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PERSONAL VIEWPOINT

Coronavirus disease 2019: Implications of emerging infections for transplantation

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The recent identification of an outbreak of 2019- novel Coronavirus is currently evolving, and the impact on transplantation is unknown. However, it is imperative that we anticipate the potential impact on the transplant community in order to avert severe consequences of this infection on both the transplant community and contacts of transplant patients.

KEYWORDS

donors and donation, editorial/personal viewpoint, infection and infectious agents—viral, infectious disease, preventive health care

1 | INTRODUCTION

On December 31, 2019 the Wuhan Health Commission reported clusters of people with pneumonia that were epidemiologically linked to a seafood and live animal market in Wuhan, China.[1-3] The etiology was identified as a novel coronavirus, with a presumptive zoonotic origin.[2] The virus was recently designated severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) and the disease named Coronavirus Disease 2019 (COVID-19).[4,5] While initially it seemed to have limited person-to-person spread, the ability for human-to-human transmission from symptomatic individuals became apparent later in the epidemic.[3-7] Whether transmission can occur during the incubation period or from asymptomatic infected

Abbreviations: CDC, Centers for Disease Control and Prevention; COVID-19, Coronavirus Disease 2019; FDA, Food and Drug Administration; MERS-CoV, Middle East respiratory syndrome coronavirus; OPO, Organ Procurement Organization; SARS-CoV, severe acute respiratory syndrome coronavirus; SARS-CoV-2, severe acute respiratory syndrome coronavirus-type 2; TTS, The Transplant Society; WHO, World Health Organization.

individuals is unknown. By mid-February 2020, the COVID-19 had expanded to include over 50 000 confirmed cases, (over 6000 severe), involving 28 countries around the world;[4,5] 15 cases have been confirmed in the United States thus far.[5] Comorbidities including cardiovascular disease, cerebrovascular disease, and diabetes are present in one third to one half of reported cases and these patients appear to be at greater risk of serious complications.[8] Nosocomial spread may have been aided when patients presented with less classic gastrointestinal symptoms, delaying diagnosis and attention to infection prevention precautions.[7]

To our knowledge, COVID-19 has not been described in organ transplant recipients or donors. However, related viruses such as severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) were reported in transplant recipients during prior outbreaks of these viruses.[9,10] Kumar et al.[9] reported a fatal case of a liver transplant recipient with SARS that infected several other individuals, predominantly healthcare workers, illustrating a "super-spreader" event. AlGhamdi et al[10] described MERS-CoV in 2 renal transplant recipients, 1 of whom had no fever and as such did not meet the case definition for MERS-CoV; he was tested based on respiratory distress and epidemiologic knowledge and thereby appropriately diagnosed. Due to the need for immunosuppression in solid organ transplant recipients, they may be anticipated to have more intense and prolonged shedding of virus, thus potentially increasing the risk of transmission to contacts including healthcare workers. While closely related to SARS-CoV and MERS-CoV, the mortality associated with COVID-19 may be lower than what was reported with the previous epidemic novel coronaviruses. However, caution is still required as we do not yet know the full impact of the infection as it spreads to more diverse populations.[4,5,11]

The current COVID-19 epidemic is still in its early stages and while acquisition of knowledge is rapidly accumulating, there are many unknowns for the community at large and the transplant community in particular. Nevertheless, it is imperative that we anticipate the potential impact on the transplant community in order to avert severe consequences of this infection on both the transplant community and contacts of transplant patients. As we learn more about the infection, recommendations may need to change; an essential element of any recommendation is the ability to revise them in real time.

