COVID-19

Diagnostic Performance of a Rapid Point-of-care Test for SARS-CoV-2 in an Urban Emergency Department Setting

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The ability to rapidly and accurately identify a patient's COVID-19 status has had significant impact on emergency departments (ED) and health systems globally. Since the identification of SARS-CoV-2 illness in the United States, there has been rapid development in patient testing capacity following initial challenges including sparse availability. This was made possible by increasing availability of diagnostic molecular tests in several formats, from laboratory-based traditional, RT-PCR methods to near-patient testing rapid point-of-care (POC) PCR tests. Recent reports have shown the occurrence of false negatives at a higher rate with some of these tests.[1] False-negative results can potentially result in the spread of disease in the community, hospital patients, and critical personnel. Conversely, a false-positive diagnosis can result in potential exposure of a COVID-negative patient while receiving care in a COVID ward and unnecessary use of personal protective equipment (PPE) that is currently in limited supply. Much of the attention by infectious disease services and hospital leadership has been on minimizing false-negative results; however, paramount to effective testing is the overall concept of accuracy, which minimizes both false-negative and false-positive results. Measurement of SARS-CoV-2 test accuracy is complicated by the lack of a consensus reference method (or criterion standard) to compare results from newer assays.

Initially, turnaround times for SARS-CoV-2 testing results took approximately 5 to 7 days.[2] This was because SARS-CoV-2 testing was first established in reference and academic clinical laboratories with capacity for high-complexity test development. As testing was brought in house following commercial reagent availability, batched results from high-throughput assays became available within 24 hours. While these strategies were a major step forward and still have utility in an outpatient setting, such a time frame cannot support most ED decision making. There is a need for rapid POC molecular tests that can be readily and safely deployed in an ED setting that generate reliable results in < 2 hours. Such tests provide clinically actionable results in the ED setting, facilitating diagnosis and rapid decision making. The ID NOW COVID-19 assay performed on the Abbott instrument platform is one such rapid

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Table 1
2 × 2 Table of Diagnostic Performance of ID NOW SARS-CoV-2 Assay Compared to the *m*2000 Using Dry Nasal Swabs

	Abbott *m*2000	
Abbott ID NOW	Positive	Negative
Positive	26	—
Negative	7	546

diagnostic test, capable of delivering results in 5 to 13 minutes.[3]

Because of the novelty of this virus as well as the recent introduction of these tests into the health care market, there are little comparison data in any emergency setting to measure performance. Given the criticality of maximizing accuracy and getting some quantification of a false-negative rate, the aim of this study was to evaluate the agreement of the diagnostic performance of the ID NOW COVID-19 with the Abbott *m*2000 real-time PCR, the institutional presumed reference standard, for SARS-CoV-2 in patients presenting to an urban ED. The ID NOW COVID-19 uses isothermal nucleic acid amplification technology for detection of SARS-CoV-2 on a POC platform.

This is a retrospective analysis of data for prospectively collected specimens from symptomatic ED patients for standard-of-care decision making and was approved by the institutional review board. The health system recommended testing all patients presenting with a COVID-19-like illness with the final decision at the clinician's discretion. All subjects had dry nasal swab (NS) testing with the Abbott COVID-19 assay on the ID Now platform (ID NOW, Abbott Diagnostics) paired with nasopharyngeal swab collected in viral transport medium tested on *m*2000 instrument (*m*2000, Abbott Molecular). All dry NSs were tested and results were obtained within 1 hour of collection. Positive results from the ID NOW were accepted as a final result. This was supported by prior in-house testing, validation data, and recent literature.[3] If ID NOW returned negative, the paired NP sample was then tested on the *m*2000 instrument for concordance. During the study period, results were used to determine patient disease status in standard care. Diagnostic performance is presented as positive agreement and negative predictive value with associated 95% CI.

