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Original Article

Utility of post-admission SARS-CoV-2 serial testing in hospitalized patients with cancer

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Abstract

Background: SARS-CoV-2 asymptomatic surveillance testing (AST) is a common strategy to minimize the risk of nosocomial infection in patients and healthcare personnel. In contrast to admission screening, post-admission AST was less widely adopted.

Objective: This study describes the diagnostic yield of post-admission serial SARS-COV-2 testing in hospitalized patients at a large cancer center with mostly double-occupancy rooms.

Design: Retrospective cohort study design. Post-admission SARS-CoV-2 tests were examined over a 18 month study period. Positive results were reviewed to determine true hospital-onset infections using a combination criteria of screening all sample cycle threshold (Ct) values >30, results of non-concordant repeat testing, and clinical symptoms.

Results: Post-admission serial testing of 15,048 hospitalized patients during an 18-month study period at a tertiary care cancer center detected hospital-onset infection in 1.6% (n = 245 patients). Among all hospital-onset positive SARS-CoV-2 RNA tests, 13% were clinically false positive. Most true infections were mild to moderate in severity.

Conclusions: In summary, post-admission serial testing in a high-risk setting is a low-yield strategy with several unfavorable effects and should no longer be routinely applied.

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Introduction

SARS-CoV-2 asymptomatic surveillance testing (AST) is a common strategy to minimize the risk of nosocomial infection in patients and healthcare personnel by identifying infected individuals who are either asymptomatic or pre-symptomatic at hospital admission.[1,2] In addition, some hospitals with immunocompromised patients or high shared-occupancy rooms also implemented serial testing to detect occult community infections missed at the time of admission.[3]

In contrast to admission screening, post-admission AST was less widely adopted and frequently part of a bundled approach, among other precautions such as admission screening, rostered employee testing, visitor restrictions, and masking. Recently published single institution studies and national UK (United Kingdom) data have critically evaluated the utility of admission screening and yielded mixed results on its impact on nosocomial transmission.[4–6] However, the practice utility of serial testing is yet to be analyzed in a non-outbreak setting. This study describes the diagnostic yield of post-admission serial SARS-COV-2 testing in hospitalized patients at a large cancer center with mostly double-occupancy rooms. The study period encompasses periods of high- and low-community SARS-CoV-2 Omicron prevalence.

Methods

The study was conducted between October 2021 and April 2023 at Memorial Sloan Kettering Cancer Center (MSKCC), a 514-bed tertiary care cancer center with two bone marrow transplant (BMT) units with a combined 50 beds. In 2022, 23,751 patients were admitted to the study institution with 170,075 inpatient days and an average length of stay (LOS) of 7.2 days. Additionally in 2022, 507 hematopoietic stem cell transplant (HCT) and 173 chimeric antigen receptor T-cell (CAR-T) treatments were performed at MSKCC. In total, 57% of beds at the study institution are double occupancy. Patients who are not in protective isolation after transplant or transmission-based precautions are eligible to be roomed in with another patient.

