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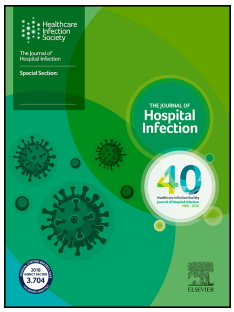

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Targeted Rapid Testing for SARS-CoV-2 in the Emergency Department is Associated with Large Reductions in Uninfected Patient Exposure Time

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Summary

Opportunity exists to decrease healthcare-related exposure to SARS-CoV-2, preserve infection control resources and increase care capacity by reducing the time to diagnosis of COVID-19. We performed a retrospective cohort analysis to measure the effect of targeted rapid molecular testing for SARS-CoV-2 on these outcomes. In comparison to standard-platform testing, rapid testing was associated with a 65.6% reduction (12.6 hours) in median time to removal from isolation cohort for patients with negative diagnostic results. This translated to an increase in COVID-19 treatment capacity of 3,028 bed hours and 7,500 less patient interactions that required consumption of personal protective equipment per week.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes COVID-19, has infected over 30 million and caused over one million deaths worldwide. Provision of care to patients with or suspected of having COVID-19 requires specialized infection control resources including dedicated diagnostic and treatment spaces equipped for negative pressure isolation, trained healthcare personnel and large quantities of personal protective equipment (PPE).[1,2] While most attention has been paid to healthcare resource allocation for patients with confirmed COVID-19,[3,4] most diagnostic tests performed for SARS-CoV-2 are negative.[5] Infection control requirements for persons under investigation (PUIs) for COVID-19 are the same as those for patients who have tested positive. Further, PUIs are commonly cohorted alongside patients with confirmed SARS-CoV-2 infection while awaiting diagnostic test results. This places uninfected patients at excess risk for healthcare-related exposure to SARS-CoV-2.[1,2,6] There is opportunity to preserve constrained resources, reduce avoidable healthcare costs and limit time of infection-risk exposure by decreasing time spent under investigation for COVID-19 in hospital settings.

More than 120 molecular tests for SARS-CoV-2 have now been granted *in vitro* diagnostic emergency use authorization (EUA) by the U.S. Food and Drug Administration (FDA) (https://www.fda.gov/medical-devices/emergency-use-authorizations-medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices). Analytical performance of approved nucleic acid amplification tests (NAATs) for SARS-CoV-2 is universally high, but processing times are variable.[7] While rapid (<1hr) NAATs for influenza and other respiratory viruses have had positive effects on patient throughput and appropriateness of antiviral and antibiotic prescribing by physicians,[8–11] the benefits of rapid testing for COVID-19 is not well-understood.

In this study, we sought to assess the impact of targeted rapid molecular testing on hospital infection control procedures and risk of COVID-19 exposure for uninfected patients. We compared the amount of time that PUIs without microbiologic evidence of infection, tested using standard and rapid molecular diagnostics, spent in isolation cohorts alongside patients with confirmed COVID-19. We hypothesized that rapid testing would drive large decreases in the interval to removal from COVID-19 isolation cohort, thus decreasing risk of nosocomial infection, preserving infection control resources and increasing COVID-19 treatment capacity.

METHODS

Study Design, Setting and Participants

We performed a retrospective cohort analysis of ED visits to two urban academic hospitals (Site 1 and 2) and a suburban community hospital (Site 3) within a single university-based health system in Maryland between March 29 and June 30, 2020. All adult patients ($\geq$18 years old) who had a laboratory diagnostic evaluation for SARS-CoV-2 infection initiated during their ED stay and remained in the hospital (ED or inpatient) until their test resulted were included. Patients who were discharged prior to diagnostic test result were excluded because the clinical decision to remove from the isolation cohort was independent of SARS-CoV-2 diagnostic test result. The Johns Hopkins Medicine Institutional Review Board approved this study (IRB Number: IRB00246741).

