



PERSONAL VIEWPOINT

Utilization of deceased donors during a pandemic: argument against using SARS-CoV-2-positive donors

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has rapidly become an unprecedented pandemic that has impacted society, disrupted hospital functions, strained health care resources, and impacted the lives of transplant professionals. Despite this, organ failure and the need for transplant continues throughout the United States. Considering the perpetual scarcity of deceased donor organs, Kates et al present a viewpoint that advocates for the utilization of coronavirus disease 2019 (COVID-19)-positive donors in selected cases. We present a review of the current literature that details the potential negative consequences of COVID-19-positive donors. The factors we consider include (1) the risk of blood transmission of SARS-CoV-2, (2) involvement of donor organs, (3) lack of effective therapies, (4) exposure of health care and recovery teams, (5) disease transmission and propagation, and (6) hospital resource utilization. While we acknowledge that transplant fulfills the mission of saving lives, it is imperative to consider the consequences not only to our recipients but also to the community and to health care workers, particularly in the absence of effective preventative or curative therapies. For these reasons, we believe the evidence and risks show that COVID-19 infection should continue to remain a contraindication for donation, as has been the initial response of donation and transplant societies.

KEYWORDS

donors and donation, editorial/personal viewpoint, ethics and public policy, infection and infectious agents – viral, infectious disease, organ allocation, organ procurement, organ procurement and allocation, organ transplantation in general

1 | INTRODUCTION

Since its initial emergence in Wuhan, coronavirus disease 2019 (COVID-19) has grown to pandemic proportions. As of April 14, there were 1 844 863 cases of severe acute respiratory

syndrome coronavirus 2 (SARS-CoV-2) with 117 021 deaths worldwide, with 553 822 cases and 21 972 deaths in the United States as reported by the World Health Organization.¹ This crisis has impacted society, disrupted routine hospital functions, caused significant resource strain in the health care industry, and touched transplant providers' lives personally and professionally.²⁻⁴ Despite these unprecedented stresses in modern health care, transplant providers continue our commitment to

Abbreviations: ACE2, angiotensin-converting enzyme 2; COVID-19, coronavirus disease 2019; MERS-CoV, Middle East respiratory syndrome-related coronavirus; OPO, organ procurement organization; PPE, personal protective equipment; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

the almost 113 000 people currently awaiting transplant.⁵ While life-saving transplant operations continue during this pandemic, the supply of deceased donors continues to significantly lag behind the demand of the waitlist. The Association of Organ Procurement Organizations, The Transplantation Society, and the Canadian Blood Services have stated that patients who are COVID positive should not be considered for donation.⁶⁻⁸ In efforts to maximize all potential deceased donor organs, some in the transplant community have asked whether there should be consideration for the utilization of organs from donors who are COVID-19 positive.

We have read the personal viewpoint of Kates et al⁹ titled "Use of SARS-CoV-2 Infected Deceased Organ Donors: Should We Always 'Just Say No?'" which presents arguments for considering COVID-positive donors with great interest. They present a review of current literature pertaining to SARS-CoV-2 transmission and organ involvement as well as detailing experiences with previously known respiratory viruses. They suggest that there should be consideration for highly selected COVID-positive donors for patients in need of kidney, liver, and heart transplant. At this time, unfortunately little is known about the biologic behavior, transmission, pathogenesis, and long-term morbidity of COVID-19. We will review the current literature to provide additional points and considerations as to why COVID-19-positive deceased donors should not be considered for donation at this time.

2 | ORGAN-SPECIFIC CONSIDERATIONS

In this section, we will review several aspects of SARS-CoV-2 viremia and end organ involvement, as well as potential risks to transplant recipients.

