EXPERT REVIEW OF MOLECULAR DIAGNOSTICS
https://doi.org/10.1080/14737159.2021.1944807

Taylor & Francis
Taylor & Francis Group

EDITORIAL

Molecular testing as a tool to combat the COVID-19 pandemic

Christina Liscynesky [a,b] and Joan-Miquel Balada-Llasat[c]

[a]Internal Medicine, Division of Infectious Diseases, Department of Internal Medicine, The Ohio State University Columbus, OH, USA; [b]Department of Clinical Epidemiology, Comprehensive Cancer Center, The Ohio State University, Columbus, OH, USA; [c]Clinical Pathology, Department of Pathology, The Ohio State University Columbus, OH, USA

ARTICLE HISTORY Received 1 March 2021; Accepted 15 June 2021

Our tools in fighting the coronavirus disease 2019 (COVID-19) pandemic were initially limited. The first step was identifying who was infected by the virus. New molecular testing was quickly created to diagnose disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Now with over a year's worth of experience, testing indications have changed and resources need to be considered.

At the beginning of the pandemic, data was lacking on molecular test types, where to swab and who should swab. All these unknown variables were compounded by testing turnaround time. Molecular diagnostic laboratories were quickly expanded because the demand and intense focus was placed on which test and specimen types to use. Laboratories had to expand testing in a very brief period of time, bringing on board new assays, either as laboratory developed or emergency use authorized assays where instrumentation and reagents were difficult to be acquired. Nasopharyngeal (NP) samples are standard of care for influenza testing. Extrapolating this knowledge, we initially instituted NP specimens as the only option for SARS-CoV-2 testing. Real life taught us the NP swabs can be harmful in fully anticoagulated patients, leading to the use of alternative specimen sites of combined anterior nares/oropharynx.

Current Infectious Disease Society of America (IDSA) Guidelines recommend a SARS-CoV-2 nucleic acid amplification test (NAAT) obtained from NP swab, mid-turbinate swab, anterior nasal swab, saliva or a combined anterior nasal/oropharyngeal swab in symptomatic individuals[1]. NP specimens must be obtained by a trained healthcare worker (HCW) and are briefly uncomfortable, leading to a patient reluctance for testing. In addition, SARS-CoV-2 NAAT are qualitative, not quantitative. Unfortunately, viral loads are not reported routinely, but clinicians have access to cycle thresholds (CT). CTs are not uniform and can vary upon specimen type and collection technique. Recently published data compared NP swabs versus oropharyngeal (OP) swabs for SARS-CoV-2 in patients with ≤ 7 days of symptoms and reported 95.2% concordance[2]. Specimens were tested using the Centers for Disease Control (CDC) reverse transcription–polymerase chain(RT-PCR) detecting three genetic markers: N1, N2, and N3 nucleocapsid gene regions. The median cycle thresholds were lower for NP swabs, 24.3 vs 29.9 for N1 and 25.0 vs 31.4 for N2. This data is one reason why IDSA does not recommend oral swabs alone.

The use of NP collection that may have higher viral load was the specimen of choice at our institution, but hesitance focused on the use of rapid transcription mediated amplification testing versus traditional RT-PCR, since these tests may show lower sensitivity. For this reason, our institution implemented the Abbott ID NOW COVID-19 assay only for inpatients that were symptomatic because the rapid turnaround time benefited patient care. In order to evaluate the Abbott ID NOW COVID-19 assay (NP collected in dry swab), we performed a performance comparison with the Simplexa COVID-19 Direct Kit (NP collected in viral transport media), if results were discrepant the laboratory developed CDC RT-PCR was used. The Abbott ID NOW COVID-19 showed a similar performance to the Simplexa COVID-19 Direct Kit. COVID-19 is indistinguishable from other respiratory viral syndromes by symptoms alone. Symptoms consistent with COVID-19 include cough, shortness of breath, fever, chills, fatigue, muscle pain, headache, sore throat, new loss of taste or smell, congestion, nausea, vomiting or diarrhea[3]. Anti-viral therapy cannot be prescribed until the diagnosis is confirmed via testing, hence the need for a rapid result.

Patients, especially those with medical comorbidities and advanced age (>70 years old), acutely infected with SARS-CoV-2 were quickly recognized as having a higher post-operative mortality after major surgical procedures. [4]. Due to this early data and expert opinion, all patients were screened pre-operatively for SARS-CoV-2. In December 2020, the American Society of Anesthesiologists released guidelines postponing all elective procedures for COVID positive patients based off their illness severity [5]. Patients who were asymptomatic or had mild, non-respiratory symptoms should wait 4 weeks, while a patient requiring care in the intensive care unit should be postponed 3 months. Interestingly, they lump together diabetics, immunocompromised and otherwise hospitalized patients together and suggest an 8 to 10 week waiting time. Prior to this guidance, elective surgery timing was based on discontinuation of isolation.

