COVID-19 Serial Testing among Hospitalized Patients in a Midwest Tertiary Medical Center, July–September 2020

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Abstract

We implemented serial COVID-19 testing for inpatients with a negative test on admission. The conversion rate (negative to positive) on repeat testing was one percent. We identified patients during their incubation period and hospital-onset cases, rapidly isolated them, and potentially reduced exposures. Serial testing and infectiousness determination were resource intensive.

Background:

Coronavirus disease 2019 (COVID-19) is a multisystemic illness caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS CoV-2). Due to adverse patient outcomes and high costs associated with unrecognized COVID-19 transmission in hospitals, many centers have implemented admission COVID-19 testing protocols. However, COVID-19 testing on admission may miss cases if the patient is in the incubation period at the time of admission. Patients may also acquire COVID-19 during their hospitalization. Serial testing of hospitalized patients may be a plausible strategy to detect COVID-19 cases missed during admission screening. However, SARS CoV-2 testing can remain positive for months [1][2], and a positive test in an asymptomatic patient may represent remnant viral RNA from a past infection. Differentiating past from current infection is important because isolation and contact investigations may not be necessary for those with past infection.

Though the utility of COVID-19 admission testing has been assessed [3, 4], limited data exists on the impact of serial testing for inpatients. We assessed the value of COVID-19 serial testing for hospitalized patients after a negative COVID-19 admission test.

Methods:

The University of Iowa Hospitals & Clinics (UIHC) is an 811-bed academic medical center. In addition to admission COVID-19 testing, in July 2020 we implemented COVID-19 serial testing for inpatients every 5 days regardless of symptoms. Patients having surgical procedures also underwent pre-procedural testing if a COVID-19 test had not been obtained in the previous 48 hours. Patients with COVID-19 signs or symptoms were tested at the discretion of their treating provider. All admitted adults and children from July 7 to September 22, 2020 were included in this study. Testing was performed using the TaqPath COVID-19 Combo Kit (ThermoFisher Inc.) according to the latest Instructions for Use under Food and Drug Administration Emergency Use clearance.

In this paper we 1) assess the frequency of conversion from a negative admission COVID-19 test to a subsequent positive in repeat testing: serial, pre-procedural, or symptomatic testing during the same admission; 2) describe the clinical characteristics of patients found to be infected; 3) quantify exposure events; and 4) identify COVID-19 among contacts of infected persons. We obtained data from the electronic health record including age, sex, admission diagnosis, time from admission to positive repeat testing, symptoms, Mean RT-PCR cycle threshold (CT) values, SARS-CoV2 serum antibodies (IgG), and infectiousness as determined by the Program of Hospital Epidemiology. We used the Roche Diagnostics assay for total antibodies to SARS-CoV-2. All specimens positive by the Roche assay are tested by a separate DiaSorin SARS-CoV-2 IgG assay. An nasopharyngeal nucleic acid amplification test (NAAT) for COVID-19 was used for admission and repeat testing[5]. Tests performed 2 days before to one day after admission were considered the admission test. Information on exposure events for health care personnel (HCP), patients, and their follow up COVID-19 test results were obtained.

Infectiousness was categorized into 4 groups: active infection (definite: CT values ≤24; possible: CT values 25–29), prior infection (possible: CT values ≥30, definite: CT values ≥30 and positive serology or history of a positive result in the last 90 days). We routinely retested patients with CTs ≥30 1–2 days later to assess CT value kinetics: if repeat CTs were <30, the case was labeled as an acute infection; if repeat CTs were ≥30 or negative, the case was labeled as a past infection. Active infections remained on isolation precautions and contact tracing was performed. Cases who converted <14 days after admission were considered to have possibly been in the incubation period. Patients who converted ≥14 days after admission were considered hospital-associated. All HCP wore medical grade face masks and face shields for all patient care. HCPs wore N95 respirators and face shields during all aerosol generating procedures (AGPs) performed on patients known or suspected to have COVID-19. All inpatients were recommended to wear a mask in our hospital but adherence to recommendations was not assessed. Only one visitor was allowed per patient

for up to two hours per day. Face masks were required. If patients were identified as active infection, no visitors were allowed by our hospital policy. This study was approved by the Institutional Review Board of the University of Iowa.