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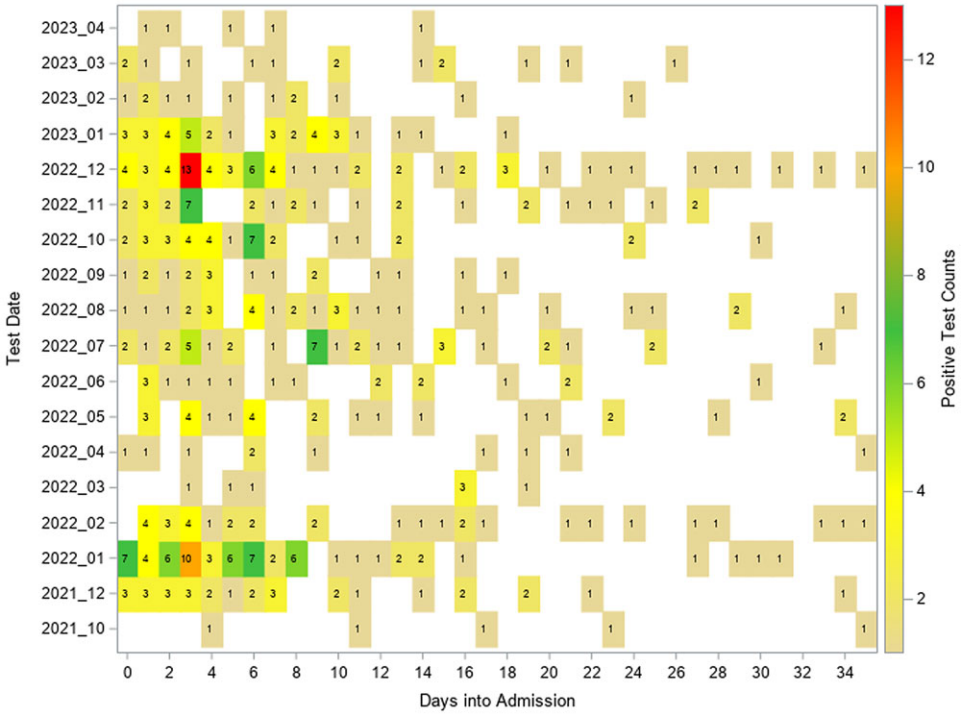

Figure 1. Heat map showing the frequency of hospital-onset SARS-CoV-2 cases by month throughout the study period (October 2021–April 2023).

SARS-CoV-2 reverse transcription polymerase chain reaction testing of asymptomatic hospitalized patients

Since April 2020, all hospital admitted patients were tested for SARS-CoV-2. Those with an initial negative test were routinely retested every 3 days throughout their hospital stay. This testing was performed on nasopharyngeal swabs. Patients with a known history of COVID-19 within the preceding 120 days of admission were excluded from testing based on electronic medical record-based logic that was anchored either on a positive test done at the study institution or an electronic record of a self-reported infection. Clinical false positives were adjudicated by an independent review conducted by an infection preventionist and a hospital epidemiologist based on one or more of the following criteria (1) screening tests with initial sample cycle threshold (Ct) values >30, (2) results of non-concordant repeat testing, and (3) lack of clinically compatible history and symptoms. Only the first threshold cycle was used to graphically depict the differences between true and false clinical positives.

Exposed roommates of a positive case were placed on droplet precautions until 14 days from the last exposure. To calculate the number of infections prevented by this approach, we multiplied the lowest number of roommates of index cases with the observed secondary attack rate.

All healthcare personnel and visitors followed universal masking in all clinical locations throughout the study period. Patients who test COVID-19 positive are placed in airborne contact precautions. Cohorting of positive patients is not done at the study institution.

Laboratory methods

SARS-CoV-2 RNA was detected using two commercially available EUA tests, the TaqPath COVID-19 Combo Kit (Thermo Fisher Scientific) and the Roche Cobas SARS-CoV-2 test. The TaqPath test targets the N, S, and ORF genes. The Cobas test targets the E and the ORF a/b gene. Samples were reported as positive, negative, or presumptive per manufacturers' instructions.[7,8] The Ct value for each positive sample was retrieved from the instrument record. Ct values by groups are reported as means with standard deviation. Means between groups were compared using a two-tailed t-test.

MSKCC's Institutional Review Board reviewed the study and granted a Health Insurance Portability and Accountability Act waiver of authorization.

Results

During the 18-month study period from October 1, 2021, to April 30, 2023, 56,338 post-admission surveillance tests from 15,048 hospitalized patients detected 282 new infections. Of these 282 new infections, 37 (13%) were deemed to be clinical false positives per criteria defined in the methods section. The overall yield on post-admission tests was 1.6%. The frequency distribution of positive surveillance tests correlated with SARS-CoV-2 community incidence and was highest during the winter months in both study years. The number of hospital-onset infections by month and the time to the first positive test from admission is shown in Figure 1. Only 14% of patients were symptomatic with COVID-19 at the time of first detection. For the clinical false positive test results, Ct values are shown in Figure 2.