Diagnostic Testing Strategy

On March 29, 2020, targeted rapid molecular testing using the Xpert Xpress SARS-CoV-2 test (Cepheid, Sunnyvale, CA, USA) was implemented across our healthcare system. The Xpert testing platform allows diagnostic test results to be generated in approximately 45 minutes by combining specimen processing, nucleic acid extraction, RT-PCR and amplicon detection in a single random-access cartridge.[13,14]

Limited rapid tests were prioritized for the evaluation of PUIs in the ED who were expected to be hospitalized or could not be discharged to self-isolate at home while awaiting diagnostic test results (e.g., homeless or residing in a group home or assisted living facility). Standard platform NAATs including RealStar® SARS-CoV-2 RT-PCR Kit 1.0 (Altona Diagnostics; Hamburg, Germany), NeuMoDx™ SARS-CoV-2 assay (NeuMoDx, Ann Arbor, Michigan), Becton Dickinson SARS-CoV-2 Reagents for the BD MAX™ System (Becton Dickinson, Sparks, MD) and GenMark ePlex SARS-CoV-2 test (GenMark, Carlsbad, CA) continued to be used for all others.

All diagnostic orders were placed by treating emergency clinicians. Decision support that included testing algorithms and rapid test prioritization criteria was distributed electronically and made available in real time via electronic health record (EHR)-embedded guidelines and printed guidelines posted at clinical workstations. SARS-CoV-2 testing inclusion criteria were managed by our Department of Hospital Epidemiology and Infection Control and were standardized across all sites. Testing inclusion criteria broadened over time as guidance from the Centers for Disease Control and Prevention evolved and local capacity increased (ie, initially high-risk individuals only and then all symptomatic patients) but was standardized across all sites. Rapid test prioritization criteria, described above, remained constant over the entire study period.

Methods of Measurement and Analysis

Timestamped clinical data were queried from a relational database that underlies the common electronic health record (EHR) (Epic®, Verona, WI) used at all three study sites. Summary statistics, including demographics (age, sex, race and ethnicity) and rates of test positivity and hospitalization for all patients tested for SARS-CoV-2 infection at one of the three EDs over the study period were compiled. Daily SARS-CoV-2 testing volume was combined across study sites and stratified by standard-

and rapid-platform (Xpert Xpress) NAAT. Hospitalization was defined as admission to any inpatient unit (e.g. medical or surgical).

Uninfected patient exposure time was defined as the amount of time patients with negative SARS-CoV-2 NAAT results spent as PUIs subject to isolation precautions and geographically cohorted with SARS-CoV-2 infected patients. It was calculated as the time difference between diagnostic test order entry and first intra-hospital treatment space movement (removal from geographic cohort) after negative SARS-CoV-2 test result. Uninfected patient exposure time was compared between patients who tested negative by standard and rapid-platform NAAT. Exposure times were pooled across sites and compared using boxplot analysis and the logrank test for time-interval data. All data processing and analyses were performed using Python (V 2.7).

RESULTS

A total of 12,263 ED patients were tested for SARS-CoV-2 across three sites during the study period. Of these, 3,245 patients were discharged prior to result availability and were excluded from our cohort. Of the 9,018 who remained in the hospital (ED or inpatient) until their results became available, 3,502 (38.8%) patients were tested using rapid platform NAAT (Xpert Xpress SARS-Cov-2) with the remainder tested using standard platform NAAT (Table 1). Rates of rapid test use were slightly higher at our urban academic EDs (40.8% for Site 1 and 43.6% for Site 2) than at our suburban community ED (32.1%). Demographics across sites were similar, though patients tested at our suburban community ED (Site 3) were slightly older and a higher proportion of patients at study site 1 self-identified as black or African American (Table 1). The overall SARS-CoV-2 positivity rate for our cohort was 9.9% and a majority (60%) of patients included were hospitalized after departure from the ED (Table 1).

