

Discontinuation of Transmission Precautions for COVID-19 Patients

Polymerase Chain Reaction Diagnostics, Patient Delays, and Cycle Threshold Values

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Background: The decision of when it is safe to discontinue transmission-based precautions for SARS-CoV-2 coronavirus disease 2019 (COVID-19) hospitalized patients has been controversial. The Centers for Disease Control and Prevention offered reverse transcriptase polymerase chain reaction (PCR) diagnostic test- or symptom-based guidelines.

Methods: A retrospective chart review of Vidant Health system, Eastern North Carolina, was conducted. Length of stay, days in isolation unit, and date appropriate for discharge or isolation discontinuation based on the symptom-based strategy were recorded.

Results: Of 196 COVID hospitalized patients, 34 had repeated COVID PCR tests 3 or more days from their first positive test result. Half of these patients experienced delays in release from transmission-based precautions because of repeated positive PCR test results and use of the test-based approach. This resulted in an additional 166 days of hospitalization, costing an estimated \$415,000. Furthermore, 2 subjects had a combined 16-day delay in necessary medical procedures. Most of the COVID PCR platforms yield quantitative results in the form of cycle threshold (Ct) values, the number of cycles needed to detect the genome. These values have also been used to assess whether patients are likely to remain contagious. None of our patients who met the criteria for symptom-based strategy for transmission-based precaution discontinuation had positive PCR test results with Ct values lower than 25, but 4 had Ct values lower than 30.

Conclusions: Concerns surround immunocompromised patients and those treated with steroids who might be delayed or incapable of stopping viral replication and thus remain contagious. Our results suggest that clinicians use all available data including Ct values to evaluate the safety of discontinuation of transmission precautions.

Key Words: COVID-19, SARS-CoV-2, PCR, isolation precautions, diagnostics

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Coronavirus disease 2019 (COVID-19) is caused by SARS-CoV-2 and was first identified in the city of Wuhan, Hubei Province, China.^{1,2} Similar to the first SARS outbreak in 2003,³ the disease primarily presents as an acute respiratory illness, but it may have a number of clinical presentations including thrombosis and gastrointestinal symptoms.⁴ Evidence suggests that the virus infects the kidney, liver, gastrointestinal tract, blood vessels,

and heart^{5,6} and has killed more than 1 million people as of October 6, 2020.⁷ Virus has also been detected in, and can be spread by asymptomatic individuals.^{8–11} Although continued coronavirus spillover events were predicted and much vaccine work was done in animals for SARS-CoV,^{12–15} there is currently no approved vaccine for SARS-CoV-2. The rapid spread of the disease around the world has resulted in far-reaching impacts on many aspects of society. Notably, health care systems have been overwhelmed with a large influx of patients with COVID-19, scarcity of personal protective equipment (PPE), and staff shortages due to economic hardships faced by the hospitals.

Diagnostic testing for COVID-19 depends on the detection of SARS-CoV-2. The first and most of the tests rely on the detection of viral ribonucleic acid (RNA) using reverse transcription real-time polymerase chain reaction (PCR). The PCR test for viral RNA is the mainstay of testing in the United States. The Centers for Disease Control and Prevention (CDC) has provided guidelines for interpreting COVID-19 test results, both for viral detection (current infection) and detection of patient antibodies to SARS-CoV-2.¹⁶ Detection of serum antibody (immunoglobulin M or G) indicates that the patient has been infected, or may still be infected and has mounted an immune response to SARS-CoV-2.¹⁷ The serological antibody test has not been validated to document immunity or to make clinical decisions on infectivity.¹⁶ Antigen tests detecting viral proteins are also coming into production. However, antigen tests are often less sensitive, resulting in more false-negatives. A positive COVID antigen result is conclusive, but a negative result may require follow-up PCR testing.¹⁶ Nasopharyngeal samples are most commonly collected for diagnostics, but saliva also provides reliable diagnostic results.¹⁸ Saliva has additional advantages; it is less invasive and can easily be self-administered, obviating the need for health care professionals and PPE. When a patient is first infected, a patient will test negative for the virus during the incubation period until viral titers reach the threshold for detection. As infection progresses, viral replication in the upper respiratory tract decreases as the immune system clears the virus; over time, this clearing will result in a negative test result.¹⁹