Based on the experiences with previous coronaviruses, we anticipate that an exposed transplant recipient would be infected; however, less is known about the risk of transmission from donor to recipient. The chance of a donor-derived infection may be influenced by donor exposures as well as infectivity of people in the incubation period and of asymptomatic individuals. The degree and duration of viremia and viability of the virus within blood or specific organ compartments would also impact the risk of donor transmission. Attention to donor epidemiological risk factors may help to diminish the risk of donor transmitted infection. The incubation period for COVID-19 is estimated to be 2-14 days.[2-8] In a report of 41 patients admitted with confirmed COVID-19, 6 (15%) had RNA detected in plasma.[12] RNA has also been detected in stool of an infected individual; thus sites other than the respiratory tract can be affected.[13] The implications of these findings remain unclear and as noted by the US Food and Drug Administration (FDA), as of now there have not been reported cases of transfusion-transmitted coronaviruses.[14] There is no formal FDA guidance for blood donors; however, it is anticipated that a person with an acute respiratory illness of any kind would be recused from blood donation. Therefore, while offering some reassurance, it does not negate the need for caution with a new coronavirus. In addition, the American Red Cross and European Centre for Disease Prevention and Control (ECDC) recommend a 28-day and 21-day delay, respectively, for donation for individuals with travel to high-risk areas or contact with a person with suspected or proven COVID-19.[15,16] The ECDC recommends 28-day delay after recovery from a confirmed infection.[16] Moreover, unlike many donor-derived infections where the risk is largely limited to the recipient, COVID-19 may present a risk to the Organ Procurement Organizations (OPOs) and procurement team; likewise nosocomial spread to other patients and healthcare workers as noted with the 2002 SARS-CoV remains a concern.[9]

Optimal management strategies have not been determined. Supportive care is the mainstay of therapy. Clinical trials evaluating potential therapies including with remdesivir (an experimental antiviral medicine) and lopinavir/ritonavir are also being conducted.[5] Drug–drug interactions of lopinavir/ritonavir with calcineurin inhibitors may limit its use in transplantation.

The emergence of COVID-19 is not the first time the transplant community has had to contend with emerging viruses, nor will it be our last. Consequently, we should learn from past experiences with novel viruses and put safeguards in place for transplant centers and OPOs to protect transplant recipients and healthcare workers in advance of a first case being reported and to mitigate the impact of this epidemic on transplant outcomes.

2 | LEARNING FROM THE PAST

When West Nile virus emerged in the United States in 1999, we quickly learned that transplant recipients were at particular risk for significant morbidity and mortality from blood transfusions and organs obtained from donors with either asymptomatic infection or (for donors) encephalitis of unclear etiology.[17] Concerns of Zika virus having similar impact have thus far not been borne out despite a viremic phase and reminds us that being cautious in an uncertain situation must be balanced with the alternative risk of not transplanting. Unlike the above flaviviruses, the impact of outbreaks of novel zoonotic coronaviruses, SARS-CoV in 2002 and MERS-CoV in 2012, was amplified because of their ability to transmit via respiratory droplets. Accordingly, the risk of nosocomial transmission with coronaviruses is greater and need for strict attention to infection prevention strategies paramount. During the 2002-2003 SARS-CoV outbreak, screening tools were required for assessing people coming into the hospital, as well as for staff and for potential donors.[9] When facilities had local transmissions of SARS-CoV or MERS-CoV, several transplant centers

TABLE 1 Targeted screening for patients for organ donors and transplant candidates and recipients should include both evaluation of symptoms and epidemiologic exposures

Signs and symptoms	Epidemiology
Fever	Traveled out of mainland China in the last 14 d and/or
Cough	Had close contact with someone known or suspected of having COVID-19
Shortness of breath or evidence of lower respiratory tract disease	

Abbreviation: COVID-19, Coronavirus Disease 2019.

were closed and at least 1 candidate died on the waiting list.[9,10] Despite the risk of negative consequences, temporary cessation of transplantation may be necessary in areas where the virus is heavily circulating. This was an important control issue in Toronto as a transplant recipient infected with SARS-CoV appeared to be a super-spreader.[9] At this time, screening, detection, and isolation of potentially infectious patients with COVID-19 are necessary. As recommended by the Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO), strict adherence to standard, contact, and airborne precautions including eye protection, may minimize the risk of nosocomial transmission[4,5] (Table 1).

Lessons from these prior epidemics should inform current and future outbreaks. Specifically, the past outbreaks revealed the need to promptly develop and have protocols in place for: (1) targeted screening of patients, visitors, and for OPOs of potential donors; (2) plans for placement and evaluation of recipients with risk factors for the emerging pathogen when they are sick and requiring evaluation; (3) back-up plans for recipients requiring evaluation for other reasons if the transplant center is temporarily closed; (4) consideration for candidates to be listed at alternate centers for transplant if an epidemic is geographically confined; and (5) the ability to communicate with transplant recipients and potential living donors to keep them apprised of updated information and recommendations and to offer reassurance as needed. The ECDC has recommended that epidemiologically at-risk potential organ donors be tested for the presence of SARS-CoV-2.[16]

Toward these ends, it is incumbent upon transplant centers to have links with their local infectious disease specialists and infection prevention practitioners. Most institutions in North America and Europe have tools in place for travel and symptom screening. In addition, transplant centers should be cognizant of local and national public health policies on reporting suspected cases of COVID-19. Broader organ sharing in the United States also raises the need to be cognizant of epidemiology in geographic areas that may be distinct from the transplant center.