Results:

We tested 4,580 patients on admission. A total of 4,438 (96.9%) had negative results. Of those, 1,950 (42.6%) had at least one repeat test during their admission (Appendix 1). Overall compliance with serial testing was 96%. We identified 19 patients (1.0%) who converted from negative to positive during their admission.

Table 1 summarizes these 19 patients: median age was 57 years (range 16–85) and 11 (61%) were male. Median time between admission to first positive test was six days (3–38). The indications for repeat testing were: serial testing 15 patients (79%), pre-procedural testing two patients (10.5%), and symptomatic testing two patients (10.5%). Fourteen patients (74%) were asymptomatic (12 detected on serial testing, and two in pre-procedural testing). Median CT value on first positive test was 30.5 (8–37).

Final interpretation revealed nine (47%) active infections (seven definite and two possible) and 10 prior infections (five definite and five possible). Six (67%) were likely in their incubation period at the time of admission and three (33%) were hospital-associated. Of the nine active infections, seven (78%) were detected via serial testing: five remained asymptomatic and two had symptoms that could be explained by their reason for admission (e.g., lung mass).

Infectious cases were associated with 46 exposures: 32 patients (20 of them were in a communal inpatient psychiatric unit) and 14 HCP. Twelve of them were associated with an emergent aerosol generating procedure in a patient later discovered to have CT values of 21 and 17. Many of the same HCPs also ate together in the same breakrooms. Of 46 exposed

persons, 42 had follow-up testing 10–12 days after exposure. Among 42 persons with follow up testing, 9 (21%) had a positive NAAT result: two patients (22%), one visitor (11%), and six HCP (67%).

Discussion:

We implemented a serial testing strategy for inpatients with a negative COVID-19 admission screening test. The conversion rate from negative to positive was one percent. Nine patients (47%) were infectious. The serial testing strategy helped us identify seven infectious COVID-19 patients, most of them asymptomatic. We detected COVID-19 cases sooner and potentially prevented further in-hospital exposure events. However, serial testing and infectiousness determination were time and resource intensive.

Implementing serial testing of inpatients for COVID-19 was feasible. While the conversion rate from negative to positive was relatively low (1.0%), this strategy identified asymptomatic patients who developed COVID-19 during their hospitalization and potentially prevented exposure events. Some studies have assessed the impact of repeating tests in symptomatic patients or those undergoing a surgical procedure. They found that 1–3% were positive on retesting after an initial negative result. [6-8]. However, their approach was different from ours because they repeated tests in patients with a high suspicion of COVID-19 or in whom they suspected a false negative result. Studies focusing only on admission screening or pre-procedural testing could have missed patients in their incubation period or hospital-onset COVID-19 patients.

This strategy helped us identify patients that became infectious during their hospital stay. However, nearly 50% were likely past infections and therefore not infectious. These findings highlight the limitations of using SARS-CoV2 NAAT in asymptomatic individuals for screening purposes. Patients may continue having a positive NAAT even months after an acute infection. Some authors postulate that different CT limits may be needed or alternative

testing methods be used for public health screening efforts [2][9]. We were able to assess case infectiousness by serial testing and discontinue isolation precautions in those with prior infections. This approach helped better utilize scarce resources (e.g., private rooms, personal protective equipment) and facilitated medical care for patients (e.g., allowing visitors, avoidance of delays for certain procedures).

COVID-19 infection can be asymptomatic in 30–40% of patients. [10, 11] Because of the long incubation period (up to 14 days) and the possibility of hospital onset, a negative admission test may not guarantee absence of risk during the hospitalization. Furthermore, detecting asymptomatic or presymptomatic cases early can avoid outbreaks in healthcare facilities. Patients who have recently converted are more likely to have higher viral loads and may be more infectious. Symptomatic patients may have other diagnoses (e.g., chronic cardiac or pulmonary disease) that may make it difficult for providers to suspect COVID-19.