The PCR test has been used for diagnosing COVID-19, for screening patients before procedures and before patient discharge to a skilled nursing facility (SNF), and for determining discontinuation of transmission-based precautions. The CDC outlined 2 strategies for discontinuing COVID-19 transmission-based precautions in Spring 2020, symptom- and test-based strategies.²⁰ The symptom-based strategy states that patients should remain on transmission-based precautions until 10 days after symptom onset, at least 24 hours without a fever (updated August 10, 2020, previously 72 hours), and improvement in respiratory symptoms, whereas the test-based strategy includes resolution of fever, improvement in respiratory symptoms, and 2 negative Food and

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Drug Administration–approved molecular assays for the detection of SARS-CoV-2 RNA collected 24 hours or more apart (Fig. 1).

Interpretation of tests in recovering patients presents a significant diagnostic challenge and can influence the availability of certain therapies, timing of procedures, and length of hospitalization. Patients who met the symptom-based criteria to discontinue transmission isolation but have a positive PCR test result may be deemed infectious and kept in isolation. Delayed discharge represents a significant emotional and financial burden to patients and can lead to delayed medical procedures and increased costs to the health care system. Bartsch and colleagues²¹ estimate the total cost for COVID direct medical care in the United States could reach \$650 billion. Uninsured patients alone could cost the health care system as much as \$40 billion.²² The cost of treating COVID-19 patients is underscored by the federal government's first Coronavirus Aid, Relief, and Economic Security Act, which provides \$175 billion in funding for health care providers.

In this report, we evaluate the impact of the test-based strategy for discontinuation of COVID-19 transmission precautions. We report findings from almost 200 hospitalized patients, 20 of whom experienced delays in procedures, transfer from the COVID unit, or discharge due to repeated positive SARS-CoV-2 PCR test results. We discuss these patient experiences in the context of evolving research showing that detection of viral RNA is not adequate to conclude that a patient is still infectious and that reliance on such tests causes significant problems for patients and the health care system. Although COVID PCR test results are often reported simply as positive or negative, we evaluated the quantitative data in terms of the number of PCR cycles needed to reach detection, the cycle threshold (Ct), which provides additional information on whether the patient likely has residual viral RNA or infectious virions being released.

METHODS

Of 196 COVID-19 hospitalized patients within the Vidant Health system in Eastern North Carolina, 34 subjects had repeated PCR tests 3 or more days from their first positive test result. Nasopharyngeal swabs were analyzed for SARS-CoV-2 genome by reverse transcriptase polymerase chain reaction (RT-PCR) on the Cepheid Infinity, Genmark ePlex Cov2, BD Max, or Quidel Lyra platforms. The Cepheid Infinity and BD Max PCR assays detect 2 PCR targets, whereas the other platforms detect 1. Using patient charts in the electronic health record, we retrospectively evaluated date of symptom onset, date of hospitalization, number and results of COVID tests, symptom timeline, and number of days that a procedure, transfer, or discharge was delayed. In addition, we evaluated available Ct values for COVID PCR diagnostic tests. Vidant Health is a hospital system constituting 1 tertiary care center and 7 rural secondary care centers. The tertiary care center contained a non-intensive care unit (ICU) COVID isolation unit designated for COVID-infected patients only, whereas the secondary care centers did not contain an isolation unit.

Improvement of respiratory symptoms was defined as a clear improvement in presenting symptoms, minimal or no supplemental oxygen requirement, and overall clinical readiness for discharge. Statements regarding disposition in progress notes, normal vital signs, and absence of intravenous therapies were all clinical indicators of discharge readiness. Increased length of stay was calculated comparing date of discharge with the date identified as clinically appropriate for discharge. Total extra days of hospitalization (delayed discharge) were calculated using date identified as appropriate for discharge using the symptom-based approach and date of actual discharge. For patients hospitalized at the tertiary care center, where both COVID ICU and non-ICU wards were used, total days spent in the non-ICU COVID isolation unit were also calculated.

