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BRIEF REPORT

Assessment of Oropharyngeal Specimens for Discontinuation of Transmission-Based COVID-19 Precautions

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We compared oropharyngeal swab test performance with nasopharyngeal testing for discontinuation of transmission-based COVID-19 precautions. We performed a retrospective review of confirmed COVID-19-positive patients who received paired nasopharyngeal and oropharyngeal SARS-CoV-2 tests for clearance from isolation from May 4, 2020, to May 26, 2020. Using nasopharyngeal swabs as the reference standard, we calculated the sensitivity, specificity, and negative predictive value of oropharyngeal swabs. We also calculated the kappa between the 2 tests. A total of 189 paired samples were collected from 74 patients. Oropharyngeal swab sensitivity was 38%, specificity was 87%, and negative predictive value was 70%. The kappa was 0.25. Our study suggests that oropharyngeal swabs are inferior to nasopharyngeal swabs for test-based clearance from COVID-19 isolation.

Keywords.: COVID-19; coronavirus PCR; discharge strategies; oropharyngeal swabs; residential substance use treatment; transmission-based precautions.

According to the US Centers for Disease Control and Prevention (CDC), the decision to discontinue transmission-based novel coronavirus 2019 (COVID-19) precautions can be made using a symptom-based or time-based strategy except in rare situations [1]. The test-based strategy, which is limited in its utility due to prolonged viral shedding but can be considered for patients who are severely immunocompromised, entails all of the following: (1) resolution of fever without the use of fever-reducing medications, (2) improvement in respiratory symptoms, and (3) negative results of a US Food and Drug Administration (FDA)–approved COVID-19 molecular assay for detection of SARS-CoV-2 RNA from at least 2 consecutive respiratory specimens collected ≥24 hours apart. Alternatively, a symptom-based strategy entails that at least 24 hours have passed since recovery (defined as resolution of fever without the use of fever-reducing medications and improvement in symptoms) and that at least 10 days have passed since symptoms first appeared. The time-based approach is used in patients with laboratory-confirmed COVID-19 who have not had any symptoms. This strategy simply requires that 10 days have passed since the date of the patient's first positive COVID-19 diagnostic test. Until recent changes were made with preference for the symptom-based strategy, there had been limited guidance about the preferred "clearance" strategy for persons returning to congregate living situations such as those in nursing homes, residential substance use treatment facilities, and persons experiencing homelessness returning to shelters. Out of an abundance of caution, many congregate living situations have required or held strong preference for the test-based strategy, and by extrapolation, polymerase chain reaction (PCR) using nasopharyngeal (NP) swab collection, based on guidance for diagnostic testing [2, 3]. However, PCR testing during the COVID-19 crisis has been plagued by significant NP swab supply shortages. In addition, NP swabs are notable for their relative discomfort to patients during specimen collection. Both factors prompted interest in alternative specimens that might mitigate these disadvantages without compromising the clinical sensitivity of PCR by NP swab collection [4]. One alternative is the oropharyngeal (OP) swab. Compared with NP swabs, the accuracy of OP swabs for detecting SARS-CoV-2 RNA by PCR for diagnostic purposes has been less favorable [5], though at least 1 study demonstrates that OP swabs may be comparable [6]. Based on overall evidence to date, current guidance favors NP swab collection for routine diagnostic PCR testing [3]. However, data for the performance of OP swab collection for "clearance" test purposes are lacking. Given the NP swab limitations and the desirability of using the test-based strategy to discontinue transmission-based precautions in persons returning to congregate shelters, we sought to understand OP swab test performance compared with NP swab PCR testing for this purpose. We hypothesized that OP swabs would have similar accuracy to NP swabs for the purpose of utilizing them for a test-based clearance strategy for previously positive COVID-19 patients whose symptoms resolved.

METHODS

We performed a retrospective chart review of patients at the Boston Medical Center (BMC) COVID Recuperation Unit (CRU) who received paired NP and OP SARS-CoV-2 tests for clearance

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from isolation and discharge from May 4, 2020, through May 26, 2020. The CRU was a respite facility that opened on April 9, 2020, and provided non-acute-level care for persons experiencing homelessness who tested positive for COVID-19. On May 4, 2020, a protocol was instituted to collect paired NP and OP specimens on all patients at the CRU who were not considered "immunocompromised" or at high risk of prolonged viral shedding (test-based clearance was already required for these patients). Patients who were excluded from the paired specimen collection included (1) persons with HIV with CD4 <200, (2) solid organ and bone marrow transplant patients, (3) individuals on chronic steroids (≥20 mg for adults for at least 1 month), (4) individuals who received other significantly immunocompromising medications including biologics for treatment of COVID-19 or active chemotherapy, (5) individuals with hematologic malignancies or other severe immunodeficiency syndromes, (7) patients receiving hemodialysis, and (8) patients with prolonged intubation for acute respiratory distress syndrome due to COVID-19 or who received care in the intensive care unit.

