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Clinical features of discharged COVID-19 patients with an extended SARS-CoV-2 RNA positive signal in respiratory samples

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Studies have begun to focus on the fact that some of the discharged coronavirus disease 2019 (COVID-19) patients could have positive reverse-transcriptase polymerase chain reaction (RT-PCR) test results a few days after discharge from the hospital (Lan et al., 2020). To summarize the clinical features of this population, we followed up 71 patients discharged from a hospital receiving COVID-19 pneumonia cases in Chongqing, China. We also explored whether a stricter discharge criterion would result in a lower rate of positive detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA in the last 27 patients after discharge.

The 44 patients discharged earlier, assigned to Group A, met the following criteria (China National Health Commission, 2020) and were allowed to leave from 2 February to 20 February 2020: (1) normal temperature lasting longer than 3 days, (2) resolved respiratory symptoms, (3) substantially improved acute exudative lesions on chest computed tomography (CT) images, and (4) 2 consecutive negative RT-PCR test results separated by at least 1 day. The last 27 patients, assigned to Group B, required 3 consecutive negative RT-PCR test results to be included, in addition to conditions (1) to (3) above, and were allowed to leave from 24 February to 4 March in 2020.

All 71 patients had a history of epidemiological exposure to COVID-19, and all met the discharge criteria. Among them, throat swabs from 19 (26.76%, 16 in Group A and 3 in Group B) patients were positive for SARS-CoV-2 RNA by RT-PCR within 10 days after discharge (mean days, 4.4; range, 1 to 10). Notably, the 19 patients who were SARS-CoV-2-RNA positive had a low viral load (inversely related to the cycle threshold [Ct] value). Furthermore, the duration that throat swabs were positive for SARS-CoV-2 RNA could be longer than two weeks after discharge (mean days, 5.5; range, 2 to 16). In the second week after discharge, tests for SARS-CoV-2 RNA were again negative (mean days, 8.4; 2 to 18) in 16 of the 19 patients (Table 1). The median age of the 19 patients was 48 years (IQR, 42.0-64.5; range, 18 to 71). Of these, 7 were women, 12 were men, 4 were in critical condition, and 4 had received

glucocorticoid therapy. The median durations of hospital stay and course of disease were 17.0 days (IQR, 12.0-19.5) and 20.0 days (IQR, 16.0-24.5), respectively. Notably, there were no significant differences between patients with positive SARS-CoV-2 RNA results and patients with persistently negative SARS-CoV-2 RNA results in age, gender, hospital stay, course of disease, disease severity, or glucocorticoid therapy (all $P > 0.05$) (Table 2).

Furthermore, in Group A, 16 patients (36.36% of the 44 patients) were positive for SARS-CoV-2 RNA on throat swabs after discharge. One of the 16 patients presented with a mild cough, one had occasional chest tightness, and neither had fever or progressed to pneumonia. The mean durations from patient discharge to first testing positive for SARS-CoV-2 RNA, from first testing positive to testing negative for SARS-CoV-2 RNA after discharge, and from discharge to negative for SARS-CoV-2 RNA again were 3.9 days (range, 1-17), 5.4 days (range, 2-16) and 8.4 days (range, 2-18), respectively. In Group B, 3 patients (11.11% of the 27 patients) were positive for SARS-CoV-2 RNA, and all were asymptomatic. The mean durations from patient discharge to first testing positive for SARS-CoV-2 RNA, from first testing positive to testing negative for SARS-CoV-2 RNA after discharge, and from discharge to testing negative for SARS-CoV-2 RNA again were 6.7 days (range, 3-10), 3.0 days (range, 2-4) and 8.3 days (range, 4-12), respectively. Notably, compared with that of patients in Group A, a lower proportion of patients in Group B tested positive for SARS-CoV-2 RNA after discharge ($P = 0.02$) (Table 1), and Group B required longer hospital stays (Group A vs. Group B; median days, 14.5 (IQR, 10.0-17.0) vs 25.0 (14.5-27.0); $P < 0.0001$) (Table 2). Moreover, antibody detection showed that 8 of 16 patients in Group A were positive for IgM and IgG, and none of the 3 patients in Group B were both IgM and IgG positive (Table 1), suggesting that the patients in Group B may have already been in the middle or late stages of infection, while some patients in Group A may have still been in the active phase of infection.

Based on the above, we would like to recommend the following: (1)

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Table 1
Changes in RT-PCR test results for 19 discharged patients.

