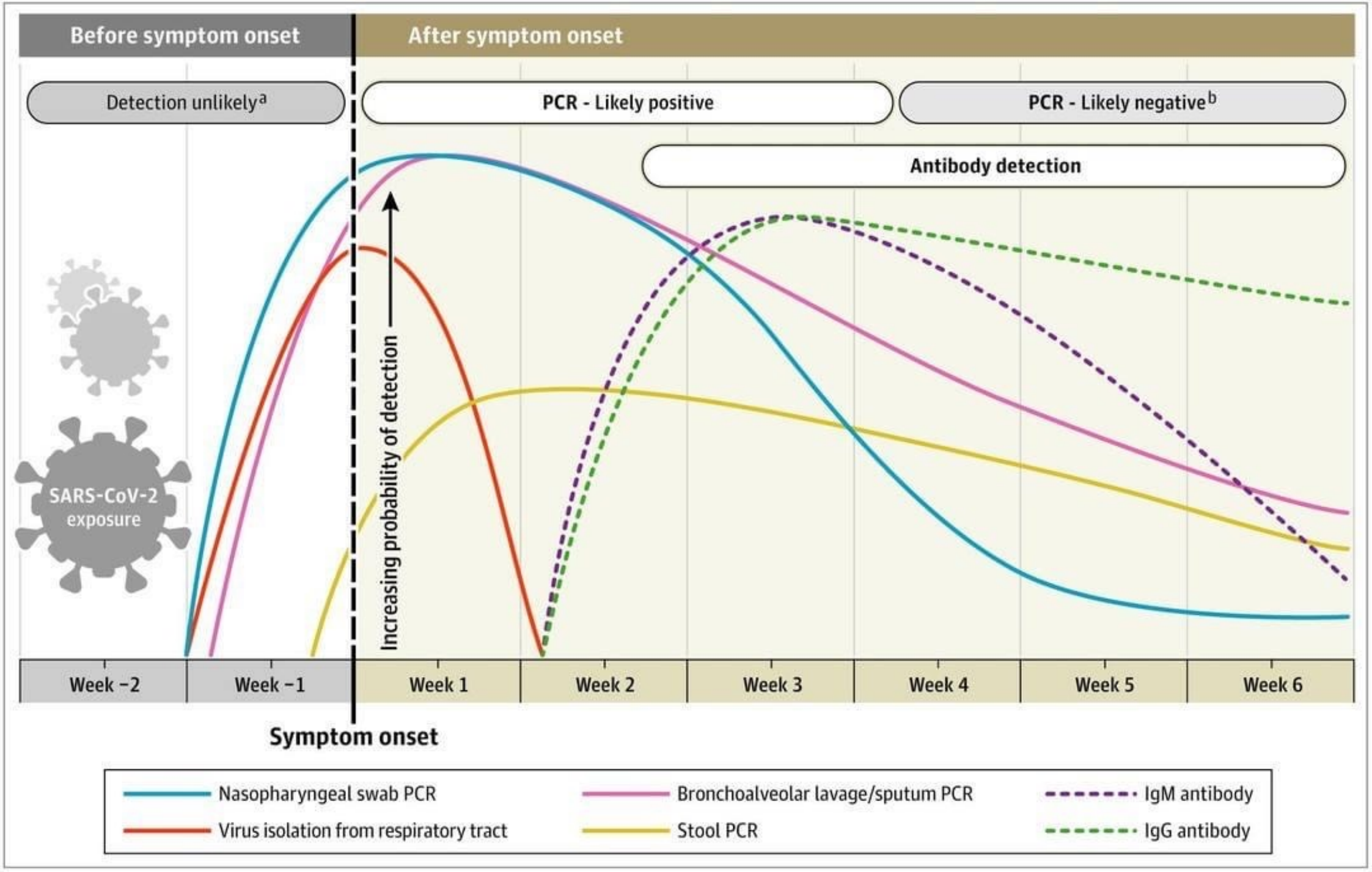
ABSTRACT

The 2019 coronavirus disease (COVID-19) has drawn global intensive attention[1-3]. Most of studies paid attention to epidemiological, clinical, and radiological features of inpatients with COVID-19[1-3]. However, little studies have focused on clinical characteristics of discharged patients with severe COVID-19, especially the duration of viral shedding.


Before symptom onset
After symptom onset
Detection unlikely[a]
PCR - Likely positive
PCR - Likely negative[b]
Antibody detection
Increasing probability of detection
SARS-CoV-2 exposure
Week −2
Week −1
Week 1
Week 2
Week 3
Week 4
Week 5
Week 6
Symptom onset
Nasopharyngeal swab PCR
Virus isolation from respiratory tract
Bronchoalveolar lavage/sputum PCR
Stool PCR
IgM antibody
IgG antibody

Methods

We enrolled 41 discharged patients with severe COVID-19 on the 7th floor ward in the west district, Union Hospital of Tongji Medical College from February 5th to March 16th, 2020. The patients were evaluated with real-time reverse transcriptase-polymerase chain reaction (RT-PCR) tests for COVID-19 nucleic acid. The RT-PCR tests were performed on throat swabs following a previously described method[3]. The RT-PCR test kits (BioGerm) were recommended by the Chinese Center for Disease Control and Prevention.

