

## False negative of RT-PCR and prolonged nucleic acid conversion in COVID-19: Rather than recurrence

Dear Editor,

A novel coronavirus disease (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) threatens the world. We read with interest the recent report by Li et al<sup>1</sup> that included 610 patients with COVID-19. They reported a high false-negative rate of real-time reverse transcription-polymerase chain reaction (RT-PCR) results for SARS-CoV-2 detection. In addition, a recent report regarding SARS-CoV-2 “turn positive” in recovered cases with COVID-19 was published.<sup>2</sup> Here, we studied the characteristics of nucleic acid conversion for SARS-CoV-2 from 70 COVID-19 patients. We found that 15 (21.4%) patients experienced a “turn positive” of nucleic acid detection by RT-PCR test for SARS-CoV-2 after two consecutive negative results, which may be related to the false negative of RT-PCR test and prolonged nucleic acid conversion.

A total of 70 patients (admission date from 21 January to 12 February 2020) with confirmed SARS-CoV-2 infection at Tongji Hospital in Wuhan were included in this study. Throat swab samples or deep nasal cavity swab samples were collected from patients on different dates after the onset of symptoms. SARS-CoV-2 was detected by RT-PCR assay using a COVID-19 Nucleic Acid Detection Kit according to the manufacturer's protocol (Shanghai Huirui Biotechnology Co, Ltd).<sup>3</sup> According to the current guideline, all included patients were mild to moderate.<sup>4</sup> No patient was transferred to the intensive care unit. Nucleic acid conversion time is defined as the period from the date of symptoms onset to the date of first-negative RT-PCR test result (in some cases, patients got positive RT-PCR results

following false-negative results, which were considered non-effective negative results in this study). Our results showed that 15 (21.4%) patients had a positive test result of RT-PCR after two consecutive negative results. Compared to patients with two consecutive false-negative RT-PCR results, patients in the control group were more likely to be younger ( $P = .093$ ) and had significantly shorter nucleic acid conversion time (21 vs 36 days;  $P < .001$ ) (Table 1). Details of RT-PCR test results were shown in Table S1. One patient (patient no. 5) has a positive test result of RT-PCR for SARS-CoV-2 on 45 days after symptoms onset.

The pandemic of COVID-19 threatened the whole world with more than 1 000 000 infected cases. Evidence suggested that the outbreaks of COVID-19 may be correlated to its rapid person-to-person transmission ability.<sup>5</sup> Since specific treatment had not been validated for COVID-19, traditional public health tactics— isolation, quarantine, and community containment are critical to control the spread.<sup>6,7</sup> Another recent report by Lan et al<sup>8</sup> found positive RT-PCR test in cases of recovered patients with COVID-19. According to our result, a certain number of COVID-19 patients may experience a prolonged nucleic acid conversion regardless of the relief in symptoms or radiography. Current guideline suggested two consecutive negative RT-PCR test results is one of the criteria for discharge. However, due to the high false-negative rate of viral test and underestimated proportion of patients with prolonged nucleic acid conversion, the above patients may experience from false-negative RT-PCR results or prolonged viral clearance rather than “turn positive”

**TABLE 1** The demographic and clinical characteristics of patients with COVID-19

Variables	All patients (N = 70)	Nonconsecutive false negative (n = 55)	Consecutive false negative (n = 15)	P value
Age, median (IQR), y	57 (44-65)	57 (43-65)	64 (51-73)	.093
Sex, male, n (%)	31 (44.3%)	22 (40.0%)	9 (60.0%)	.172
Severity on admission				.935
Moderate	66 (94.3%)	52 (94.5%)	14 (93.3%)	
Severe	4 (5.7%)	3 (5.5%)	1 (6.7%)	
Onset of symptom to nucleic acid conversion, median (IQR), d	22 (19-32)	21 (18-26)	36 (28-40)	<.001

Note: For P value: The boldface type indicates a significant difference.

Abbreviations: COVID-19, coronavirus disease 2019; IQR, interquartile range.

or “recurrence.” Traces of virus detected by RT-PCR were not necessarily correlated with the ability of transmission. However, a longer observation periods should be considered for a certain groups of patients with COVID-19.

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#### CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

#### AUTHOR CONTRIBUTIONS


All authors have agreed on the final version and meet the major criteria recommended by the ICMJE (<http://www.icmje.org/>).

#### DATA AVAILABILITY STATEMENT

The database used and/or analyzed during the current study is not publicly available (to maintain privacy) but can be available from the corresponding author on reasonable request.

#### ETHICS STATEMENT

This study was approved by the Ethics committee of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology. All procedures followed in this study were in accordance with the 1964 Helsinki Declaration and later versions. Oral consent was obtained from patients involved before enrollment when data were collected retrospectively.

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#### SUPPORTING INFORMATION

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