Statistics

Mean days from symptom onset to second COVID test result were compared using an independent-sample *t* test. Total length of hospitalization was compared with the day appropriate for discharge using an unpaired *t* test. A *P* value of < 0.05 was considered statistically significant. Statistical analyses were performed using SPSS software version 25 (IBM Corp, Armonk, NY).

This study was approved by the East Carolina University Institutional Review Board in compliance with the Declaration of Helsinki.

RESULTS

To evaluate the effects of repeated testing, we identified 34 of our 196 COVID-19 subjects who had at least 1 repeat PCR test 3 or more days from their first positive test result. Each subsequent test result and the impact of the tests were recorded (Table 1). Of the 34 patients, 26 (76%) had 2 repeat positives, 11 (32%) tested positive on a third test, and 6 (18%) tested positive on a fourth test. Two of the 6 patients who tested positive 4 times or more had previously tested negative. Twenty patients (59%) experienced delays in transfer from a COVID isolation unit, a necessary medical procedure, or discharge to a SNF or inpatient rehabilitation (IPR) because of the requirement of 2 consecutive negative PCR test results. Of the 20 patients, 18 had a delay in discharge or procedure and may also initially have had delayed transfer out of the COVID isolation unit, whereas 2 patients only had delayed transfer out of the COVID isolation unit (patients 16 and 33) (Table 1). Fourteen patients (41%) did not have a delay due to repeat testing. Despite the results of the first subsequent test being negative, patients still may have experienced a delay owing to a following test result being positive, as seen in patient 17.

To evaluate the effect of time of symptom onset to repeat positive test result, days from the first symptom onset to the time of second test was assessed. Of the 34 subjects with repeat testing, 8 (24%) tested negative on the first repeat test (Table 1). Among the 8 subjects, the mean (SD) length of stay from symptom onset until the negative test result was 21.3 (10.2) days. Of the 26 (76%)

Symptom-based	Test-based*
<ul style="list-style-type: none"> • 10 days since symptom onset • ≥ 24-hours afebrile • improved respiratory symptoms 	<ul style="list-style-type: none"> • 10 days since symptom onset • ≥ 72-hours afebrile • 2 negative RNA tests ≥24 hours apart

*Not currently recommended as of Aug 10, 2020

FIGURE 1. Strategies for discontinuation of COVID-19 transmission-based precautions in patients with mild to moderate illness who are not severely immunocompromised (updated August 10, 2020).

TABLE 1. Repeat PCR Tests and Delays in Patients Diagnosed With COVID-19

Pt	Test 2			Test 3			Test 4			Add. Tests	Total Tests	Length of Stay
	Result	Days	Delay	Result	Days	Delay	Result	Days	Delay			
1	–	38	COVID	+	40	COVID	–	42	COVID	3	7	40
2	+	7	–	+	15	SNF/IPR	–	22	SNF/IPR	1	5	20
3	–	27	–							–	2	25
4	+	20	–	–	29	SNF/IPR	+	30	SNF/IPR	2	6	34
5	+	37	SNF/IPR							–	2	25
6	+	40	–	–	48	–				–	3	27
7	+	46	SNF/IPR	+	63	SNF/IPR	+	77	SNF/IPR	3	7	99
8	+	15	–							–	2	22*
9	+	17	–	–	23	–				–	3	20
10	+	20	SNF/IPR	+	24	SNF/IPR				–	3	20
11	+	21	–	–	25	COVID	–	27	COVID	–	4	44†
12	–	25	SNF/IPR	+	26	SNF/IPR	+	27	SNF/IPR	–	4	26
13	+	13	–	–	29	SNF/IPR	+	31	SNF/IPR	1	5	19
14	+	18	–							–	2	11
15	+	10	–							–	2	9
16	+	25	COVID	–	27	COVID	–	28	COVID	–	4	49
17	–	20	SNF/IPR	+	21	SNF/IPR	–	22	SNF/IPR	–	4	18
18	–	26	SNF/IPR	–	27	SNF/IPR				–	3	22
19	+	15	Care	+	17	Care	–	21	Care	5	9	39
20	–	10	SNF/IPR	+	12	SNF/IPR	–	13	SNF/IPR	2	6	20
21	+	17	COVID	+	20	COVID	–	22	COVID	3	7	42†
22	+	4	–	+	26	SNF/IPR	–	28	SNF/IPR	4	8	29
23	–	6	SNF/IPR	–	7	SNF/IPR	–	9	SNF/IPR	–	4	8
24	–	18	–							–	2	17
25	+	29	Care	–	33	Care	–	34	Care	–	4	40*
26	+	12	SNF/IPR							–	2	11
27	+	11	COVID	–	16	COVID	–	17	SNF/IPR	–	4	22
28	+	11	–							–	2	9
29	+	7	SNF/IPR							–	2	14
30	+	6	COVID	–	13	COVID	–	15	SNF/IPR	1	5	28
31	+	4	COVID	+	6	SNF/IPR	+	7	SNF/IPR	7	11	22
32	+	5	SNF/IPR	+	7	SNF/IPR	+	8	SNF/IPR	1	5	21†
33	+	12	COVID	–	21	COVID	–	23	COVID	–	4	21†
34	+	3	–							–	2	24†