2.1 | Risks of blood transmission of SARS-CoV-2

Huang et al¹⁰ demonstrated the presence of viremia in 15% of patients, albeit with low viral RNA levels. A recent study by Chang et al¹¹ showed the presence of intact viral RNA in asymptomatic blood donors who were later found to be positive for COVID-19. It is important to be cognizant of the fact that these are early-generation tests for SARS-CoV-2. When looking at the SARS-CoV-1 outbreak in 2003, 78% of patients had detectable viral RNA within the first week of illness, while lymphocytes had a high concentration of SARS-CoV-1 with viral replication occurring within lymphocytes.¹² Considering our limited knowledge of the current virus, we believe that it is premature to suggest that the risk of transmission via blood components is negligible. Additionally, while the presence of viral RNA in blood may not lead to the risk of direct transmission via blood, it could possibly suggest another mechanism of end organ involvement by SARS-CoV-2.

2.2 | Detection of coronaviruses in nonlung tissues

2.2.1 | Liver and gastrointestinal tract

Wang et al¹³ demonstrated that SARS-CoV-2 RNA was detected in 29% of stool specimens. Additionally, a review of several studies suggested that hepatocellular injury was present in 14%-53% of patients with severe COVID-19, in which the mechanism of liver injury ranged from direct viral infection, drug-induced liver injury, and systemic inflammatory response syndromes.¹⁴ A recently reported study demonstrated that 11.4% of hospitalized COVID-19 patients had gastrointestinal symptoms, whereas 17.6% of those patients had liver injury and shock.¹⁵ These data are of concern to the utilization of liver from COVID-19-positive donors due to the potential of direct viral infection of liver, as well as the possibility of first-pass absorption through the gut. While data do not exist regarding the absorption of SARS-CoV-2, there is evidence that intestinal absorption occurs and may serve as an alternate route of infection for the related Middle East respiratory syndrome-related coronavirus (MERS-CoV).¹⁶ Taken together, these data indicate that liver injury and involvement may be due to SARS-CoV-2, whether it be from direct infection or by related systemic inflammatory responses, and suggest that the utilization of livers from COVID-19-positive donors should not be considered.

2.2.2 | Kidney

Angiotensin-converting enzyme 2 (ACE2) has been identified as the receptor for SARS-CoV-2, and it is well known that ACE2 is expressed in the kidneys.¹⁷ In fact, based on expression levels of ACE2, the kidney has been classified as a high-risk organ for potential SARS-CoV-2 involvement and infection.¹⁸ A retrospective study of convalescent patients with COVID-19 showed evidence of SARS-CoV-2 RNA in the urine of 6.9% of patients.¹⁹ Additionally, clinical and autopsy data provided by Zhang et al²⁰ on the SARS-CoV-2 and related coronavirus outbreaks indicate renal involvement by SARS. Taking the data available at the present time, it seems likely that there is a reasonable concern for renal involvement by SARS-CoV-2, which would be a strong argument against utilization of kidneys from COVID-19-positive donors.

2.2.3 | Cardiac

It has been suggested that pathophysiology of viral myocarditis begins with viral replication within the myocardium resulting in myocardial inflammatory injury, despite the presence of viral nucleic acid in only 30% of endomyocardial biopsies.²¹ While it has been suggested that patients with severe cases of COVID-19 have high rates of cardiac dysfunction, it is our opinion that the absence of cardiac dysfunction does not necessarily rule out the absence of

SARS-CoV-2 involvement of the myocardium. As discussed earlier, the ACE2 receptor is an entry point for SARS-CoV-2, which is also present within the cardiovascular system.¹⁷ The related SARS-CoV-1 was present in 7 of 20 heart samples from patients on autopsy.²² More recently, a case report of a COVID-19–positive patient showed presence of low-grade myocardial inflammation and viral particles on endomyocardial biopsy.²³ We believe that there is no adequate evidence to support the utilization of hearts from COVID-positive donors.

2.2.4 | Summary

While it could be interpreted that end organ involvement of SARS-CoV-2 is only present in the most severe cases and that potential donors with COVID-19 who are asymptomatic or mildly symptomatic could be considered for donation, our viewpoint is that the absence of severe symptoms or laboratory derangements does not rule out involvement of solid organs. Additionally, a potential donor is a patient with a catastrophic injury causing death. The necessarily unforeseen and rapid presentation of these patients precludes assessment of symptomatology and exposures of the potential donor prior to their end of life-causing event.