Hospital-onset infections in patients housed in shared rooms led to 201 roommate exposures (median exposed per index: 1, range 1–4), and 46 (22.8%) among these developed a secondary infection. The secondary cases ranged in severity: 14 (30%) were asymptomatic (never developing symptoms), 25 (54%) were mildly symptomatic without any supplemental oxygen requirement, and 7 (15%) were moderately ill with low oxygen requirement via nasal cannula for at least 24 hours with or without lower tract involvement on chest imaging. Notably, none of the secondary infections were severe (ie, requiring high flow nasal cannula), or critically ill (ie, requiring intubation due to respiratory failure). Based on the observed secondary attack rate of

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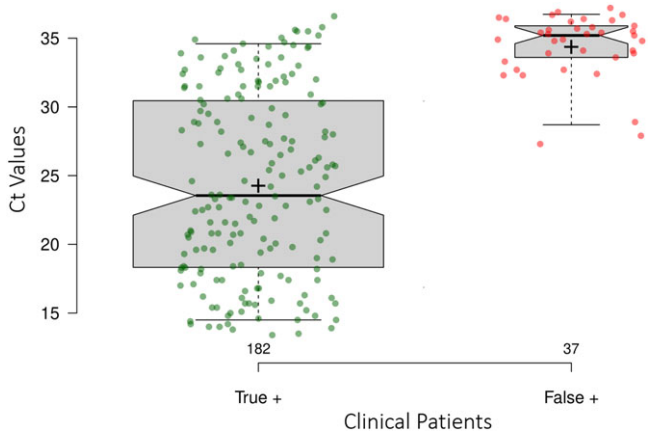

Figure 2. Polymerase chain reaction cycle threshold (Ct) value for clinically confirmed hospital-onset infections: true positive (True +) and false positive (False +) cases.

22.8%, early identification and quarantine of the 46 exposed roommates who subsequently developed COVID-19 is estimated to have prevented 10 additional cases of COVID-19.

Discussion

Our study on serial SARS-CoV-2 testing of hospitalized patients in a high-risk environment showed low overall yield (1.6%) with clustering towards the early part of the hospital stay and general low detection of nosocomial infections. Among all SARS-CoV-2 lab detections on AST, 13% were clinically false positives. Although we saw high secondary infection rates from unrecognized cases, the resulting condition was mild to moderate throughout the study, with no intensive care unit admissions or deaths. Taken together, the findings from the present study demonstrate the low utility of post-admission AST in high-risk environments from both a transmission and outcome standpoint. However, with the consistently high secondary transmission rates after in-room exposure, we believe that targeted AST in the event of exposure to a newly infected person is a reasonable step to break chains of transmission in shared environments. Additionally, there is value in the AST of patients and healthcare personnel for case finding during an outbreak.[9] Our study demonstrates the potential downsides of broad testing with the frequent occurrence of clinical false positive results, which in an oncology setting, often leads to delays in essential treatments and transplants, cause undue patient stress, and increased costs.[10]

Our study has several limitations. First, we may have underestimated hospital-acquired infections that manifested after discharge. Second, the study findings should be interpreted in the context of facility layout, the proportion of shared rooms, community risks, local masking practices, and high-risk populations. Finally, our study focuses exclusively on the utility of post-admission testing in a high-risk setting—a less widely adopted practice than admission screening only. Despite this, our study provides valuable evidence to support de-escalation of testing in similar settings with high-risk patients in a shared environment or in hospitals that decide to maintain AST practices in their oncology units. Furthermore, it can be considered for future planning and preparedness for a shift in SARS-CoV-2 epidemiology or other threats.

In summary, post-admission serial testing in a high-risk setting for early detection of COVID-19 cases is a low-yield strategy that has rendered minimal clinical benefit in the Omicron era and poses substantial challenges with several unfavorable effects. Serial testing should no longer be routinely applied in high-risk settings, shared-occupancy hospital environments, or during high SARS-CoV-2 community transmission.

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Competing interests. M.K. has acted as a consultant for Regeneron and has received speaker fees for WebMD/Medscape and MJH Life Sciences.

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