Preprocedural COVID-19 screening: Do rhinologic patients carry a unique risk burden for false-negative results?

The most prevalent method for severe acute respiratory syndrome–coronavirus-2 (SARS-CoV-2) testing is based on reverse transcriptase–polymerase chain reaction (RT-PCR) for the presence of viral RNA. With more established testing protocols, evidence has emerged that accurate results are predicated on the 3 principle concepts of proper timing, proper site, and proper sample acquisition. There are multiple factors that bear on test interpretation and account for geotemporal differences in prevalence such as the negative predictive value and false omission rate. However, within the health-care setting and against the background of a virus with no reliable treatment or vaccine, the false-negative rate represents one of the most important metrics. This results from the fact that failure to identify a coronavirus-2019 (COVID-19)–positive patient could result in inadvertent spread to both the health-care team and other vulnerable patients.[1] From the perspective of proper timing, a recent meta-analysis[2] confirmed that the highest risk for a false-negative result occurs in the presymptomatic period up to 4 days before symptom onset. With regard to proper site, several studies, including one with 353 patients, confirmed that the nasopharynx is the optimal sampling location relative to the nasal cavity and oropharynx.[3,4] This is consistent with earlier data demonstrating high viral loads within the nasopharynx in both symptomatic and asymptomatic patients.[5] Finally, with respect to proper sampling, adequate viral material must be obtained to be amplified and subsequently detected by RT-PCR. Consequently, the US Centers for Disease Control and Prevention recommends use of flocked swabs over calcium alginate swabs[6] because, along with having other advantages, flocked swabs improve sample yield through increased surface area within the multilength (ie, "flocked") swab fibers.

In light of recent evidence regarding the aerosolization risk during both clinical and surgical rhinologic procedures,[7,8] multiple societal guidelines[9-11] have endorsed use of various levels of high-level personal protective equipment (PPE) (eg, N95 respirators, gown, and eye protection), source control, and environmental controls, such as adequate room air changes per hour after these potential aerosol-generating procedures. Given the ongoing scarcity of PPE and the potential for subsequent infectious waves, some institutions have explored a strategy of preprocedural COVID-19 screening tests with the presumption that a negative test would enable preservation of provider PPE and ameliorate the burden of source/environmental controls. However, this tactic may be hazardous as the rhinologic patient population poses unique challenges to all 3 tenets of effective RT-PCR–based testing. These patients may therefore assume a distinct excess false-negative risk as a consequence of the very sinonasal disorders for which they are seeking care.

Assuming that preprocedural testing was coupled with symptom screening, we may assume that the patients proceeding to sampling would largely be asymptomatic. According to a meta-analysis by Kucirka et al,[2] this would therefore *a priori* bias the population toward sampling during the worst-performing timing window, where the presymptomatic median false-negative rate is at least 3-fold higher than in the symptomatic population. Rhinologic patients further carry an array of diagnoses that have the potential to obstruct access to the optimal sampling site within the nasopharynx. These include baseline structural issues such as a deviated septum, turbinate hypertrophy, and concha bullosa; inflammatory conditions, including nasal polyps and antro/sphenochoanal polyps; and neoplastic disease, such as sinonasal and skull base tumors. As screening testing could occur before endoscopy and/or imaging in many cases, these factors may not be known at the time of testing and could not be accounted for by sampling technique. This limitation of access to the proper sampling site may have contributed our own recent experience of a false-negative result in a patient with severe chronic rhinosinusitis with nasal polyps. In this case, the patient presented with large nasal polyps obstructing the nasopharynx (Fig. 1A) and underwent preoperative RT-PCR–based testing 48 hours before the operation. After the polyps were resected, it became clear that the nasopharynx could not have been sampled correctly and a thorough swab of the nasopharynx was obtained during the operation. Before termination of the case, the staff was notified by the laboratory that the swab was positive for SARS-CoV-2, which prompted closure of the operating room. Because the use of N95 respirators was not required in the setting of a negative preoperative screen, all health-care workers

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Potential conflicts of interest: B.S.B.: consultant for Olympus, Medtronic, Karl Storz, Sinopsys, Baxter, and 3D Matrix; consultant and royalties from Theime. He holds patents for "Treatment of Sinusitis Through Modulation of Cell Membrane Pumps" (nonprovisional US Patent [USP] assigned to Massachusetts Ear and Eye Infirmary), "Inhibition of Cystatins for the Treatment of Chronic Rhinosinusitis" (nonprovisional USP), and "Methods of Delivery Pharmaceutical Agents" (USP 13/561,998). B.S.B. is also working with industry to develop source control solutions for endoscopic procedures, which may include an equity position in the future. K.C.W. has consultant relationships with Baxter, Acclarent, and Optinose.