3 | INFORMED CONSENT

Informed consent requires dialogue between the physician and patient. The purpose of informed consent is to establish trust, accurately explain the risks and benefits of a proposed procedure and understand patient concerns. Unfortunately, considering the limited data of SARS-CoV-2, our community is unable to provide guidance and proper informed consent. We do not yet have a clear understanding of the risks associated with viral transmission, nor can we provide an informed opinion regarding mitigation of the risk of transmission should the recipient become infected.

4 | NO KNOWN EFFECTIVE THERAPIES

In order to provide proper informed consent, it is our belief that potential recipients should be able to receive proper mitigation strategies for the risk of donor-derived transmission. There are numerous studies under way examining the potential benefits of antiviral and immunomodulating agents with some promising preliminary results, but none are established as standards of care. This point is of particular importance when considering that unlike HIV and hepatitis C virus, where effective treatment and/or curative options exist, no such prophylaxis or treatment options exist for recipients receiving organs from COVID-positive donors. While we discuss the potential negative consequences to health care workers later, it is worth mentioning here that no therapies exist for these exposed individuals as well.

5 | OTHER CONSIDERATIONS

5.1 | Exposure of health care and recovery teams

The general recommendations from state officials, Centers for Disease Control and Prevention, and public health officials involve self-isolation for disease containment to prevent viral spread.²⁴ Unfortunately, the very nature of donation and transplant violates the principles of disease containment, and evaluation of COVID-positive donors places our team members and donation coordinators in direct contact with SARS-CoV-2. In a study by Wang et al,²⁵ hospital-associated transmission was the presumed mechanism for infection in 29% of health care professionals, although it is worth mentioning that many of these providers were not wearing appropriate personal protective equipment (PPE). It is generally thought that transmission of SARS-CoV-2 can be prevented with optimal infection control measures and utilization of PPE. However, Krein et al²⁶ demonstrated 283 incidents of failure of proper use of PPE in 325 observations. This indicates that the use of PPE is no guarantee of reduction in transmission.

5.2 | Disease transmission via transport materials, contamination, and propagation

A recent case report by Ong et al²⁷ suggested extensive environmental contamination by a COVID-19 patient with mild upper respiratory tract involvement, which included ventilation system ducts, sinks, toilets, and PPE. As in all recoveries for solid organs for transplant, each organ is packaged in preservation solution, then placed within several layers of sterile container and subsequently placed within a box for transportation. This is all done within the same room as the donor operation. A study by van Doremalen et al²⁸ suggested that the SARS-CoV-2 virus can remain viable in aerosols and surfaces for hours, if not days. These results suggest that packaging materials used to store deceased donor organs could potentially serve as vectors for fomite transmission of virus. By virtue of exposure of health care workers and recovery teams and the transportation of COVID-positive organs, multiple communities can be negatively impacted by the recovery of a single COVID-positive donor. Subsequent and related to the extensive local contamination described here, data suggest that hospital-associated transmission rates are approximately 12.3%.²⁵

5.3 | PPE and hospital resource utilization

It is well documented in both the literature and media that there are critical shortages of PPE throughout the United States and shortages of ICU beds and ventilators in numerous communities.²⁹ Knowingly exposing transplant teams and recipients to COVID-19–positive donors exacerbates this critical shortage by the consumption of large amounts of PPE. It risks additional utilization of ICU beds and

ventilators should members of the health-care delivery teams become infected. If members of the transplant team, operating room staff, nursing staff, organ procurement organization (OPO) staff, and ancillary service members become infected, then they would presumably be removed from duty for several weeks at best case scenario. It is also worth noting that should COVID-positive donors be recovered, the exposure may mandate quarantine of the individuals present at the case as a precautionary measure to prevent disease spread. At a time when health care staffing is critically low in some parts of the country, recovering COVID-positive donors could remove health care workers from the work force.

