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Using Serologic Testing to Assess the Effectiveness of Outbreak Control Efforts, Serial PCR Testing, and Cohorting of Positive SARS-CoV-2 Patients in a Skilled Nursing Facility

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Abstract: We characterized serology following a nursing home outbreak where residents were serially tested by RT-PCR and positive residents were cohorted. When tested 46-76 days later, 24/26 RT-PCR-positive residents were seropositive; none of the 124 RT-PCR-negative residents had confirmed seropositivity, supporting serial SARS-CoV-2 RT-PCR testing and cohorting in nursing homes.

Key words: COVID-19; SARS-CoV-2 serology; long-term care facility; infection control

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Background

Since the emergence of 2019 coronavirus disease (COVID-19) in the United States in January 2020, skilled nursing facilities (SNF) have been a repeated site of SARS-CoV-2 (the virus that causes COVID-19) outbreaks [1,2]. As older populations are the most severely affected by COVID-19 [3], the ability to identify and contain these outbreaks is critical.

Despite numerous outbreaks, the performance of serologic testing for SARS-CoV-2 in residents of skilled nursing facilities (SNF) is not well described; its utility in epidemiologic sero-surveillance studies and outbreak reporting is under evaluation. To assess unrecognized SARS-CoV-2 exposure, we reviewed serologic testing in a cohort of SNF residents who had been serially tested for SARS-CoV-2 infection by nasopharyngeal swab RT-PCR following a COVID-19 outbreak at this SNF [1].

Methods

Study design and setting. From March 28 – 30, symptom-based RT-PCR testing identified 3 COVID-19 cases at a SNF at the Veterans Affairs Greater Los Angeles Healthcare System West Los Angeles (WLA) campus [1]. In response, all remaining SNF patients (N=96) underwent universal testing with nasopharyngeal RT-PCR (Roche COBAS 6800) for SARS-CoV-2, repeated approximately weekly on each ward and discontinued when all ward residents tested negative. In addition, staff and residents underwent temperature and symptoms screening, visitors were restricted, and universal masking of staff was initiated. Between March 29-April 6, 16 additional cases were identified [1]. These 19 patients were transferred to the acute care hospital for treatment or a designated COVID Recovery Unit (CRU) with cohorted staff, located within the SNF [4]. No further cases were identified upon additional serial testing the weeks of April 13 and April 20, and serial testing was discontinued. Surveillance testing on May 11 and May 18 did not yield any cases. By June,

all cases had been transferred back to the SNF or CRU. An additional 9 patients from the community who were diagnosed with COVID-19 by RT-PCR and treated in the acute care hospital were transferred to the CRU by June 5 and were included in this analysis. SNF staff were tested once between March 29 and April 10; 8/136 were positive and self-isolated at home [1].

SARS-CoV-2 serology testing. All residents in the CRU and SNF (SARS-CoV-2 RT-PCR positive and negative) underwent one-time serologic (antibody) testing from June 5 - 12. We tested 150 residents: 26 RT-PCR positive and 77 RT-PCR negative WLA SNF residents and 47 RT-PCR negative residents from a satellite campus (Sepulveda Ambulatory Care Center, SACC) (Figure). During the WLA SNF COVID-19 outbreak in March, the SACC SNF underwent universal RT-PCR testing with no cases identified. Twenty-seven residents, including two of the known RT-PCR positive cases, were excluded as they were on hospice, refused blood draw, received convalescent plasma, or had died. Serologic testing for IgG antibody to SARS-CoV-2 Spike (S1/S2) protein was performed using the DiaSorin LIAISON[®] Assay due to availability at our facility. As our objective was to identify potentially missed cases of COVID-19 during serial surveillance testing, samples from residents with historically negative SARS-CoV-2 RT-PCR tests with DiaSorin IgG-positive results were re-tested on a second serologic testing platform (Abbott SARS-CoV-2 IgG Immunoassay) for IgG antibody specific to SARS-CoV-2 nucleocapsid.

Clinical data collection. Resident demographics, comorbidities, and symptomatology attributed to SARS-CoV-2 were obtained by retrospective review of provider notes from March 20 to June 20.

Patients were classified as asymptomatic and symptomatic based on the development of symptoms at any time during their RT-PCR positive period. Symptoms attributed to COVID-19 included fever (either subjective or documented $>38^{\circ}$ Celsius), myalgia, headache, new

or worsening cough, dyspnea, nausea, emesis, diarrhea, or new or worsening loss of appetite.

Results

SARS-CoV-2 RT-PCR positive residents:

Nineteen SARS-CoV-2 RT-PCR positive residents were identified during the outbreak and an additional 9 were transferred from the acute care hospital. One died and 1 received convalescent plasma, resulting in 26 SARS-CoV-2 RT-PCR positive residents eligible for serologic testing (Figure).