Patient ID	Discharge Time	Date of first positive after discharge	Duration from discharge to first positive, d	ORF1ab (Ct value) *	N (Ct value) *	Date of negative	Duration from first positive to negative, d	Duration from discharge to negative, d	IgM /IgG#
Group A									
CQ03	7-Feb-20	12-Feb-20	6	36.36	37.02	19-Feb-20	7	12	Pos /Pos
CQ14	14-Feb-20	17-Feb-20	4	32.16	38.08	21-Feb-20	4	7	Pos /Pos
CQ16	14-Feb-20	16-Feb-20	3	38.51	36.92	19-Feb-20	3	5	Pos /Pos
CQ17	15-Feb-20	21-Feb-20	7	34.73	39.05	24-Feb-20	3	9	Pos /Pos
CQ21	16-Feb-20	19-Feb-20	4	39.61	35.41	23-Feb-20	4	7	Neg /Pos
CQ22	16-Feb-20	19-Feb-20	4	35.68	36.57	2-Mar-20	12	15	Pos /Pos
CQ24	16-Feb-20	21-Feb-20	6	28.31	31.14	24-Feb-20	3	8	Pos /Pos
CQ26	17-Feb-20	19-Feb-20	3	35.58	38.9	6-Mar-20	16	18	Neg /Pos
CQ27	17-Feb-20	18-Feb-20	2	39.41	38.03	21-Feb-20	3	4	Neg /Pos
CQ28	17-Feb-20	20-Feb-20	4	34.2	25.38	5-Mar-20	14	17	Neg /Pos
CQ30	17-Feb-20	21-Feb-20	5	31.7	31.72	24-Feb-20	3	7	Neg /Pos
CQ31	17-Feb-20	20-Feb-20	4	31.26	31.74	24-Feb-20	4	7	Pos /Pos
CQ34	18-Feb-20	20-Feb-20	3	35.81	39.4	23-Feb-20	3	5	Pos /Pos
CQ39	18-Feb-20	21-Feb-20	4	32.6	33.37	24-Feb-20	3	6	Neg /Pos
CQ40	19-Feb-20	21-Feb-20	3	33.99	32.77	24-Feb-20	3	5	Neg /Pos
CQ44	20-Feb-20	20-Feb-20	1	39.53	39.18	22-Feb-20	2	2	Neg /Pos
Group B									
CQ47	28-Feb-20	1-Mar-20	3	35.37	33.29	3-Mar-20	2	4	Neg /Pos
CQ51	26-Feb-20	3-Mar-20	7	37.17	36.58	6-Mar-20	3	9	Neg /Pos
CQ60	3-Mar-20	12-Mar-20	10	32.3	28.78	15-Mar-20	4	12	Neg /Pos

Abbreviations: RT-PCR, reverse transcriptase-polymerase chain reaction; d, day(s); Pos, positive; Neg, negative; * cycle threshold (Ct) value for the first positive RT-PCR test results after discharge. # IgM and IgG results at the Date of RT-PCRs positive at the first time after discharge.

Table 2
Characteristics of 71 discharged patients recovered from COVID-19.

	No. (%)							P1 value ^c	P2 value ^d
	Total (N = 71)	Group A (n = 44)	Group B (n = 27)	Positive recovery ^a			Persistent negative ^b (n = 52)		
				Total (N = 19)	Group A (n = 16)	Group B (n = 3)			
Age, Median (IQR), y	47 (39.5-56.5)	47 (39.0-56.0)	48 (42.5-61.5)	48 (42.0-64.5)	54 (46.3-66.3)	20 (18-44)	46 (39.0-53.0)	0.29	0.7
Gender									
Female	29 (40.8)	14 (31.8)	12 (44.4)	7 (9.9)	6 (8.5)	1 (1.4)	22 (31.0)	0.79	0.32
Male	42 (59.2)	30 (68.2)	15 (55.6)	12 (16.9)	10 (14.1)	2 (2.8)	30 (4.2)		
Length of hospital stay (IQR), d	16 (12.0-22.0)	14.5 (10.0-17.0)	25 (14.5-27.0)	17 (12.0-19.5)	15.5 (12.5-19.0)	25 (10-29)	16 (12.0-24.0)	0.64	< 0.0001
Course of disease (IQR), d	20 (16.0-27.0)	18 (15.0-23.0)	27 (19.0-30.5)	20 (16.0-24.5)	17.5 (15.5-23.0)	30 (20-32)	21 (16.0-28.0)	0.44	0.0005
Severity									
Severe	10 (14.1)	6 (13.6)	4 (14.8)	4 (5.6)	3 (4.2)	1 (1.4)	6 (8.5)	0.44	1
Mild	61 (85.9)	38 (86.4)	23 (85.2)	15 (21.2)	13 (18.3)	2 (2.8)	46 (64.7)		
Glucocorticoid therapy	18 (25.4)	11 (25.0)	7 (25.9)	4 (5.6)	3 (4.2)	1 (1.4)	14 (19.7)	0.76	1

Abbreviations: IQR, interquartile range; COVID-19, coronavirus disease 2019; a indicate patients with SARS-VoC-2 RNA turned to positive, and b indicate patients with SARS-VoC-2 RNA remained negative; c P1 values indicate differences between the patients with positive SARS-VoC-2 RNA and patients with consistently negative SARS-VoC-2 RNA; d P2 values indicate differences between the Group A and Group B. P < 0.05 was considered statistically significant.

Patients may remain positive for SARS-CoV-2 RNA in respiratory samples for some time after hospital discharge; (2) stricter criteria for hospital discharge may be warranted; (3) the patients who remained positive for SARS-CoV-2 RNA were nearly asymptomatic and had a low viral load that did not represent reactivation of SARS-CoV-2. However, due to the urgency of the epidemic, we did not conduct viral culture to find direct evidence that this phenomenon will cause infection, but their potential infectiousness needs further attention. Therefore, it seems safe to quarantine recovered patients for at least two weeks to reduce their transmission potential, as they may excrete the virus intermittently (Pan et al., 2020; Zou et al., 2020).

The study was approved by the Ethics Committee of the First Affiliated Hospital of Chongqing Medical University and the Yongchuan Hospital of Chongqing Medical University. And, no informed consent is required.

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Jiajun Li: Conceptualization, Methodology, Writing - review & editing. **Xiaoyu Wei:** Data curation. **Wenguang Tian:** Visualization, Investigation. **Jingbo Zou:** Validation, Data curation. **Yue Wang:** Writing - review & editing. **Wei Xue:** Software, Validation. **Qing Xiao:** Writing - original draft. **Wenxiang Huang:** Supervision, Conceptualization, Methodology.

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