During the evaluation period, April 28, 2020 to May 13, 2020, a total of 585 patients were tested having 597 samples collected and evaluated on both the ID NOW and the *m*2000 platforms. This represented 100% of all COVID tests in the ED during this time and 43% of all ED encounters. The cohort had a mean (±SD) age of 53 (±19) years with an admission rate of 62%. Of those who were admitted, 9% were admitted to the ICU. Only the first valid sample pairs per encounter were included in the analysis. Additionally, six observations were removed due to an invalid result on the ID NOW or no corroborating *m*2000 result leaving a total of 579 samples. Within this cohort, the prevalence of COVID-19 was 5.7% (95% CI = 4.0% to 7.9%). There were a total of seven false-negative tests (7/33) using the ID NOW with a positive agreement of 78.8% (95% CI = 61.0% to 91.0%). The negative predictive value was 98.7% (95% CI = 97.4% to 99.5%) (Table 1).

Our study described the diagnostic performance of a rapid molecular test that was introduced to improve the evaluation of patients with symptoms concerning for COVID. Findings suggested ID NOW has a positive agreement of 79% when comparing to RT-PCR testing with the *m*2000 instrument, resulting in a probability of false-negative testing in 1% to 2% of patients when disease prevalence is around 6%. Our results are similar to those reported in other studies comparing the ID NOW to the Abbott *m*2000.[3] A subsequent smaller comparison study reported the sensitivity to be 87%.[4] However, a preprint study recently reported a sensitivity of ID NOW to be 51.6% when using the Cepheid Xpert Xpress SARS-CoV-2 as the reference standard.[5]

Statistically, no test will likely result in 100% accuracy in all settings and thus some level of discordance can be anticipated, particularly for a disease in which optimal clinical and diagnostic testing parameters have yet to be defined. In a higher prevalence of disease setting when 20% to 25% of tests are positive, this false-negative rate would have significant implications. However, in the context of a 6% pretest prevalence of disease, this likely 1% to 2% rate of false-negative results can be mitigated by thoughtful operational decisions.

While there is rising discussion with concern for false-negative testing, it remains to be shown whether this is a clinically significant failure to detect active disease or merely failure to detect low levels of viral RNA of uncertain clinical significance. Additional work could be performed to determine where patients are in the course of their illness trajectory and how a bedside clinician could utilize this knowledge to better direct testing modalities to mitigate misleading testing information.

There are several potential approaches to address the lower accuracy of ID NOW testing in the ED

setting. Requiring all negative test results to be verified on an auxiliary platform (i.e., *m*2000) is one strategy. Patients who are discharged can simply be discharged with strict self-isolation precautions until confirmatory results are available the following day utilizing standard follow-up mechanisms. Unfortunately for admitted patients, most hospitals want strict separation in wards of COVID-positive or COVID-negative patients. This would result in significant ED boarding while awaiting confirmatory testing. For effective implementation, hospitals need to have a data-driven risk stratification step after an initial negative result to determine specific hospital location or simply assign all patients to a COVID ward with prompt deescalation procedures with a concordant negative test performed by the reference standard. This strategy of reflexing all negative result samples to a traditional RT-PCR test would require retesting almost 94% to 95% of patient samples. At our current disease prevalence, this may be of questionable value.

Alternatively, one could also simply rely on the more rapid ID NOW and tolerate a 1% to 2% false-negative rate in populations with low disease prevalence as ours, with lesser impact for discharged patients who receive self-isolation instructions and could be verified with additional testing for inpatients who deteriorate or fail to improve. This requires maintaining awareness of the current region's disease prevalence.

We choose to rely on the ID NOW with the caveat that an ED physician can confirm result using Abbott *m*2000 if there is suspicion that ID NOW test is a false negative. This results in repeat testing in only those patients where there remains a high posttest probability and relies on physician gestalt estimation or a priori knowledge of disease probability. This raises the potentially important role that formal or scientifically validated pretest probability tools are developed appropriate for the acute care setting.

In our ED cohort of patients, we found 1% to 2% will have a false-negative result when using ID NOW compared to the Abbott *m*2000. Developing a process for retesting those patients in whom the physician identifies as having a high pretest probability of disease may address the concerns around false-negative results.

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