Daily SARS-CoV-2 testing volume increased over time for both standard and rapid testing platforms as seen in Figure 1A. The median order to result time, defined as the interval between test order entry by a treating clinician and negative/positive result viewable in the EHR, was 7.8 (IQR 3.71 – 11.68) hours for standard and 1.90 (IQR 1.40 – 2.82) hours for rapid platform tests (P < 0.001). Results were available prior to ED departure for 50.7% (n = 2,718) of patients tested using standard NAAT and 92.2% (n = 3,228) of those tested using rapid NAAT. As shown in Figure 1B, the median uninfected patient exposure times for those tested using standard and rapid platforms was 19.20 (IQR 9.45 – 44.59) and 6.62 (IQR 4.13 - 13.57) hours, respectively (P < 0.001). Thus, rapid testing for SARS-CoV-2 infection was associated with a 12.6-hour decrease (65.6% absolute reduction) in median uninfected patient exposure time.

DISCUSSION

Strategic delivery of SARS-CoV-2 rapid tests to a subset of ED patients with anticipated prolonged stays (e.g., hospitalization or limited capacity to self-isolate) resulted in large decreases in time spent as a PUI by patients without microbiologic evidence of SARS-CoV-2 infection. While important, our finding that rapid platform NAAT results were available an average 5.9 hours earlier than standard platform NAAT results is not surprising. However, our finding that rapid testing led to larger decreases (12.6 hours) in the interval from test order to removal from isolation cohort was somewhat unexpected. The magnitude of this effect is likely explained by patient location at time of diagnostic result and operational constraints of bed reassignment in each setting. Over 90% of rapid NAAT results became available during the ED encounter, enabling immediate intradepartmental transfers and optimal initial inpatient cohort assignment. On the converse, results for nearly half of patients tested in the ED using standard platform NAAT were delayed until after their arrival in the inpatient setting, where removal from isolation is complicated by need for transfer between distinct wards and clinical teams.

Targeted ED rapid testing was associated with considerable decreases in healthcare-associated exposure to SARS-CoV-2 for uninfected patients. Over the study period, we observed an aggregate savings of 40,106 hours (3,028 hours per week) in time that uninfected patients were treated in COVID-19 isolation units alongside confirmed positive patients. The intervention was also associated with drastically decreased infection control resource consumption and healthcare expenditures. Using a conservative estimate of 2.5 healthcare worker-patient contacts per hour,[12,13] this simple intervention prevented over 100,000 patient interactions under isolation precautions that would have required consumption of non-reusable infection control supplies (e.g., N95 respirators, gloves, gowns, sanitizing wipes) and decontamination of reusable equipment (e.g., face shields, goggles and powered air purifying respirators). Under assumptions of conventional surge capacity[15] and current supply costs[14], with each interaction consuming one N95 respirator (mean estimated cost $4.02 each), four gloves ($0.20), one gown ($2.33) and two sanitizing wipes ($0.08), our intervention translated to cost-savings of over $650,000 in non-reusable PPE alone. Under assumptions of contingency or crisis capacity, with repeated use of disposable N95 respirators across multiple encounters, [15] more than $250,000 in PPE costs were saved. Further, this intervention increased negative pressure isolation bed capacity in our ED and inpatient units, increasing capacity to care for additional patients who were under investigation for or had been diagnosed with COVID-19.

Prior studies on the effectiveness of rapid testing for respiratory viruses have primarily focused on influenza and have evaluated impacts on therapeutic decision-making and reductions in ED and hospital lengths of stay.[9,10,16] To our knowledge, this study is unique in that it is the first to evaluate the clinical effectiveness of rapid testing for SARS-CoV-2 and because it focuses on both infection risk exposure time and resource savings. Our demonstration that a relatively small number of rapid tests, if properly targeted, can be used to drive large decreases in time that patients spend under investigation

for infectious disease in the hospital setting is novel. These findings are particularly relevant to the management of COVID-19 but are also broadly applicable to seasonal respiratory viruses and emerging viruses.

