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Utilization of rapid antigen assays for detection of severe acute respiratory coronavirus virus 2 (SARS-CoV-2) in a low-incidence setting in emergency department triage: Does risk-stratification still matter?

Liang En Wee MRCP¹ , Edwin Philip Conceicao BSc², Jean Xiang-Ying Sim MRCP^{1,2}, Indumathi Venkatachalam MRCP^{1,2}, Paul Weng Wan MMed³, Nur Diana Zakaria MCEM³, Kenneth Boon-Kiat Tan MCEM³ and Limin Wijaya MRCP¹

¹Department of Infectious Diseases, Singapore General Hospital, Singapore, ²Department of Infection Prevention and Epidemiology, Singapore General Hospital, Singapore and ³Department of Emergency Medicine, Singapore General Hospital, Singapore

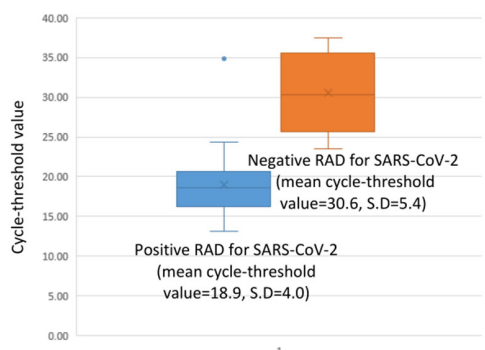
To the Editor—We read with interest the article by Smith *et al*¹ describing the use of rapid antigen detection (RAD) for severe acute respiratory coronavirus virus 2 (SARS-CoV-2) in guiding hospital admission triage. Given the rapid turnaround of point-of-care testing, various studies have utilized RAD tests at the point of entry into the healthcare system.^{1–4} However, most of these studies have occurred during periods of heightened transmission, with detection rates of 5%–21%.^{1–4} RAD testing in clinical scenarios with lower incidence, such as asymptomatic individuals, may potentially result in low detection rates with high false-positive rates.⁵ False-positive RAD tests have resulted in SARS-CoV-2–negative patients being admitted to coronavirus disease 2019 (COVID-19) cohort wards, with subsequent nosocomial transmission.² Conversely, given broad variations in potential infectivity among individuals with false-negative RAD tests,⁴ negative RAD tests need to be interpreted cautiously, especially in the context of significant contact history or clinical syndromes compatible with COVID-19. We describe our institution's experience with the implementation of RAD testing for SARS-CoV-2 to guide

admission triage in a low-incidence setting. RAD testing was utilized in tandem with pre-existing triage strategies that stratified admissions according to epidemiological risk and clinical syndromes,⁶ which allowed a comparison of these approaches.

In Singapore, a Southeast Asian city-state, hospitals instituted admission triage strategies early on to segregate patients presenting with clinical syndromes compatible with COVID-19.⁶ At our institution, the largest hospital campus in Singapore, patients with epidemiological risk were admitted directly to the isolation ward; patients without epidemiological risk who presented with clinical syndromes compatible with COVID-19 were isolated in modified cohort cubicles with reduced bed density in the “respiratory surveillance ward (RSW)” until SARS-CoV-2 was excluded by polymerase chain reaction (PCR) testing.⁶ During the first wave of COVID-19 from January to June 2020, these admission triage strategies were extremely successful in correctly placing suspected COVID-19 cases. Although $\geq 1,500$ cases of COVID-19 were managed in our institution, $< 5\%$ of cases were admitted outside isolation areas.⁷ However, with the emergence of more transmissible variant strains, a second wave of COVID-19 began at the end of April 2021, providing the impetus for universal screening of inpatients via PCR testing of respiratory samples on admission and every 7 days subsequently. On June 27, 2021, our institution began utilizing RAD testing to screen all admissions for SARS-CoV-2. Thereafter, patients with a positive RAD result were transferred

Author for correspondence: Dr Wee Liang En, The Academia, 20 College Road, Singapore 169856. E-mail: ian.wee.le@singhealth.com.sg

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Data derived from all patients with concurrent RAD and PCR tests for SARS-CoV-2 from 24/5/21-8/8/21

Fig. 1. Cycle-threshold value on polymerase-chain-reaction (PCR) testing for SARS-CoV-2 E-gene of PCR-confirmed COVID-19 cases, stratified by rapid-antigen-detection (RAD) result.

to isolation areas in the emergency department and then admitted to negative-pressure single rooms for confirmatory PCR testing. Patients with negative antigen tests were still risk-stratified for admission to isolation areas based on epidemiological risk and clinical syndromes. Our institution utilized the Veritor SARS-CoV-2 antigen rapid test kit (Becton Dickinson, Franklin Lakes, NJ), with a positive percentage agreement of $\geq 80\%$ and a negative percentage agreement of 99.5% compared to PCR testing.⁸