All patients tested positive for test 1. Days denote days since symptom onset; Add. Tests, number of additional tests after the fourth test; Care, delay in care; SNF/IPR, delay discharge to SNF/IPR; and COVID, delay in transfer out of COVID unit. Blank cells indicate no further testing.

* Patient passed away during hospitalization.

† Ongoing hospitalization at time of writing.

Pt indicates patient.

subjects whose first repeat test result was positive, the test was performed a mean (SD) of 15.9 (10.2) days from symptom onset. Independent sample *t* test showed that there was no significant difference between mean days from symptom onset and repeat COVID test result ($t_{32} = 1.298, P = 0.204$).

Of the 18 subjects identified as having a delay in a procedure or discharge to an SNF or IPR, 16 subjects had delayed discharge, 1 subject had a delay in both discharge and procedure, and 1 subject had a delay in a procedure because of repeat positive COVID test results (Table 2). Patient 25 experienced a 6-day delay in a necessary procedure because of a positive test result and died in the ICU. The other 17 subjects all met the symptom-based CDC approach for transmission precaution discontinuation criteria

and were clinically ready for discharge. These patients could have been discharged earlier; however, they were discharged using the test-based strategy, causing 166 days of extra hospitalization (Table 2, Fig. 2), with a mean extra stay of 9.8 days per patient. The total length of hospitalization with the test-based strategy used versus the length of stay if the symptom-based strategy was used did not result in a statistically significant difference ($t_{23} = 1.73, P = 0.092$); however, the total hospitalization was longer than if the symptom-based strategy was used. The mean (SD) length of stay for patients who were discharged using the test-based strategy was 27.6 (21) days, whereas mean (SD) hospitalization would have been 17.8 (11) days if the symptom-based approach were used. Furthermore, because of the test-based

TABLE 2. Delays in Hospital Discharge and Required Procedures Owing to the Test-Based Strategy Being Used

Pt	Total LOS	Day Patient Appropriate for Discharge	Extra LOS Due to Repeat Testing	Days in COVID Unit	Discharge/Result
1	40	25	15	21	SNF
2	20	11	9	10	SNF Pt insisted on going home
4	34	25	9	11	IPR
5	25	20	5	15	SNF
6	27	19	8		SNF
7	99	44	55		SNF
10	20	13	7		SNF
13	19	14	5	6	IPR*
17	18	17	1	3	IPR*
19	39	38	1	18	LTAC Procedure delayed 10 days
22	29	23	6	8	SNF*
23	8	4	4	5	SNF
25	40	–	–		Procedure delayed 6 days Pt passed away in ICU
26	11	8	3		SNF
29	9	8	1		SNF
30	28	13	15	6	SNF
31	22	10	12	22	SNF
32	21+	11	10+	22+	SNF
Total	509+		166+	141+	

SNF denotes discharged to SNF; IPR, discharged to IPR; and LTAC, discharged to long-term acute care hospital. “Days in COVID Unit” denotes that the patient was hospitalized in the COVID Isolation Unit at a tertiary care center. + means ongoing hospitalization; –, not appropriate for discharge.