NP and OP specimen collection was conducted in accordance with CDC guidelines [7]. Testing was performed at the BMC Clinical Laboratory using a reverse transcriptase polymerase chain reaction (RT-PCR) molecular assay (either the Roche Molecular Systems cobas SARS-CoV-2 test performed on the cobas 6800 instrument or the DiaSorin Simplexa COVID-19 Direct Kit) for detection of SARS-CoV-2 virus as allowed under the FDA Emergency Use Authorization (EUA). We used the nasopharyngeal swab as the "reference standard." Clinical decisions regarding discharge were based on the NP swab regardless of OP swab results, although both results were reported to the patient electronic medical record and were accessible to the clinical provider. When patients were eligible for either symptom-based or time-based discontinuation of precautions, NP and OP swabs were collected. If that NP test was positive for SARS-CoV-2, then the next set of specimens was collected 3 days later. If, however, the first NP test result was negative, then a second set of tests was collected at least 24 hours later. If the second NP test result was negative, then the patient was cleared from isolation and discharged. If the second NP test was positive, then the "clock reset" and a new set of swabs was collected 3 days later. The protocol was discontinued on May 26, 2020, and a switch was made to a predominately symptom-based approach given resource limitations.

We analyzed both the NP and OP specimen results to calculate percent positive agreement, overall concordance, and overall discordance. We assumed that the NP swab was the "reference standard" for detection of SARS-CoV-2 viral RNA. We calculated the positive and negative percent agreements (sensitivity and specificity) and negative predictive value of the OP test at the time of test-based clearance. We also calculated the unweighted kappa statistic as another measure of concordance. To do this, we included tests that were positive, negative, and indeterminate.

Patient Consent Statement

This study was reviewed by the Boston University Medical Campus Institutional Review Board and determined to be exempt.

RESULTS

Between May 4, 2020, and May 26, 2020, a total of 74 patients at the CRU had at least 1 paired NP and OP specimen collected. Patient demographics are outlined in Table 1. Fourteen patients received only 1 paired sample, 35 received 2 paired samples, 10 received 3 paired samples, 8 patients received 4, 2 received 5, 2 received 6, and 3 patients received 7 paired samples (Figure 1). A total of 189 paired samples were collected, and 43% of the dual tests had at least 1 positive result (NP or OP). Overall, 36% of the NP swabs and 7% of the OP swabs were positive. Of the paired samples, 121 (64%) were concordant (NP negative/OP negative = 95, NP positive/OP positive = 25, NP indeterminate/OP indeterminate = 1). Of the discordant tests, 40 (58%) were NP positive and OP negative and 13 (19%) were NP negative and OP positive, while at least 1 test was indeterminate in the remaining discordant samples (n = 15). The threshold cycle (Ct) values for positive NP swabs (when OP swab was negative) are included in Supplementary Table 1. If we exclude indeterminate tests and assume that NP is the "reference standard," then the OP test has a positive percent agreement (sensitivity)

Table 1. Patient Demographics for Those who Received Paired Nasopharyngeal and Oropharyngeal Swab for Test-Based Clearance From Isolation

Patient Characteristic	Value
Total patients	74
Age, mean (SD), y	51.7 (13.2)
Gender, No. (%)	
Male	47 (64)
Female	26 (35)
Unknown	1 (1)
Race/ethnicity, No. (%)	
Black/African American	23 (32)
Asian	1 (1)
Hispanic/Latinx	9 (13)
White	26 (36)
Other/unknown/declined to answer	13 (18)
Length of stay at CRU, median (IQR), d	11 (9–14)
Primary language, No. (%)	
English	61 (83)
Spanish	8 (11)
Amharic	1 (1)
Haitian Creole	2 (3)
American Sign Language	1 (1)
Unknown	1 (1)

Abbreviations: CRU, COVID Recuperation Unit; IQR, interquartile range.

