RESEARCH LETTER

Prolonged Live SARS-CoV-2 Shedding in a Maintenance Dialysis Patient

To the Editor:

Dialysis patients with coronavirus disease 2019 (COVID-19) have 20% mortality,[1-3] making prevention of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in this immunocompromised population paramount. Prevention strategies include cohorting infected patients in alternative settings for their hemodialysis care.[4] Accordingly, identifying when a dialysis patient is no longer infectious minimizes the risk for virus transmission on return to their usual care. The Centers for Disease Control and Prevention (CDC) transitioned from a test-based to a time-based approach for removing individuals with COVID-19 from isolation settings based on limited data showing that replication-competent virus has not grown from samples beyond 10 days in general populations and beyond 20 days in severely immunocompromised patients; the former group includes dialysis patients.[5,6] Critically, data reviewed by the CDC did not include patients receiving maintenance dialysis.[7,8]

Dialysis Clinic Inc (DCI) uses a test-based strategy whereby patients return to the general population of the hemodialysis clinic after resolution of symptoms and 2 negative molecular test results using either reverse transcription–polymerase chain reaction (RT-PCR) or transcription-mediated amplification (TMA) performed at least 24 hours apart. To assess whether a time-based protocol was appropriate for in-center hemodialysis patients, we initiated a quality improvement (QI) project in collaboration with Tufts New England Regional Biosafety Laboratory to perform SARS-COV-2 viral cultures on concurrent nasopharyngeal swabs collected from a convenience sample of patients and staff with recent COVID-19 diagnosis who are being tested for ongoing positivity through the DCI laboratory, under contract with PathGroup Lab. A positive molecular test result the week prior (at any time during the clinical course of COVID-19), with planned repeat molecular testing scheduled the following week, triggered eligibility for concurrent viral culture between September 1 and October 2, 2020. Patients with persistently positive molecular test results could participate with weekly sampling for up to 4 consecutive weeks. In some cases, a negative molecular test result during QI sampling was followed by a positive local test more than 24 hours later, leading to continued participation. Detailed methods are included in Item S1. This QI project was deemed exempt by Western Institutional Review Board (WIRB#20202425).

Among 44 dialysis patients with COVID-19, median age was 58.8 (range, 39.9-82.7) years, 52% were women, 45% Black/34% White/21% other race, 9% Hispanic, with 89% with diabetes mellitus, 34% with atherosclerotic cardiovascular disease, 20% with congestive heart failure, 7% with chronic obstructive pulmonary disease, 2% with peripheral vascular disease, and receiving dialysis for median of 49.7 months. Most patients were treated as outpatients with mild disease (or a few were asymptomatic with exposure), with 48% hospitalized; among them, length of stay was a median of 7 days. Overall, 77 nasopharyngeal samples were obtained and screened with both molecular test and viral culture (Fig 1). There were 32 samples from 15 patients with negative simultaneous molecular test results and negative virus cultures. Of 45 samples from 29 patients that were positive by molecular testing, 2 samples (4%) from 2 unique patients (7%) had positive viral cultures for SARS-CoV-2, with 1 patient sampled 29 days after his initial diagnosis. Contemporary samples were also obtained from 9 dialysis facility staff with COVID-19. All 11 samples with positive molecular test results from staff, obtained between 7 and 27 days from initial diagnosis, failed to culture virus.

Case 1 is a man in his 50s with diabetic kidney disease and a prior failed kidney transplant whose wife tested positive for SARS-CoV-2 infection. Although asymptomatic, he also tested positive. Seven days after his initial positive test result, both molecular test and viral culture results were positive. Subsequent molecular tests on days 16, 21, and 28 were all positive but all accompanying viral cultures were negative. Case 2 is a man in his 70s with diabetes and hypertension with initially symptomatic SARS-CoV-2 infection. He remained positive on a subsequent molecular test at day 24. On day 29 after his initial positive test result, both a molecular test and viral culture were positive. The patient refused further nasopharyngeal swabs. Serum antibody tested at day 38 was positive. He subsequently agreed to have a single nasal swab on day 58, with the resulting molecular test negative at that time. No repeat culture was obtained.

In maintenance dialysis patients treated at outpatient hemodialysis facilities, prolonged SARS-CoV-2 RT-PCR/TMA positivity is common although seldom associated with viable virus, in our experience to date. We cultured virus at day 29 after the initial diagnosis and in the absence of symptoms, albeit with only low levels of viral growth near the limit of detection.[9] The other patient showed a positive viral culture early in the disease course at day 7, while all other patients and staff had negative viral cultures in the setting of positive molecular test results beyond day 7, consistent with prior reports in the general population.[5,6] Whether the positive culture obtained at day 29 represented sufficient viral load to be transmissible remains uncertain, particularly in the setting of universal mask use among hemodialysis patients and staff, yielding uncertainty about the optimal duration for separately cohorting hemodialysis patients with COVID-19. Notably, the process of obtaining and shipping samples for virus culture would likely bias toward no growth due to the variability of transit time, temperature fluctuations, freeze-thaw exposure, and sampling technique.