Early on in the United States, the CDC recommended 2 negative RT-PCRs prior to discontinuing isolation. RT-PCR positivity does not equate infectivity. We had anecdotal experience with this prior to COVID-19 in our chronic lymphocytic leukemic patients who would repeatedly test positive for Rhinovirus on respiratory viral PCR platform during consecutive hospital admissions. Patients persistently positive for SARS-CoV-2 were subject to continued

CONTACT Christina Liscynesky Christina.Liscynesky@osumc.edu Internal Medicine, Division of Infectious Diseases, Department of Internal Medicine, The Ohio State University Columbus, N1147 Doan Hall, 410 West 10th Avenue, Columbus, OH 43201, USA

isolation. We began utilizing CTs as a marker for infectivity, with higher numbers signifying lower viral loads, and thus discontinuing isolation. Data from South Korea demonstrated viable SARS-CoV-2 in viral culture in samples with a cycle-threshold value of 28.4 or less and up to 12 days post-symptom onset[6]. In addition, a meta-analysis, reported that no study detected viable SARS-CoV -2 beyond 9 days of symptoms, but mean duration of shedding was 17.0 days with a maximum duration of 83 days, further supporting RT-PCR positivity does not equate infectivity[7]. Immunocompromised hosts are an outlier to the above, with documented viable virus beyond 20 days, but CTs were not reported [8]. Reporting out actual SARS-CoV-2 viral loads, would negate all this extrapolation. Until that is available, we will continue to use CTs and symptoms to inform clinical judgment.

In addition to diagnosing illness, routine testing for SARS-CoV-2 has been used as a tool to relax social distancing, such as in professional sports, or as marker of safety to keep post-secondary institutions open. These surveillance programs are costly. For example, the American National Football League (NFL) invested 100 USD million dollars in mitigation measures, testing and contact tracing for the 2020 football season[9]. From 9 August 2020 to 21 November 2020, 623,000 RT-PCR tests were performed on 11,400 players and staff[10]. Three hundred and twenty nine infections with SARS-CoV-2 were laboratory confirmed. Never has the access to abundant, convenient, expedited testing proven to be such a luxury.

Professional sports are entertaining but not essential. In contrast, surgeries and cancer therapeutics cannot pause due to a global pandemic. Never before have patients been molecularly screened for a respiratory virus prior to therapeutic intervention. Screening is done both for patient outcome as well as to decrease HCW exposure. The immense resources that have been stood up to accomplish this are not sustainable. How do you transition this current testing model, with focus on the safety of both the HCW and patients, to a process that benefits the most vulnerable? The basic guiding principle should be that testing be performed to protect the patient.

Testing is a valuable resource that should be utilized to enhance patient outcomes. Quantitative results would ameliorate issues with shedding. As testing has been a major asset in our toolbox during the COVID-19 pandemic, we anticipate it will take center stage for future emerging infectious pathogens. When looking back over the last year, the diagnostic deployment and evolution is nothing less than amazing.

Declaration of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Reviewer disclosures

Peer reviewers on this manuscript have no relevant financial or other relationships to disclose

Funding

This paper was not funded.

ORCID

Christina Liscynesky http://orcid.org/0000-0003-3548-5653

References

1. Hanson KE, Caliendo AM, Arias CA, et al. The infectious diseases society of America guidelines on the diagnosis of COVID-19: molecular diagnostic testing [published online ahead of print, 2021 Jan 22]. Clin Infect Dis. 2021;ciab048. DOI:10.1093/cid/ciab048.
2. Patel MR, Carroll D, Ussery E, et al. Performance of oropharyngeal swab testing compared with nasopharyngeal swab testing for diagnosis of coronavirus disease 2019-United States, January 2020-February 2020. Clin Infect Dis. 2021;72(3):403–410. doi:10.1093/cid/ciaa759
3. Centers for Disease Control and Prevention. Symptoms of Coronavirus. [cited 2021 Feb 15]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html
4. COVIDSurg Collaborative. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study [published correction appears in Lancet. 2020 Jun 9;:]. Lancet. 2020;396(10243): 27–38. doi:10.1016/S0140-6736(20)31182-X
5. American society of anesthesiologists and anesthesia patient safety foundation joint statement on elective surgery and anesthesia for patients after COVID-19 infection. American Society of Anesthesiologists and Anesthesia Patient Safety Foundation Joint Statement on Elective Surgery and Anesthesia for Patients after COVID-19 Infection - Anesthesia Patient Safety Foundation (apsf.org); 2020 Dec 8.
6. Kim MC, Cui C, Shin KR, et al. Duration of culturable SARS-CoV-2 in hospitalized patients with Covid-19. N Engl J Med. 2021;384 (7):671–673. doi:10.1056/NEJMc2027040
7. Cevik M, Tate M, Lloyd O, et al. SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis. Lancet Microbe. 2021;2(1):e13–e22. doi:10.1016/S2666-5247(20)30172-5
8. Aydillo T, Gonzalez-Reiche AS, Aslam S, et al. Shedding of viable SARS-CoV-2 after immunosuppressive therapy for cancer. N Engl J Med. 2020;383(26):2586–2588. doi:10.1056/NEJMc2031670
9. Seifert K. How how the NFL navigated COVID-19 this season: 959,860 tests, $100 million and zero cancellations. https://www.espn.com/nfl/story/_/id/30781978/how-nfl-navigated-covid-19-season-959860-tests-100-million-zero-cancellations
10. Mack CD, Wasserman EB, Perrine CG, et al. Implementation and evolution of mitigation measures, testing, and contact tracing in the national football league, August 9-November 21, 2020. MMWR Morb Mortal Wkly Rep. 2021;70(4):130–135. doi:10.15585/mmwr.mm7004e2