Twenty-four of the 26 (92%) RT-PCR-positive residents tested positive for IgG by the DiaSorin assay 46-76 days after their initial diagnosis. One seronegative infected resident had an asymptomatic infection during the initial SNF outbreak. After an initial positive result (March 29), five subsequent RT-PCR tests (April 19 to June 16) were negative. The other seronegative resident was transferred from the WLA SNF at the time of the initial SNF outbreak to a non-VA acute care hospital for urinary tract infection and septic shock requiring intubation and vasopressor support. Testing for SARS-CoV-2 by RT-PCR at the non-VA hospital was negative March 29. He was then transferred to WLA acute care hospital, was extubated and tested positive by RT-PCR April 10 as a part of hospital surveillance; subsequent RT-PCR testing (April 18 and 23) was negative.

SARS CoV2 RT-PCR negative residents:

There were an additional 124 residents in the SNF who underwent serial SARS-CoV-2 RT-PCR testing and were persistently negative. Of this cohort, 69 were residing in the WLA SNF and 44 were residing at SACC at the time of the initial COVID-19 outbreak in March (Figure).

Among these 124 SNF residents with negative RT-PCR, all but two were seronegative for IgG antibody to SARS-CoV-2 spike protein by the DiaSorin assay. The two seropositive residents had no detectable IgG antibody to SARS-CoV-2 nucleocapsid when reflex tested by the Abbott assay performed the same day. One of these residents had 7 previous negative RT-PCR results; the other had 3. The latter was transferred to the WLA SNF from a non-VA acute care hospital, where he had been admitted for gastrointestinal and other symptoms attributed to urinary tract infection and was thus not present during the initial WLA SNF outbreak. All 47 SACC residents were IgG negative.

Discussion

In a cohort of 150 nursing home residents tested for SARS-CoV-2 infection by RT-PCR, including 26 previously diagnosed with COVID-19, the sensitivity of the DiaSorin assay was 92% (24/26) and the specificity was 98% (122/124). The two individuals seropositive by DiaSorin assay despite multiple negative RT-PCR tests likely represented false positive results, as reflex serologic testing using the Abbott assay indicated seronegativity. The absence of confirmed seropositivity in the RT-PCR negative cohort supports that universal and serial RT-PCR testing and early cohorting strategies in the SNF were effective at reducing further SARS-CoV-2 transmission.

Multiple factors may affect sensitivity and specificity of serologic testing to identify SARS-CoV-2 infection, including temporal dynamics in antibody response and possibly immunosenescence. SARS-CoV-2 antibody development (IgG and IgM) has been

demonstrated in the first 2 weeks of illness [5,6], with IgG more reliably detectable two weeks after symptom onset and persisting at least 3-4 weeks into the illness [5,7,8]. There is a paucity of data using IgG to evaluate history of infection two months later, as was performed in our study. The role of immunosenescence and COVID-19 IgG response also remains unclear but may be especially pertinent in older SNF residents. Despite these factors, DiaSorin assay performance was within the confidence intervals reported by the manufacturer [9].

Although RT-PCR is the most common method of diagnosing COVID-19, serologic testing has been shown to aid in retrospective diagnosis [5,10]. RT-PCR may be falsely negative due to inconsistent sampling, time and temperature of specimen transport, inhibitors to nucleic acid amplification, and kinetics of viral shedding [11]. Our objective was to use serology to identify COVID-19 cases missed by RT-PCR, as was observed in an epidemiologic investigation in Singapore where serological testing provided laboratory evidence linking two clusters that RT-PCR results had not [10]. Though our cohort had two residents who were RT-PCR negative but seropositive by DiaSorin, they likely do not represent cases missed by RT-PCR, as reflex testing was negative by the Abbott assay, which is unlikely to yield an overlapping false positive result [12].

The utility of serological testing has also been highlighted by large scale epidemiological studies [8] and to retrospectively evaluate outbreak control strategies [10]. Our results support that the infection control strategies employed during the WLA SNF COVID-19 outbreak were effective, including universal RT-PCR testing of residents and staff, and serial RT-PCR testing of residents with subsequent rapid isolation and cohorting of positive individuals, which limited transmission of infection. Additionally, the establishment of a CRU allowed cohorting of clinically stable residents

with COVID-19 [4], which provided an ideal cohort to evaluate known positive patients using serology.

Limitations of this report include small cohort size and a predominantly male, older population with a specific comorbidity profile that may be difficult to extrapolate to other populations. Relatedly, the size of the cohort may also limit the ability to assess the true accuracy of PCR and serology tests on a population-wide scale. As the outbreak control methods included a multipronged infection prevention/control approach, we are unable to exclude the contributions of these methods in preventing further spread of cases and note that testing resources can limit the utility of specific diagnostic tools.

Conclusion

Serial RT-PCR testing and rapid cohorting and isolation in a dedicated COVID-19 unit are effective measures to suppress further COVID-19 infection in a skilled nursing facility. Serologic evidence further supports no new cases of COVID-19 after initial case-finding activities.

Notes

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Conflict of Interest. The authors declare that there are no conflicts of interest

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Figure. Study Cohort for SARS-CoV-2 Molecular Diagnostic (RT-PCR) and Serologic Surveillance Testing of SNF Residents in the VA

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Figure 1

Figure. Study Cohort for SARS-CoV-2 Molecular Diagnostic (RT-PCR) and Serologic Surveillance Testing of SNF Residents in the VA Greater Los Angeles Healthcare System