Over a 6-week study period from June 27, 2021, to August 8, 2021, 6,665 admissions were systematically tested for SARS-CoV-2 with RAD tests and PCR. Moreover, 40 patients tested positive for SARS-CoV-2 by RAD; among them, 29 tested positive by PCR, with a mean cycle-threshold value for SARS-CoV-2 E-gene of 18.9 (Fig. 1). Two patients who tested negative for SARS-CoV-2 by RAD subsequently tested positive by PCR; however, they were admitted initially to isolation due to epidemiological risk. The sensitivity of RAD was 93.6% (95% CI, 78.6%–99.2%), with specificity of 99.8% (95% CI, 99.7%–99.9%). The positive predictive value of RAD was 72.5% (95% CI, 59.2%–82.7%), and the negative predictive value was 99.9% (95% CI, 99.8%–99.9%). Over the same period, 812 (12.2%) of 6,665 admissions fulfilled epidemiological criteria and/or presented with a clinical syndrome compatible with COVID-19, and these patients were initially admitted to isolation areas while awaiting the results of PCR testing; 29 (3.6%) of these 812 patients subsequently tested positive. The sensitivity of combined epidemiological and clinical criteria was 93.6% (95% CI, 78.6%–99.2%), with a specificity of 88.2% (95% CI, 87.4%–88.9%). The positive predictive value of epidemiological and clinical criteria was 3.6% (95% CI, 3.2%–4.0%), while the negative predictive value was 99.9% (95% CI, 99.8%–99.9%). Two asymptomatic patients with no known epidemiological risk tested positive for SARS-CoV-2; 1 patient was admitted to isolation due to a positive RAD test. The sole case of COVID-19 admitted outside isolation occurred in an asymptomatic patient with no known epidemiological risk, for whom RAD testing was not performed due to previous nasal surgery.

Before the implementation of RAD testing, COVID-19 cases detected outside the isolation ward over a 6-month period (January–June 2020) spent an average of 16.5 hours (N = 32; SD, 9.76) from admission to isolation, with an average of 2.1 (SD, 3.25) inpatient close contacts identified for each index case.^{7,9} Of 68 inpatient close contacts identified, 1 patient subsequently tested positive within the incubation period.^{7,9} In contrast, after

introduction of RAD testing, COVID-19 cases initially detected on RAD testing spent an average of 0.2 hours (N = 29; SD, 0.68) from admission to isolation (mean difference, -16.3 ; 95% CI, -19.9 to -12.7 ; $P < .001$), with an average of 0.3 (SD, 0.84) inpatient close contacts identified for each index case (mean difference, -1.8 ; 95% CI, -3.5 to -0.06 ; $P = .004$). Of 8 inpatient close contacts identified, none tested positive subsequently. No nosocomial COVID-19 clusters were detected among staff or by inpatient universal surveillance during the study period.

In conclusion, RAD testing for SARS-CoV-2 as part of an admission-triage strategy demonstrated high sensitivity and specificity, even in a low-incidence setting. Although a triage strategy based on epidemiological risk and clinical syndrome was resource-intensive, the potential for false-negative RAD tests and the possibility that patients with epidemiological risk could still be incubating at point of admission meant that RAD testing could not be used alone for isolation triage. The introduction of RAD testing substantially reduced potential exposure, in terms of both time to isolation and number of exposed inpatients. A robust admission triage strategy based on epidemiological risk and clinical syndrome, supported by an expansion of hospital isolation facilities¹⁰ and RAD testing for earlier isolation of positive cases, successfully limited nosocomial exposures.

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Frequent detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA on hands and skin of patients with coronavirus disease 2019 (COVID-19)

Sarah N. Redmond MD¹, Daniel F. Li MD^{1,2}, Muhammed F. Haq MD², Lucas D. Jones BS³, Alexandria M. Nguyen MSHS⁴, Margaret Tiktin DNP⁴, Jennifer L. Cadnum BS³, Maria E. Navas MD⁵, Jessica Bingham RN⁶, Brigid M. Wilson PhD⁷ and Curtis J. Donskey MD^{1,7}

¹Case Western Reserve University School of Medicine, Cleveland, Ohio, ²Research Service, Louis Stokes Cleveland VA Medical Center, Cleveland, Ohio,

³Department of Molecular Biology and Microbiology, Case Western Reserve University School of Medicine, Cleveland, Ohio, ⁴Clinical Research Center, Louis