Given the quickly changing dynamics of the current outbreak, links to the factual information on the reliably updated websites of the CDC (https://www.cdc.gov/coronavirus/2019-ncov/index.html)[5] and the WHO (https://www.who.int/emergencies/diseases/novel-coronavirus-2019)[4] should be readily available and frequently reviewed. Additionally, The Transplantation Society (TTS) has put forward interim recommendations for transplantation.[18] Based on prior experience and current knowledge, TTS's

TABLE 2 Interim recommendations for transplant centers[a]

Standard recommendations	Patients identified at risk based on Table 1 findings	Potential donors: attention to travel and exposure history as well as symptoms
Emphasize cough and sneeze etiquette with signage Frequent hand hygiene Vaccinate against vaccine-preventable infections (eg, PCV13 to prevent secondary bacterial infection)	Mask the patient Move the patient to a private room with the door closed. Ideally, place the patient in an airborne infection isolation room, if available Use airborne and contact precautions with face shield when entering the patient room If infection with COVID-19 suspected, report concern to local infection prevention personnel and local health department immediately Follow updated guidelines from the CDC https://www.cdc.gov/coronavirus/2019-ncov/infection-control.html	Asymptomatic living donors with travel to China or exposure to a person with known or suspected COVID-19 should postpone elective donation for 14 d based on current data[a] Living donors for emergent donation with above exposures should be decided on a case-by-case basis[a] Deceased donors with known active COVID-19 should not be used at this time[a] Deceased donors with epidemiologic risks above but without history of fever or respiratory illness should be used only with caution for organs other than the lungs or intestines and with careful consideration of risk: benefit on a case-by-case basis Decision-making should include the candidate or their proxy[a] Donors who have recovered from COVID-19 at least 28 d ago should be used only with caution as noted above. Benefit on a case-by-case basis. Decision-making should include the candidate or their proxy[a]

Abbreviations: CDC, Centers for Disease Control and Prevention; COVID, Coronavirus 2019.

[a]In a rapidly changing environment, these recommendations may need to be updated and revised.

document recommends against using a deceased donor who has died with COVID-19 and not performing living donation within 14 days or return from Wuhan, China. For transplant candidates, they likewise recommend against undergoing transplantation within 14 days of returning from China/Wuhan. The United States Organ Procurement Transplantation Network also put out information with the endorsement of the American Society of Transplantation and American Society of Transplant Surgeons.[19] We agree with avoiding the use of organs from donors with confirmed or suspected active COVID-19; not only is there a risk to the recipient, but likewise the OPO, procurement team, healthcare providers, and family members. We also agree with deferring elective transplant procedures for individuals who could be in the asymptomatic incubation period based on epidemiologic exposures. Modifications are likely to be required as the epidemic spreads and more information comes to light. At this time, data are lacking to make definitive recommendations regarding donors who may have recovered from infection in the past, or for patients requiring emergent transplantation in which they or a potential donor have an epidemiologic exposure but no symptoms (Table 2). While further data are accumulating, decisions in these cases need to thoughtfully consider the urgency of the need for the transplant, the organ being used, and the particular exposure risk of the donor as well as the consequence of not performing the transplant when an organ becomes available. If a transplant is performed during a potential incubation period or in a country with endemic circulation of SARS-CoV-2, it would be prudent to include isolation procedures to protect the patient, family, and hospital personnel. In addition, we should be mindful that blood and tissue banks may require a more intensive strategy and longer moratorium of exposed donors. In rapidly changing epidemics such as the current COVID-19, the gravity of the situation would change dramatically if widespread secondary or tertiary cases not associated with travel appear and if viremia is confirmed in infected individuals. As the epidemic evolves, we should all anticipate modifications to the current recommendations in real time. It is imperative for the transplant community to be prepared and regularly update their protocols; this will undoubtedly not be the last novel coronavirus to cross our path.

DISCLOSURE

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