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Concise Communication

The utility of paired upper and lower respiratory tract sampling for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) testing in patients with artificial airways

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Abstract

Early in the coronavirus disease 2019 (COVID-19) pandemic, the CDC recommended collection of a lower respiratory tract (LRT) specimen for severe acute respiratory coronavirus virus 2 (SARS-CoV-2) testing in addition to the routinely recommended upper respiratory tract (URT) testing in mechanically ventilated patients. Significant operational challenges were noted at our institution using this approach. In this report, we describe our experience with routine collection of paired URT and LRT sample testing. Our results revealed a high concordance between the 2 sources, and that all children tested for SARS-CoV-2 were appropriately diagnosed with URT testing alone. There was no added benefit to LRT testing. Based on these findings, our institutional approach was therefore adjusted to sample the URT alone for most patients, with LRT sampling reserved for patients with ongoing clinical suspicion for SARS-CoV-2 after a negative URT test.

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The Centers for Disease Control and Prevention (CDC) recommends upper respiratory tract (URT) polymerase chain reaction (PCR) testing for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) as the initial diagnostic test for coronavirus disease 2019 (COVID-19).[1] In April 2020, at the time this work was undertaken, lower respiratory tract (LRT) testing was also recommended for patients requiring mechanical ventilation.[1] Given the potential for discordant results and uncertainty surrounding the optimal approach early in the pandemic, our institution elected to recommend paired sampling from both the URT and LRT for all mechanically ventilated patients.

However, this recommendation resulted in an unintended consequence of significantly disrupted clinical workflows. These included uncertainties surrounding timing of initiation and discontinuation of isolation precautions when 1 of the 2 tests were pending and/or were not performed and the need to have skilled personnel capable of performing LRT sampling in outpatient, drive-through testing sites. As part of our ongoing operational work evaluating these workflows and to re-evaluate our testing strategy considering these unintended consequences, we compared concordance between paired URT and LRT specimens in children undergoing SARS-CoV-2 testing at our institution.

Methods

This descriptive analysis included a convenience sample of all children with artificial airways who had paired URT and LRT SARS-CoV-2 PCR testing performed between April 1, 2020, and July 8, 2020. SARS-CoV-2 testing was performed universally on admission and prior to any procedure involving an aerosol-generating procedure (AGP) throughout this time. Artificial airways included a tracheostomy or endotracheal tube. URT specimens included nasopharyngeal (NP) swabs and aspirates. LRT specimens included tracheal aspirates and bronchoalveolar lavages. URT and LRT specimens were classified as paired if the 2 specimens were collected within 24 hours. We excluded additional pairs performed within 72 hours of the index pair because these would represent duplicative information. Tests were classified as diagnostic versus screening based on the testing indication selected in the order and confirmed through medical record review performed by 3 investigators (E.K., K.C., and K.O'C.). During the study period, 2 RT-PCR tests were performed: a locally developed assay and the XPERT XPRESS SARS-CoV-2 test (Cepheid, Sunnyvale, CA). The maximum cycle threshold required for a positive result in both of these tests is 40. Statistical analyses were limited to descriptive statistics, with categorical variables summarized by number and

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Table 1. All Valid Paired Upper Respiratory Tract and Lower Respiratory Tract Samples (N = 126 pairs)

		Upper Respiratory Tract				
		Negative		Positive		Total
Lower Respiratory Tract	Negative	Screening 66 Diagnostic 45	Total 111	Screening 2 Diagnostic 6	Total 8	119
	Positive	Screening 0 Diagnostic 0	Total: 0	Screening 2 Diagnostic 5	Total 7	7
	Total	111		15		126

proportion and continuous variables summarized by median and interquartile range. Stata version 15 software (StataCorp, College Station, TX) and Excel software (Microsoft, Redmond, WA) were used for the descriptive analysis. This study was undertaken as a quality improvement project and met our institutional definition of nonhuman subjects research.

Results

We reviewed 134 paired samples during the study period. We excluded 5 pairs that had at least 1 inconclusive result contributing to their pair. The final sample included 126 paired samples from 105 unique patients.