6 | DISCUSSION

There is no doubt that the persistent shortage of deceased donor organs requires that the transplant community continues to think “outside the box” to identify ways to increase the number of life-saving transplants. In the context of deceased donor infections (eg, hepatitis C virus, bacteremia), our traditional concerns are almost solely for the potential recipients of the donors’ organs. COVID-19 poses unique risks not only to the recipient and the procurement teams but by extension also other health care workers and the community at large. The decision to pursue transplant starts with a referral of a potential donor, evaluation of the referral by the OPO clinical staff, followed by the involvement of OPO family support liaisons. Once authorization for donation has been obtained, OPO clinical coordinators generally take over the management of the potential donor. The process of clinical evaluation and management of a donor, allocation, and establishing an agreed upon donor operating room time can be lengthy and often involve multiple clinical OPO coordinators. Once the donor is in the operating room, numerous health care worker team members, including transplant surgeons, trainees, anesthesiologists, circulators, scrub technicians, and others, become involved in the case. All of these individuals have a risk of exposure to COVID during this time. Once the donor operation is complete, each transplant team member returns to their respective facilities to begin the process of transplant, and other organs such as kidneys can be shipped to various locations in distant communities. A single COVID positive donor can result in organs being transplanted at multiple different hospitals. On arrival to a given hospital, the transplant procedure is conducted. Many health care professionals, including physicians as well as nursing and ancillary service teams, can subsequently be exposed within the operating room and subsequent postoperative care units. There is a risk of in-hospital transmission between health care providers and to other hospitalized patients. And, of course, all of these providers have the potential to then transmit the infection to their close contacts and communities. In short, the number of people in contact downstream from a single COVID-positive donor is quite large. There are many potential negative consequences of exposure of these individuals, not to mention the risks to the recipient. And as noted, there are no known effective therapies or prophylaxis for

SARS-CoV-2, which adds a large degree of risk compared to donors with blood-borne communicable diseases such as HIV and hepatitis C virus.

We acknowledge that there are no conclusive data at this time to refute the proposition that donor derived COVID transmission to a recipient is unlikely. It should be understood, however, that the absence of such proof is not proof of its absence. Much of the organ-specific data strongly point to end organ involvement, which includes the heart, liver, and kidneys. While there are lessons to be learned from prior coronavirus-related pandemics such as SARS-CoV-1 and MERS-CoV, the SARS-CoV-2 (COVID-19) pandemic is one that is unprecedented in modern health care. Although all health care professionals are trained to provide the best possible health care to patients, we frequently do not consider the ramifications to our surrounding team members, nor do we consider resource expenditure. We make the assumption that our team members are willing to assume similar risks as us to provide optimal patient care. We are used to practicing in a health care system that typically does not have issues related to shortages of PPE, ventilators, and ICU beds. Although the pandemic presents new challenges to us in transplant, we must remember that systems-level considerations are inherent to our field. The chronic scarcity of organs has necessitated strategies where recipients are prioritized, be it by time accrued on the list, risk of death without transplant, or potential longevity with a graft. Given our cultural familiarity with rationing and choices in life-and-death decisions, it is our medical, moral, and ethical responsibility to think of the potential downstream negative consequences of utilization of COVID-positive donors and COVID exposure in the health care setting. Rather than solely focusing on a potential transplant recipient, it is our responsibility to consider all the people surrounding that recipient as well, including the transplant team, OPO, and associated hospital workforce. It is for these reasons that cannot endorse the use of COVID-19-positive donors, and instead support the positions taken by the Association of Organ Procurement Organizations and The Transplantation Society.

DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

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How to cite this article: Shah MB, Lynch RJ, El-Haddad H, Doby B, Brockmeier D, Goldberg DS. Utilization of deceased donors during a pandemic: An argument against using SARS-CoV-2–positive donors. *Am J Transplant*. 2020;20:1795–1799. <https://doi.org/10.1111/ajt.15969>