* Denied admission to IPR or SNF because of positive PCR test, discharged home.

Pt indicates patient; LOS, length of stay.

criteria, 3 subjects were denied admission to SNF or IPR and were discharged home when they would have clinically benefitted from SNF or IPR placement (Table 2).

Two cases illustrate the difficulties with PCR-based viral detection for discontinuation of transmission-based precautions. One patient, a 64-year-old man, was admitted to the hospital after an ischemic stroke. Although he worked well with physical and occupational therapy, the subject could not be safely discharged home because of severe neurologic deficits. Therefore, while preparing for an SNF discharge, a COVID-19 PCR nasopharyngeal swab was obtained on hospital day 34, which returned positive.

Repeat COVID-19 testing on hospital days 48 and 79 were also positive. Because of concern of unnecessary use of PCR tests for which reagent is in short supply across the country, further testing was deferred for the next 2 weeks. The patient was stable for discharge on hospital day 44 and ended up having an extra 55 days of hospitalization before discharge owing to testing requirements for discharge to a nursing facility. A second patient, a 61-year-old man, was hospitalized for acute hypoxic respiratory failure from COVID-19 pneumonia requiring intubation and ICU admission. His ICU course was complicated by a sacral wound infection requiring surgical debridement and renal failure requiring

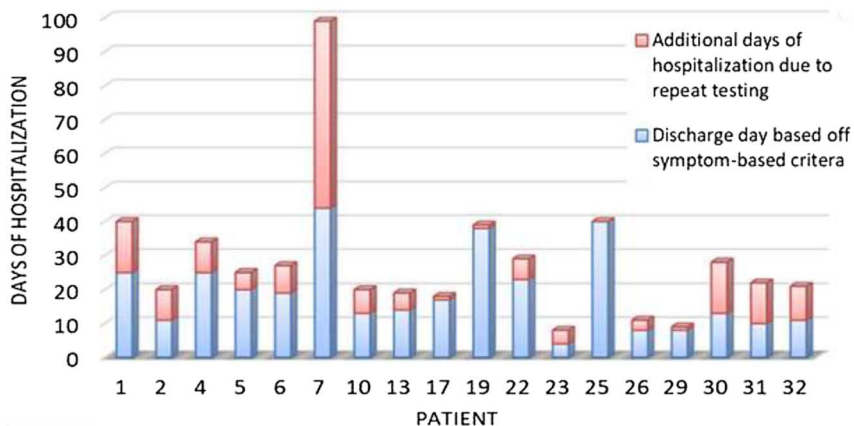


FIGURE 2. Total length and extra days of hospitalization due to test-based strategy versus symptom-based strategy.

hemodialysis. Hospital criteria for surgery required a COVID test before any procedure. He tested positive, and therefore, both procedures were delayed for 10 days. Furthermore, although he was negative before his procedures, he tested positive before discharge, requiring transfer back to the COVID isolation unit. Such test-based strategy required 18 days in the COVID isolation unit, a 10-day delay in procedures, and a 1-day increase in hospitalization.

Of the 34 subjects with at least 1 repeat COVID test, 24 were hospitalized at the tertiary care center and 10 were hospitalized at rural secondary care centers. The 24 tertiary care center subjects spent a collective 226 days in the non-ICU COVID isolation unit; the average time spent was 9.4 days. Assuming that the patients with extra length of stay due to testing were required to remain in the COVID unit (Table 2), it would indicate that 77 of the 141 days in COVID isolation were unnecessary, contributing to patient distress, increased costs, and PPE use. Patient 30 was

transferred out of COVID isolation after 2 negative test results but subsequently tested positive, delaying discharge (Table 1).