This study has several limitations. First, these data are from a single hospital system with high SARS-CoV-2 testing capacity. While other sites may not have the same testing capacity, the value of strategically targeting rapid tests to a specific population translates to other settings and may inform the use of rapid testing protocols generally. Secondly, SARS-CoV-2 testing criteria changed over the course of this study creating a heterogeneous study population. However, testing criteria were standardized across sites and the study outcome is reflective of real-world clinical management. Finally, the true clinical sensitivity of all diagnostic tests for SARS-CoV-2 is still unknown and it is possible that our study may include patients with false-negative results. This limitation was mitigated by our use of first physical transfer after a negative test result as the outer bound of our time interval outcome. This transfer served as a proxy for isolation precaution removal based on clinical determination that the patient was at low risk for SARS-CoV-2 infection.

In summary, we found a targeted rapid testing strategy to be effective in reducing in-hospital time spent under investigation for COVID-19 by uninfected patients. Implementation of this strategy was associated with decreased risk for healthcare-associated SARS-CoV-2 infection, conservation of limited infection control resources and increased COVID-19 treatment capacity.

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DECLARATION OF INTERESTS

KC and HM participated in a multicenter validation of the Cepheid SARS-CoV-2 test. SL and RR are principal investigators of a research contract sponsored by Cepheid. No financial or material support was provided from Cepheid to directly support this work.

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Table 1. Patient Characteristics

	Total	Study Site 1	Study Site 2	Study Site 3
Total Tested	9,018	3,819	2,383	2,816
Age				
18-44	2,604 (28.9%)	1,355 (35.5%)	603 (25.3%)	646 (22.9%)
45-64	3,320 (36.8%)	1,548 (40.5%)	932 (39.1%)	849 (30.1%)
65-74	1,506 (16.7%)	548 (14.3%)	433 (18.2%)	525 (18.6%)
>74	1,573 (17.4%)	367 (9.6%)	414 (17.4%)	792 (28.1%)
Female	4,453 (49.4%)	1,817 (47.6%)	1,183 (49.6%)	1,453 (51.6%)
Race				
Black or African American	3,727 (41.3%)	2,230 (58.4%)	715 (30%)	782 (27.8%)
White	3,949 (43.8%)	1,121 (29.4%)	1,332 (55.9%)	1,496 (53.1%)
Other	1,342 (14.9%)	468 (12.3%)	336 (14.1%)	538 (19.1%)
Ethnicity				
Latino	844 (9.4%)	320 (8.4%)	277 (11.6%)	247 (8.8%)
Non-Latino	8,174 (90.6%)	3,499 (91.6%)	2,106 (88.4%)	2,569 (91.2%)
Admitted	5,409 (60%)	1,951 (51.1%)	1,678 (70.4%)	1,780 (63.2%)
Standard Platform	5,516 (61.2%)	2,262 (59.2%)	1,343 (56.4%)	1,911 (67.9%)
Rapid Platform	3,502 (38.8%)	1,557 (40.8%)	1,040 (43.6%)	905 (32.1%)
SARS-CoV-2 Positive	892 (9.9%)	306 (8%)	252 (10.6%)	334 (11.9%)

All study sites are affiliated with the same university hospital sytstem. Sites 1 and 2 are urban academic emergency departments (EDs); site 3 is a suburban community ED. SARS Co-V-2: Severe acute respiratory syndrome coronavirus 2.

Figure Legends

Figure 1. Uninfected Patient Exposure Time. (A) Daily volume of patients who were tested for SARS-CoV-2 in the emergency department and remained in the hospital setting until their tests resulted, stratified by standard (light blue) and rapid (dark blue) testing platforms. (B) Box plot analysis of uninfected patient exposure time, measured as time from SARS-CoV-2 diagnostic test order to first treatment space reassignment after negative result, for both standard (light blue) and rapid (dark blue) testing platforms. Median is represented by an orange horizontal line, interquartile range by boxes and 95% of range by whiskers