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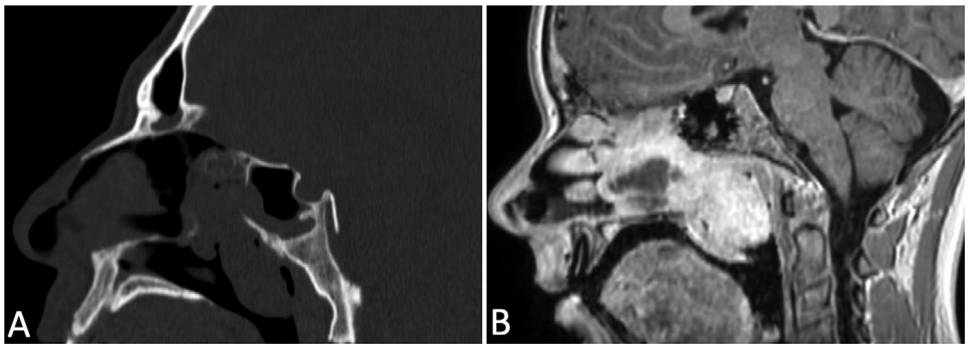

FIGURE 1. Examples of rhinologic patients at risk for false-negative RT-PCR testing. (A) Sagittal CT scan of a patient with false-negative preprocedural COVID-19 testing due to severe chronic rhinosinusitis with nasal polyps and positive intraoperative positive testing after endoscopic-guided nasopharyngeal swab. (B) T1 contrast–enhanced sagittal MRI scan of a patient with juvenile nasopharyngeal angiofibroma and nasopharyngeal obstruction who had epistaxis after COVID-19 screening. COVID-19 = coronavirus-2019; CT = computed tomography; MRI = magnetic resonance imaging; RT-PCR = reverse transcriptase–polymerase chain reaction.

who were wearing traditional surgical masks had to report to Corporate Health, undergo a 2-week period of symptom questionnaires, and required to have RT-PCR testing 5 to 7 days after the exposure. Of note, these rhinology-related pathologies may not only obstruct the nasopharynx but also increase the risk to the patient during sampling. For example, patients with vascular lesions (Fig. 1B) may be at higher risk for postsampling epistaxis. Furthermore, blind nasopharyngeal swabbing of postoperative patients with a patent sphenoid sinus and/or dissected skull base could risk injury to these exposed structures, and at least 1 post-swab cerebrospinal fluid leak has been anecdotally reported in an ear-nose-throat–related blog post, although it was not verified.

Even with optimized timing and site of collection, sample acquisition faces additional challenges in this patient population. As previously noted, sample yields are facilitated by swab designs that improve absorption and eventual release of viral material. Relative to patients without sinonasal disease, rhinologic patients are more likely to have an increased volume and viscosity of mucus within the nasal cavity resulting from an array of possible conditions, including allergy, eosinophilic inflammation, and neutrophilic infection.[12] Regardless of the primary etiology, these secretions have the potential to saturate the swab as it is advanced toward the nasopharynx, effectively displacing the intended sample with more proximal material.

These common issues faced by patients with rhinologic disease conspire to increase the potential false-negative rate at all 3 points of failure related to RT-PCR testing. This phenomenon is a function of the idiosyncratic challenges to proper sample timing, site, and acquisition associated with sinonasal disease. These latter 2 concepts have been specifically validated in the sinonasal cavity as endoscopic guidance, and guarding of flocked swabs has become the preferred method of obtaining site-specific rRNA samples for microbiome sequencing.[13] Currently, nasopharyngeal RT-PCR testing for SARS-CoV-2 may be helpful to exclude positive patients; however, a negative result should be viewed with caution when making decisions to supplant source/environmental controls and provider PPE.

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