Stokes Cleveland VA Medical Center, Cleveland, Ohio, ⁵Pathology and Laboratory Medicine Services, Louis Stokes Cleveland VA Medical Center, Cleveland, Ohio,

⁶Nursing Service, Louis Stokes Cleveland VA Medical Center, Cleveland, Ohio and ⁷Geriatric Research, Education, and Clinical Center, Louis Stokes Cleveland VA Medical Center, Cleveland, Ohio

To the Editor—Hand hygiene is a core measure recommended for prevention of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission.^{1,2} Hand hygiene is needed to eliminate SARS-CoV-2 acquired on hands during contact with infected patients or contaminated surfaces and fomites, including personal protective equipment.^{1–3} In an in vitro model, SARS-CoV-2 inoculated onto human skin survived for 9 hours after inoculation versus 2 hours for influenza A.⁴ SARS-CoV-2 was rapidly inactivated on skin by 80% ethanol.⁴

Hand hygiene may also be beneficial in reducing the burden of SARS-CoV-2 on the hands of individuals with coronavirus disease 2019 (COVID-19), and bathing may reduce SARS-CoV-2 on other skin sites. However, the burden of SARS-CoV-2 on hands and other skin sites of COVID-19 patients is unknown. Here, we tested the hypothesis that SARS-CoV-2 RNA is frequently present on the hands and the chest/abdomen of patients with COVID-19, particularly those with a high viral burden in samples collected from the anterior nares.

The study protocol was approved by the Cleveland VA Medical Center's Institutional Review Board. Between November 1, 2020, and April 26, 2021, a convenience sample of patients with symptomatic COVID-19 was enrolled. Patients were excluded if they had dementia or delirium, were admitted to the intensive care unit, and if >3 days had passed since their COVID-19 diagnosis.

Premoistened CLASSIQswabs with universal transport medium (Copan Diagnostics, Murrieta, CA) were used to collect samples from the anterior nares, oropharynx, chest/abdomen (10×10-cm surface area), and the entire surface area of both hands. Swabs were also used to sample environmental surfaces in patient rooms, including 5×20-cm areas of the bed rail and bedside table; outpatients sampled a frequently used chair and tabletop. A medical record

review was conducted to obtain information on age, sex, medical conditions, and COVID-19 treatments.

A detailed description of the methods for RNA extraction and reverse transcriptase quantitative polymerase chain reaction (RT-qPCR) is included as Supplementary Material (online). The Fisher exact test was used to compare the proportions of COVID-19 patients with positive chest/abdomen or hand SARS-CoV-2 RNA for those with anterior nares cycle threshold (C_t) values of ≤ 30 or >30 . The cycle threshold cutoff of 30 was chosen based on evidence that individuals with higher nasopharyngeal swab C_t values are less likely to have a positive cultures or to transmit SARS-CoV-2 to contacts.⁵ Analyses were performed using R version 3.5.1 statistical software (R Foundation for Statistical Computing, Vienna, Austria).

For the 16 study participants, the mean age was 60.8 years; 13 (81.3%) were male; 9 (56.3%) were receiving dexamethasone and supplemental oxygen at the time of enrollment; and 2 (12.5%) were outpatients. The anterior nares RT-qPCR result was positive for SARS-CoV-2 in all participants with an average C_t value of 29.2 (range, 18.2–40). Figure 1A shows the percentage of other sites with positive RT-qPCR results for SARS-CoV-2 RNA, stratified by anterior nares C_t value ≤ 30 or >30 . Of the 16 participants, the oropharynx, chest/abdomen, hand, and environmental samples were positive for SARS-CoV-2 RNA in 15 (93.8%), 7 (43.8%), 7 (43.8%), and 3 (18.8%) patients, respectively. All 7 patients with SARS-CoV-2 RNA on hands also had positive chest/abdomen samples. The percentage of chest/abdomen and hand samples that were positive was significantly higher in patients with anterior nares C_t values of ≤ 30 versus >30 : 6 (75%) of 8 versus 1 (12.5%) of 8 ($P = .04$).

Figure 1B shows a boxplot of the C_t values for SARS-CoV-2 RNA from all sites. Of the 7 patients with positive chest/abdomen RT-qPCR results for SARS-CoV-2, 1 patient (14.2%) had a chest/abdomen C_t value <30 and 3 patients (42.9%) had C_t values between 30 and 35. Of the 7 patients with positive hand RT-qPCR results for SARS-CoV-2, 3 patients (42.9%) had hand C_t values between 30 and 35. Only 1 (16.7%) of 6 positive

Author for correspondence: Curtis J. Donskey, E-mail: Curtis.Donskey@va.gov

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