COVID-19 was diagnosed upon admission based on the New Coronavirus Pneumonia Prevention and Control Program in China (4th edition)[4]. RT-PCR tests for COVID-19 nucleic acid were positive in all enrolled patients. Severe COVID-19 was defined as having either one of the flowing criteria: 1) Respiratory distress with respiratory rate was more than 30 times/min; 2) Oxygen saturation ≤93% in resting state; 3) PaO2/FiO2 ≤300mmHg (1mmHg=0.133kPa). All the following criteria had to be met for hospital discharge: 1) normal temperature lasting longer than 3 days; 2) resolved respiratory symptoms; 3) substantially improved acute exudative lesions on chest computed tomography (CT) images; 4) 2 consecutively negative RT-PCR test results separated by at least 1 day. Written informed consent was obtained from all patients upon enrollment according to the Declaration of Helsinki, and was approved by the ethics committee of the local hospital.

Data were presented as percentages for categorical variables and median±IQR (Inter Quartile Range) for continuous variables. Simple t test and Mann-Whitney U test was used to compare continuous variables.

Results

41 patients with severe COVID-19 upon enrollment were discharged in the west district, Union Hospital, Tongji Medical College from February 5th to March 16th, 2020. The discharged patients with severe COVID-19 consisted of male (n=22, 53.7%) and female (n=19, 46.3%). The median age of the 41 patients was 58.0 (IQR: 48.0-62.0) years, ranging from 17 years to 75 years, which were separated into two groups with <65 yrs (n=31, 75.6%) and ⩾65 yrs (n=10, 24.4%) (Table 1).

The median duration of viral shedding was 31.0 (IQR: 24.0-40.0) days from illness onset. The shortest observed duration of viral shedding was 18 days, whereas the longest was 48 days. In addition, there was no significant difference with the viral shedding time between male [29.0 (IQR: 23.3-38.0) days)] and female [32.0 (IQR: 25.5-40.5) days], and between <65 yrs [31.0 (IQR: 23.5-40.5) days] and ⩾65 yrs [31.0 (IQR: 24.3-38.0) days)] (Table 1 and Figure 1).

The median total time from illness onset to discharge (total time) was 40.0 (IQR: 32.0-46.0) days. The shortest observed time was 24 days, whereas the longest was 56 days. Moreover, there was no significant difference with the total time from illness onset to discharge between male [38.5 (IQR: 30.5-45.8) days] and female [40.0 (IQR: 35.0-45.5) days], and between <65 yrs [39.0 (IQR: 30.0-46.0) days] and ⩾65 yrs [40.0 (IQR: 35.5-43.8) days] (Table 1 and Figure 1).

Discussion

In the current study, we have focused on clinical characteristics of discharged patients with severe COVID-19. We found the median duration of viral shedding was 31.0 (IQR: 24.0-40.0) days from illness onset and the median total time from illness onset to discharge was 40.0 (IQR: 32.0-46.0) days. This has important clinical implications for making isolation decision of discharged patients and guiding the duration of hospitalization for patients with severe COVID-19. Previous study showed that the detectable SARS-CoV-2 RNA persisted for a median of 20 days in survivors and that it was sustained until death in nonsurvivors[5]. Moreover, another study displayed that four patients with COVID-19 who met the criteria for hospital discharge in China had positive RT-PCR test results 5 to 13 days later[6], suggesting that recovered patients might still be virus carriers. Thus, it is plausible that the patients with severe COVID-19 might need longer duration of symptomatic and supportive treatments due to prolonged duration of viral shedding.

Additionally, there was no significant difference with viral shedding time and the total time from illness onset to discharge between male and female, and between <65 yrs and ⩾65 yrs. Based on the results, we did not observe shortening of viral shedding time in the above groups, so it implied that all patients with severe COVID-19 should complete adequate course of treatment, regardless of sex and age.

Previously, increased age has been reported as an important independent predictor of mortality in COVID-19[5]. The current study also found that the number of discharged patients with severe COVID-19 in the group (<65 yrs) was more than in the group (⩾65 yrs), indicating that the elder patients with severe COVID-19 may have poor outcome, and we

should pay attention to the patients with severe COVID-19, especially ⩾65 yrs.

The study was limited to a small number of discharged patients with severe COVID-19, not including mild or moderate infection, because we enrolled patients from the designated hospital for severe COVID-19. Besides, the estimated duration of viral shedding is limited by the frequency of respiratory specimen collection and relatively low positive rate of SARS-CoV-2 RNA detection in throat swab. It is advisable to continue follow-up discharged patients even after discontinuing quarantine for further viral shedding information. In addition, further studies based on larger cohorts would help to understand the prognosis and the duration of the disease.

NOTES

Author Contributions: BZ, XM and YW collected the clinical and laboratory data. JS processed statistical analysis. JS and BZ drafted the manuscript. BZ, XM and YW revised the final manuscript. BZ, XM and YW is responsible for all clinical and laboratory data.

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Conflict of Interest Disclosures: We declare no competing interests.

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Figure legends

Table 1: Baseline information.

Figure 1: The duration of viral shedding from illness onset and the total time from illness onset to discharge in sex and age groups.

Table 1: Baseline information

	Median(IQR)						
	Total	Sex			age		
		Male	Female	P value	<65 yrs	≥65 yrs	P value
Age(yrs)	58.0(48.0-62.0)	(n=22, 53.7%)	(n=19, 46.3%)		(n=31, 75.6%)	(n=10, 24.4%)	
Viral shedding(days)	31.0(24.0-40.0)	29.0(23.3-38.0)	32.0(25.5-40.5)	0.33	31.0(23.5-40.5)	31.0(24.3-38.0)	0.75
Total time(days)	40.0(32.0-46.0)	38.5(30.5-45.8)	40.0(35.0-45.5)	0.44	39.0(30.0-46.0)	40.0(35.5-43.8)	0.55

Figure 1