In this study, we identified 166 days of unnecessary hospitalization for 17 patients (Table 2, Fig. 2). At a cost of \$2,500 per day,^{23,24} the total cost of these delays was estimated at \$415,000, a mean of \$24,400 per patient. The CDC reports 58,088 laboratory-confirmed COVID-19-associated hospitalizations between March 1, 2020, and September 26, 2020.²⁵ If a similar percentage of delays occurs nationally as in our patient population (~9%) with delays of 10.2 days, that would cost the United States an additional unnecessary \$129 million just between March and September 2020.

To determine whether quantitative data from PCR diagnostic tests might be useful for evaluating the potential for patient infectiousness, we assessed the Ct data from the patients (Table 3). In general, the Ct values of patients increased over time, as expected

TABLE 3. PCR Ct Values Days Post Symptom Onset

Pt	Test 2				Test 3			Test 4			Add. Tests	Total Tests
	Result	Days	Ct 1	Ct 2	Result	Ct 1	Ct 2	Result	Ct 1	Ct 2		
1	-	38	-	-	+	32.5	32.5	-	-	-	3	7
2	+	7	21.8	20.5	+	31.4	31.1	-	-	-	1	5
3	-	27	-	-	-	-	-	+	32.3	33.3	2	6
4	+	20	37.4	40.5	-	-	-	+	32.3	33.3	2	6
5	+	37	25.0	36.8	-	-	-	-	-	-	-	2
6	+	40	27.3	27.5	-	-	-	-	-	-	-	3
7	+	46	23.9	24.4	+	32.4	32.8	+	31.8	32.7	3	7
8	+	15	-	-	-	-	-	-	-	-	-	2
9	+	17	-	36.1	-	-	-	-	-	-	-	3
10	+	20	29.9	30.0	+	29.2	29.9	-	-	-	-	3
11	+	21	33.5	34.5	-	-	-	-	-	-	-	4
12	-	25	-	-	+	0.0	39.8	+	0	40.4	-	4
13	+	13	28.0	30.5	-	-	-	+	29.2	29.7	1	5
14	+	18	27.3	29.7	-	-	-	-	-	-	-	2
15	+	10	-	-	-	-	-	-	-	-	-	2
16	+	25	36.1	35.8	-	-	-	-	-	-	-	4
17	-	20	-	-	+	34.2	34.4	-	-	-	-	4
18	-	26	-	-	-	-	-	-	-	-	-	3
19	+	15	26.1	26.4	+	26.1	26.2	-	-	-	5	9
20	-	10	-	-	+	34.7	34.4	-	-	-	2	6
21	+	17	32.3	32.6	+	35.5	34.6	-	-	-	3	7
22	+	4	21.6	23.9	+	37.8	-	-	-	-	4	8
23	-	6	-	-	-	-	-	-	-	-	-	4
24	-	18	-	-	-	-	-	-	-	-	-	2
25	+	29	34.7	35.7	-	-	-	-	-	-	-	4
26	+	12	28.1	28.1	-	-	-	-	-	-	-	2
27	+	11	33.4	34.2	-	-	-	-	-	-	-	4
28	+	11	19.6	N/A	-	-	-	-	-	-	-	2
29	+	7	-	-	-	-	-	-	-	-	-	2
30	+	6	29.3	N/A	-	-	N/A	-	-	N/A	1	5
31	+	4	14.5	N/A	+	16.0	N/A	+	16.2	N/A	7	11
32	+	5	23.3	N/A	+	22.6	22.4	+	28.5	28.3	1	5
33	+	12	32.8	32.7	-	-	N/A	-	-	N/A	-	4
34	+	3	14.4	N/A	-	-	-	-	-	-	-	2

Days denotes days after symptom onset. Ct 1 is the Ct value for genome target 1, and Ct 2 is Ct value for target 2. Bold data indicate patients declared ready for discharge based on symptom-based strategy and Ct values lower than 30.