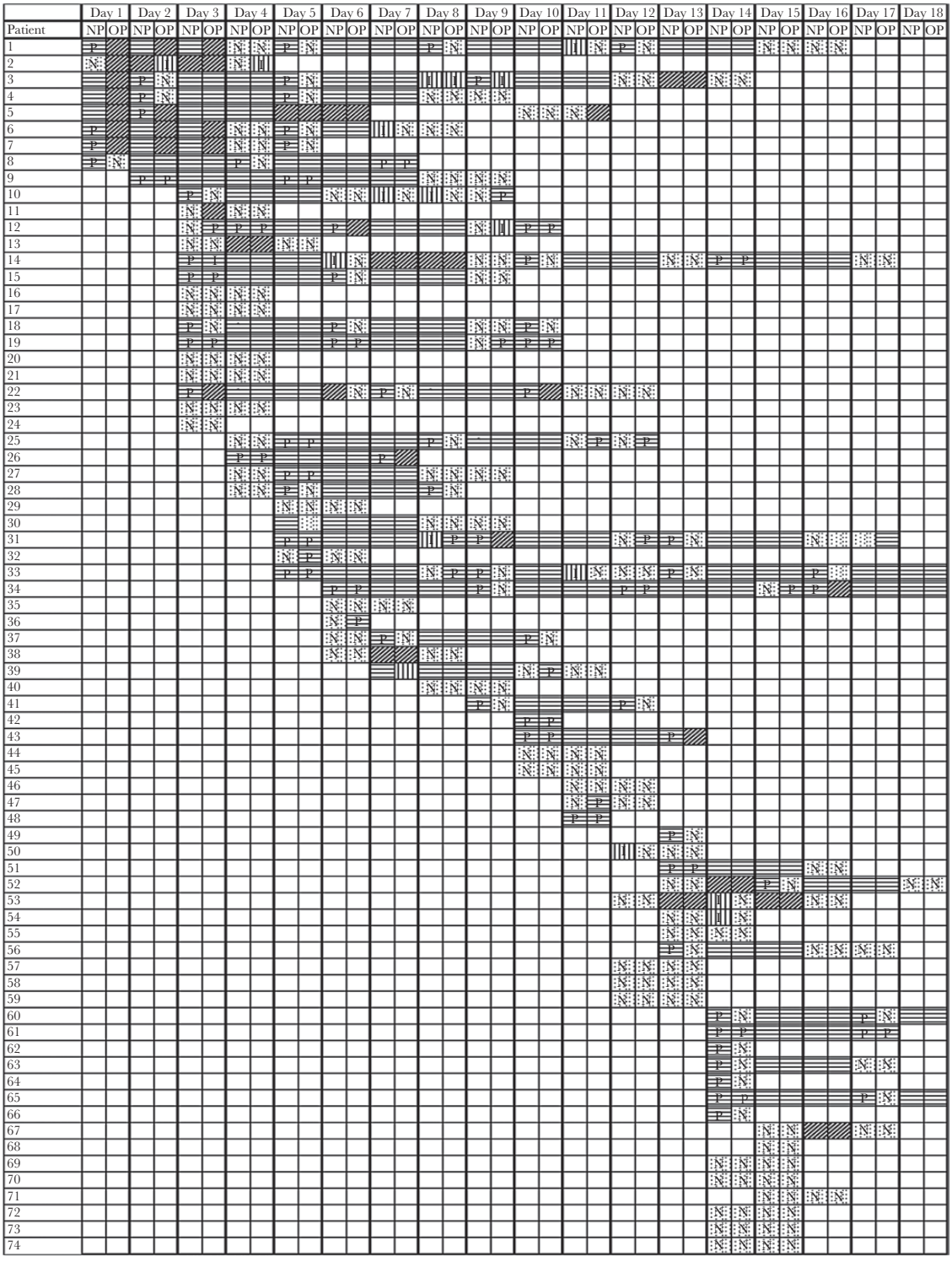

Figure 1. Results, by patient, of paired nasopharyngeal and oropharyngeal specimens for discharge from the COVID Recuperation Unit at Boston Medical Center. Results from the paired nasopharyngeal and oropharyngeal swabs by patient are depicted (row). The figure demonstrates days that the swabs were collected. Boxes with horizontal lines with the letter "P" indicate a positive test; boxes with dots with the letter "N" indicate a negative test; boxes with vertical lines with the letter "I" indicate an indeterminate test. Boxes with horizontal lines without the letter "P" indicate days when a person was not eligible for testing due to a positive nasopharyngeal test. Boxes with slanted lines indicate days that patients did not receive tests but were eligible. Largely, these were due to delayed test results. Each day at the top of the figure corresponded to a calendar day that the test was performed. Abbreviations: NP, nasopharyngeal; OP, oropharyngeal.

of 38% (25/[25 + 40]) and a negative percent agreement (specificity) of 87% (95/[95 + 13]) for detecting SARS-CoV-2 RNA when performed following symptom improvement or resolution (Figure 2). Furthermore, the OP test has a negative predictive value of 70% (95/[40 + 95]). The unweighted kappa (SE) was 0.25 (0.73), indicating only fair agreement between the 2 swabs.