Our cohort was 46% female, with a median age of 3.7 years (interquartile range [IQR], 0.5–13.9). Seventy eight samples (62%) were obtained in the PICU setting. The SARS-CoV-2 laboratory developed assay was used in 105 (83%) of 125 of cases and the Cepheid XPERT XPRESS SARS-CoV-2 assay was used in 21 cases (17%). Of the 126 pairs analyzed, 70/126 (56%) paired samples were sent for screening purposes and 54/126 (44%) were sent for diagnostic purposes. Notably, 69 (55%) of 126 samples were ordered for patients with pre-existing tracheostomies. The remainder of tests were ordered for patients with an endotracheal tube placed during admission.

Overall, 15 (2%) of 126 paired samples were positive. Most paired specimens, 118 (94%) of 126, were concordant: 111 that were negative from both sources and 7 that were positive from both sources. Of the 8 paired specimens (6%) that were discordant, all were positive from the URT and negative from the LRT. There were no instances of a positive LRT specimen with a negative URT specimen (Table 1).

Of the 7 pairs that were concordantly positive, 5 (71%) of 7 were ordered for diagnostic purposes. Symptoms were present for a median of 4 days (interquartile range [IQR], 1–22). Of the 8 discordant pairs, 6 (75%) were ordered for diagnostic purposes. Symptoms were present for a median of 6 days (range, 4–19.5 days). Radiographic signs of pneumonia were present in 4 (50%) of 8 of these discordant pairs.

Discussion

Our results demonstrated a high degree of concordance in paired sample testing throughout the study period when community prevalence of SARS-CoV-2 ranged from 5% to 35%.[2] Whether testing was performed for diagnostic or screening purposes or from a pre-existing tracheostomy or endotracheal tube, discordance was seen only when a sample tested positive from the URT and negative from the LRT.

Previous publications have raised concerns surrounding the potential for missed diagnoses of SARS-CoV-2 using URT PCR testing alone.[3–5] Wang et al[5] reported a higher test positivity rate in bronchoalveolar lavage (BAL) specimens than nasal or pharyngeal swabs. However, interpretation of these findings is limited by small sample size, with only 15 patients undergoing BAL testing, as well as a lack of clinical data available to correlate indication for and timing of testing relative to symptom onset. This latter limitation is particularly relevant because prolonged RT-PCR positivity may not always indicate transmissibility; therefore, PCR positivity is of unclear clinical value.[6] Further limiting the conclusions that can be drawn from this study, only 1 patient undergoing BAL sampling had a simultaneously collected URT specimen.[5] In a larger study of 79 adults with clinically suspected SARS-CoV-2 lower respiratory tract disease and negative or indeterminate nasal or nasopharyngeal swab, only 2 patients tested positive for SARS-CoV-2 by PCR from BAL fluid, for an overall agreement between the 2 sources of 97.5%.[7]

Overall, our results are consistent with these published data and provide additional support that URT specimens are the preferred sample for SARS-CoV-2 testing.[1] However, our work was limited by the small number of positive tests that occurred in this population as well as an overall small sample size. Furthermore, our sample was a convenience sample with URT and LRT testing sent at the discretion of treating providers, though both specimen types were routinely recommended at our institution throughout the study period. Despite these limitations, our results build upon existing data and provide "real world" data specific to the pediatric population.

Our experience with universal paired URT and LRT testing may be of value to other pediatric institutions, particularly those that care for medically complex children with tracheostomy tubes, who are disproportionately represented in pediatric hospitalizations.[8,9] Based on the data presented herein and supported by the published literature and revisions to national guidelines, which now recommend LRT sampling only if URT testing is negative and there is high clinical suspicion, we successfully shifted our testing strategy to sample the URT alone for most patients.[10] This practice change improved the safety of testing workflows by avoiding the need to disconnect a mechanically ventilated child from the ventilator to perform LRT testing, thus avoiding risk of precipitating hypoxia, as well as avoiding an AGP and risk of staff exposures, particularly in drive through testing sites. Furthermore, this approach reflects value-based care by facilitating optimal allocation of valuable testing resources in a high-utilizing population.

In conclusion, Our results demonstrate a high concordance between paired URT and LRT testing for SARS-CoV-2 in children with artificial airways, with no cases of isolated positive LRT tests. These results supported a successful local practice change to discontinue universal paired URT and LRT testing.

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