Pt indicates patient; NA, not applicable (QuantStudio 1 target).

as patients recovered from virus infection. Of the patients who had a second PCR test done at day 10 or less of symptoms, 85.7% had Ct values lower than 25, suggesting that they might still be infectious. Only 1 had a Ct value higher than 25 (29.3). For patients with a positive PCR test result at day 11 of symptom onset or later, 17.6% had at least 1 Ct value of 25 or lower (indicating a higher level of viral genome present), 35.3% had at least 1 Ct value lower than 30, and the remaining 47.1% had Ct values higher than 30. We had 4 patients who tested negative and subsequently tested positive for SARS-CoV-2 RNA: all had Ct values higher than 32 on the subsequent test. Thirteen of 34 patients (38%) tested positive by PCR on or after the day they were judged appropriate for discharge, and 4 who were more than 10 days after symptom onset had Ct values lower than 30 (bold text in Table 3), but all were 25 or higher.

DISCUSSION

Determining when a COVID-19 patient is no longer infectious is a difficult and complex task. The proper timing of discontinuing transmission-based precaution is crucial for the safety of health care workers and the community at large. When patients experience a delay in being declared free of infectious virus, they experience numerous difficulties. Chaplain visits are limited, and expert consultants who are involved in clinical decisions are deferred to phone interviews. In our study, the 24 subjects hospitalized at the tertiary care center spent 224 days in the COVID isolation unit owing to the test-based strategy, an estimated 77 being unnecessary. Delay in discharge causes emotional distress and delays in needed care. Patients cannot be discharged to appropriate care facilities (SNF) or have appropriate physical or occupational therapy. In addition, these delays cause great expense to both patients and the health care system costing millions of dollars.

Other studies are beginning to shed light on PCR detection of viral RNA versus the infectivity of recovering patients. To evaluate the risk of infectivity upon discharge, the Korean CDC identified 285 subjects who had recovered from COVID-19 but subsequently had a positive PCR RNA test.²⁶ Of the 790 individuals who came in contact with the 285 subjects, only 3 new cases were reported. Importantly, all 3 new cases had contact with other known cases. As a result, the Korean CDC discontinued the previous test-based recommendation for transmission-based precaution discontinuation. The Korean study demonstrates that recovered COVID-19 subjects with positive PCR test results may not be infectious.

Another study exploring the relationship between PCR detection of viral load, timing of seroconversion, and symptoms followed 9 patients with resolution of symptoms within 5 days.²⁷ However, despite viral RNA being detectable for weeks, live virus was detectable only until day 8 after symptom onset, indicating that these patients were not infectious. Seroconversion occurred by day 7 in 50% of patients and all patients by day 14. At time of seroconversion, there was no decrease detectable in viral RNA, suggesting that shedding of viral genome fragments may continue even after recovery and a protective immune response. Furthermore, another study of 766 subjects reported the detection of viral RNA for up to 33 days.²⁸ Such findings suggest that viral RNA is detectable for weeks after the cessation of infectiousness.

An approach to improve the testing strategy is to evaluate the amount of viral RNA present. Real-time PCR uses a quantitative measure, the Ct. The Ct is inversely proportional to the target sample amount (a lower cycle number indicates more viral genome). Bullard et al²⁹ reported that COVID-19 subjects (90) with a Ct higher than 24 and with more than 8 days from symptom onset resulted in a negative viral culture and low probability of

transmitting infection. Another study reported that a Ct of 30 or higher would result in low probability of being infectious.²⁸ Therefore, Ct values could be used to address the aforementioned limitations in test-based strategy for preoperative and nursing facility discharge screening. It should be noted that Ct values are not directly comparable between different testing platforms. Indeed, variability has been documented even between different batches of tests from the same instrument.³⁰ Our data show that those patients who were ready for discharge using the symptom-based strategy who had a subsequent positive test result all had a Ct value of 25 or higher, supporting the findings of the aforementioned studies. However, of our patients with a positive PCR test result at day 11 or after of symptom onset, but who did not meet the full symptom-based criteria, 17.6% had at least 1 Ct value of 25 or lower, suggesting that they might still have infectious virus. Therefore, simply basing decisions on days from symptom onset is not recommended.

In our study, we report the tremendous cost to patients and the health care system of the previously recommended test-based strategy in discontinuing COVID-19 transmission-based precautions and support the use of all available data (symptom improvement, cessation of fever, and PCR Ct values) to assess patient and community safety, especially in the case of patients who may be immunocompromised or immunosuppressed by steroid treatment.

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