Because serial testing is costly and time intensive, implementing it for all inpatients may not be cost-effective in facilities with a low incidence of COVID-19. Some institutions may want to consider it, especially if they have semi-private rooms or lack respirator availability for all aerosol generating procedures.

This study has limitations. It was conducted at a single center with a relative low COVID-19 incidence and the results may not be generalizable. Interpretation of infectiousness using CT values is not yet standardized. CT values vary widely between assays and gene targets and may not translate numerically to CT values obtained from other testing. We could not confirm if exposed persons who subsequently tested positive acquired COVID-19 in the hospital or in the community. However, we present one of the first experiences of COVID-19 serial testing and a framework for infectiousness interpretation using CT values and serologic status.

In conclusion, we demonstrated that a serial testing strategy for inpatients could help detect COVID-19 cases. These cases could have been in the incubation period on admission, or healthcare-associated infections. CT value kinetics enabled us to assess case infectiousness and discontinue isolation precautions in those unlikely to be infectious. Because serial testing and infectiousness determination were time and resource intensive, screening strategies should balance diagnostic and resource stewardship with patient and health care professionals safety.

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Table 1: Descriptions of patients who had negative COVID-19 screening on admission but positive results on repeat testing.

Patient	Age	Sex	Reason for admission	Admission to repeat positive test (days)	Reason for repeat testing	Concurrent symptoms	First + NAAT CT value	Follow-up NAAT (CT value)	Serum antibody	Interpretation	Isolation and contact tracing
1	28	M	Suicidal ideation	11	Pre-procedure screening	None	28	Positive (26)	Intermediate	Possible active infection	Yes
2	59	M	Seizure	6	Serial testing	None	35	Negative	Negative	Possible prior infection	No
3	70	M	Atrial fibrillation	5	Serial testing	None	33	-	Positive	Definite prior infection	No
4	51	M	Motorcycle accident	9	Serial testing	None	31	Positive (35)	Positive	Definite prior infection	No
5	85	F	Fall	12	Serial testing	None	28	Positive (19)	Negative	Definite active infection	Yes
6	16	M	Spinal cord injury	15	Serial testing	None	30	Negative	Positive	Definite prior infection	No
7	77	F	Gastroenteritis Failure to thrive	5	Serial testing	None	31	Negative	Negative	Possible prior infection	No
8	79	M	Retroperitoneal bleeding	5	Serial testing	None	17	-	-	Definite active infection	Yes
9	40	F	Choledocholithiasis	3	Pre-procedure screening	None	33	-	-	Definite prior infection (confirmed positive NAAT 2 months prior)	No
10	70	F	Lung mass	6	Serial testing	Chronic cough	15	-	Negative	Definite active infection	Yes
11	48	F	Burn	5	Serial testing	None	35	-	-	Possible prior infection	No

12	48	M	Motor vehicle accident	24	Symptomatic testing	Fever	21	Positive 17	Negative	Definite active infection	Yes
13	78	M	Endocarditis	5	Serial testing	None	14	Positive 16	Negative	Definite active infection	Yes
14	54	M	Necrotizing fasciitis	15	Serial testing	None	8	Positive 23	Negative	Definite active infection	Yes
15	51	F	Cardiac arrest	5	Serial testing	Hypoxia due to "aspiration"	37	-	Positive	Definite prior infection (confirmed positive NAAT a few months prior)	No
16	64	M	Subdural hematoma	38	Serial testing	None	22	19	Negative	Definite active infection	Yes
17	48	F	Subdural hematoma	16	Symptomatic testing	Hypoxia	32	Negative	Negative	Possible prior infection	No
18	83	M	Sepsis	5	Serial testing	Hypoxia	28	-	-	Possible active infection	Yes
19	57	M	Foot gangrene	7	Serial testing	None	34	Negative	-	Possible prior infection	No

Abbreviations: CT: cycle threshold, NAAT: nucleic acid amplification test, "-": not performed