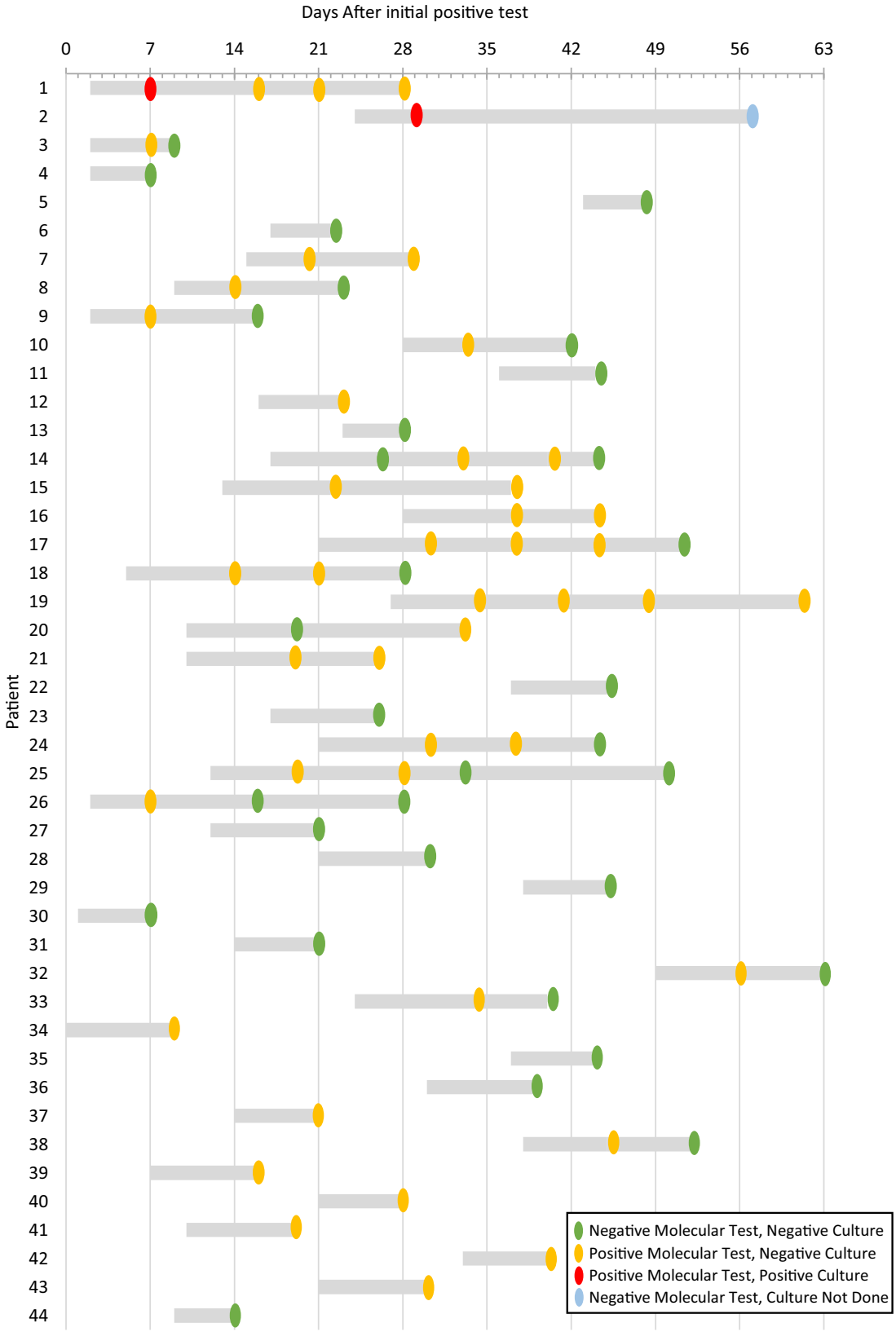

Figure 1. Individual patient summary of results from a convenience sample of maintenance hemodialysis patients with positive index molecular test results who were requested to provide concurrent samples for molecular tests and viral cultures for the quality improvement (QI) project. Each patient is represented by a timeline and columns represent the number of days from coronavirus disease 2019 (COVID-19) diagnosis during the period they participated in the QI project.

In conclusion, these results suggest that some dialysis patients, possibly due to relative immunocompromise, may have diminished ability to resolve SARS-CoV-2 infection and support policies in many dialysis facilities of maintaining moderately longer enhanced precautions that are more consistent with those recommended by the CDC for immunocompromised patients. Notably, despite many patients having positive RT-PCR/TMA test results for SARS-CoV-2, almost all viral cultures were negative; accordingly, our findings highlight limitations of both test-based and time-based strategies. Overall, there remains uncertainty regarding the optimal duration of enhanced precautions for maintenance dialysis patients with COVID-19, with the 1 individual with a prolonged positive culture having low-level viral replication, making conclusions regarding transmissibility in this setting uncertain. Further study is needed to determine whether a segment of dialysis patients who remain RT-PCR/TMA positive at remote times from initial infection could remain infectious.

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SUPPLEMENTARY MATERIAL

Item S1. Detailed Methods

ARTICLE INFORMATION

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