DISCUSSION

We reviewed the results of 189 paired NP and OP SARS-CoV-2 obtained from 74 distinct patients for the purpose of attempting to validate the OP swab for test-based clearance by RT-PCR for SARS-CoV-2. We found that the OP swab used for this purpose had a low positive agreement (sensitivity) at 38% compared with NP swabs. Our results are consistent with other reports that have shown low rates of sensitivity in OP swabs when compared with concurrent NP swab collections for diagnostic testing [8]. Our findings are unique and add substantially to the literature for 2 reasons. First, the majority of previous reports assessed the utility of OP swabs for the diagnosis of COVID-19 infection. A recent systematic review and meta-analysis using combined data from 11 manuscripts demonstrated that overall sputum specimens had the highest rate of sample positivity for the diagnosis of COVID-19, while OP swabs had the lowest [8]. In contrast, our study focused on the use of OP swabs for discontinuation of transmission-based precautions for patients who were documented to be COVID-19 positive. In light of changing recommendations for clearance from isolation, our findings suggest that OP swabs are likely not adequate, particularly for those who are asymptomatic or have mild symptoms.

Second, we attempted to validate the use of OP swabs in a vulnerable population, persons experiencing homelessness, who were discharged to congregate settings. Local and state departments of health have 2 basic options for persons returning to congregate settings: either adopt a symptom-based or time-based approach or search for potential alternative methods for sampling respiratory secretions. The former approach is aligned with current CDC guidance and has been adopted by a number of departments of health. In the setting of expanding knowledge and emerging new data in an ever-changing epidemic, our findings suggest that OP swabs are not adequate should test-based clearance be adopted again, particularly for those who are asymptomatic or have mild symptoms. For patients who remain at high risk for infections who are returning to congregate settings and in the absence of a practical alternative to viral culture to determine transmissibility, dual or serial testing may be options. The alternate imperative is to utilize a comprehensive approach involving early detection through surveillance, rapid testing, contact tracing, and isolation.

One limitation to this study was the sample size. We estimated that ~355 paired samples would have needed to be collected to validate the OP swab for test-based clearance (aiming for 95% concordance). We were unable to reach that number due to resource constraints, but it is also clear from the sample size we achieved that the OP swab is clearly inferior to the NP swab for the purpose of test-based clearance. Second, the patient population was heterogeneous in that some patients experienced symptoms and others were asymptomatic throughout their disease course [9, 10]. The generalizability is also limited by the fact that patients who were immunocompromised, received biologic therapy, or were treated in the intensive care unit were not included. Furthermore, we did not assess the utility of the OP swab in patients who might have a higher viral load (eg, severely ill in need of intubation). Nevertheless, a majority of patients returning to congregate settings likely fit the profile of our patient population rather than those who were severely ill. Next, some of the discrepant NP and OP results may have been the result of inadequate sensitivity of the EUA assay. In theory, this could have produced more discrepant results than would have been seen if we had used a different test. This is a theoretical limitation and may not have affected the findings as several EUA PCRs have, to date, all been reported to be relatively similar in performance overall with regard to clinically meaningful sensitivity [11, 12]. Finally, the CRU was established on an emergency basis in the midst of the COVID-19 surge in Massachusetts to provide recuperation to persons experiencing homelessness who were COVID positive. Patients were admitted from a number of locations across the city, and documentation of symptoms, exact date of positive COVID-19 swab, and comorbid conditions were often incomplete. As such, we are unable to perform further analyses based on days after symptom onset or in relation to comorbid conditions.

In conclusion, our study suggests that OP swabs are inferior to NP swabs for molecular-based testing for clearance from COVID-19 isolation for known COVID-19-positive patients. Rapid development of alternative testing approaches for SARS-CoV-2 is needed given the ongoing pandemic.

OP swab	NP swab		
	Positive	Negative	Total
Positive	25	13	38
Negative	40	95	135
Total	65	108	173

* Excluded tests in which one or both were 'indeterminate'
Sensitivity = 25/(25+40) = 38%
Specificity = 95/(95+13) = 87%

Figure 2. Sum of the results of NP and OP swabs. Abbreviations: NP, nasopharyngeal; OP, oropharyngeal.

Supplementary Data

Supplementary materials are available at Open Forum Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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