Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Computed tomography (CT) of the head suggested anoxic brain injury with no hemorrhage. Chest CT angiography was consistent with a right lower lobe pulmonary artery segmental embolus. On Day 2, he was found to have a large, acute left middle cerebral artery ischemic infarct. Subsequently, on Day 7, he developed sub-falcine herniation. He remained afebrile, but his white blood cell count increased from 7,600 to 17,800 cells/mm^3 of blood with no bacterial infection on respiratory and blood cultures. During organ-donation work-up, a repeat chest CT (on Day 8) showed resolution of his pulmonary embolus, but new scattered, bilateral ground-glass opacifications were noted, which prompted bronchoalveolar lavage and nasal swab specimens for coronavirus disease 2019 (COVID-19) testing. These were positive 24 hours later, and the patient was declined as an organ donor. This case raises several points regarding the assessment of donors for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Given the frequent absence of donor history, the extent of community spread, concern for the risk of nosocomial acquisition, and concomitant hazard to medical personnel, donor screening should be mandatory. The International Society for Heart and Lung Transplantation currently recommends that all donors should be tested for SARS-CoV-2 infection *if testing is available*.[1] Early screening may be prudent, particularly when medical history is sparse or absent. Admission to a facility or units known to have cases of COVID-19 increases concern for nosocomial transmission. In this case, the patient may have arrived with pre-existing asymptomatic COVID-19 infection but may also have acquired the infection after arrival at the donor hospital.[2,3] In such cases, even if an initial screening test is negative, a repeat test should be performed before the recovery of organs. For organ procurement organizations, tests may need to be sent out if the donor hospital is unable to provide in-house testing, resulting in significant delays in allocation. Although reverse transcriptase polymerase chain reaction (RT-PCR) sensitivity varies widely by sampling site, concurrent evaluation of chest CT seems to greatly increase sensitivity for the disease.[4] In this candidate donor, the final chest CT demonstrated the development of bilateral ground-glass opacities that were consistent with COVID-19, which was confirmed by respiratory RT-PCR. The chest CT was convincing evidence to defer making a decision to accept the organ until the RT-PCR result was available. Multimodality RT-PCR testing should also be considered as the virus may be present in mucosal areas such as the gut. However, availability of such testing may be limited. Although the disease primarily affects the lungs, it is not clear whether other organs may be safely transplanted. From a cardiac standpoint, the angiotensin-converting enzyme 2 receptor is required for SARS-CoV-2 entry and is expressed on cardiac myocytes. There has been evidence of fulminant myocarditis in COVID-19, and troponin elevation has been associated with increased mortality. Because the outcomes of transplanting organs from a COVID-19–positive donor and the extent of cardiac involvement in COVID-19 are currently unknown, it is our practice at the time of publication to decline organs from donors with positive RT-PCR testing, even for an isolated cardiac transplant. Other considerations include a significant risk of transmission to the procurement team, the lack of resource-effective surveillance strategies for donor transmission, absence of proven treatments for this potentially lethal condition, and potential for turning the recipient into a vector for viral transmission. Owing to the many uncertainties and rapidly evolving data regarding SARS-CoV-2, it is vital to develop donor testing protocols for COVID-19 during this pandemic.

References

1. Aslam S, Danzinger-Izakov L, Luong M, et. al. Guidance for cardiothoracic transplant and ventricular assist device centers regarding the SARS CoV-2 pandemic; 2020. Available at: https://ishlt.org/ishlt/media/documents/SARS-CoV-2_-Guidance-for-Cardiothoracic-Transplant-and-VAD-centers.pdf.
2. Bai Y, Yao L, Wei T, et al. Presumed asymptomatic carrier transmission of COVID-19. JAMA 2020;323:1406-7.
3. Vanhems P.Fast nosocomial spread of SARS-CoV2 in a French geriatric unit Lyon Study Group on Covid-19 infection [e-pub ahead of print]. Infect Control Hosp Epidemiol. doi: 10.1017/ice.2020.99, Accessed April 19, 2020.
4. Fang Y, Zhang H, Xie J, et al. Sensitivity of chest CT for COVID-19: comparison to RT-PCR [e-pub ahead of print]. Radiology. doi: 10.1148/radiol.2020200432, Accessed April 19, 2020.

COVID-19 pneumonia in a dual heart–kidney recipient

Maxine W. Stachel, MD,[a] Claudia G. Gidea, MD,[a] Alex Reyentovich, MD,[a] Sapna A. Mehta, MD,[b] and Nader Moazami, MD[c]

From the [a]Leon H. Charney Division of Cardiology, Department of Medicine, New York University Langone Health, New York, New York; [b]Department of Medicine, Transplant Infectious Disease Service, New York University Langone Health, New York, New York; and the [c]Department of Cardiothoracic Surgery, New York University Langone Health, New York, New York.

A 61-year-old African American man with a history of hypertension, coronary artery disease, end-stage renal disease (on hemodialysis since 2014), and end-stage heart failure secondary to arrhythmogenic right ventricular cardiomyopathy underwent dual organ heart–kidney transplantation in May 2019. Approximately 2 months after transplant, mycophenolate was discontinued owing to episodes of pancreatitis, leukopenia, and detectable BK polyomavirus. Since then, the patient was maintained on tacrolimus (goal level of 8 ng/ml) and low-dose prednisone (5 mg/day). Eight months after transplant, the patient developed a mild influenza A infection that was treated with oseltamivir for 10 days. After 6 weeks, approximately 10 months after heart–kidney transplantation, the patient re-presented with cough productive of yellow sputum for 3 days, associated with pleuritic chest pain, dyspnea, nasal congestion, and subjective fevers. He denied travel or exposure to known individuals infected with coronavirus disease 2019 (COVID-19). Initial vital signs were within normal limits and physical examination was unremarkable. The blood oxygen saturation on room air was 96%. Respiratory viral panel was negative, and white blood cell count and blood lactate were normal. Absolute lymphocyte count was

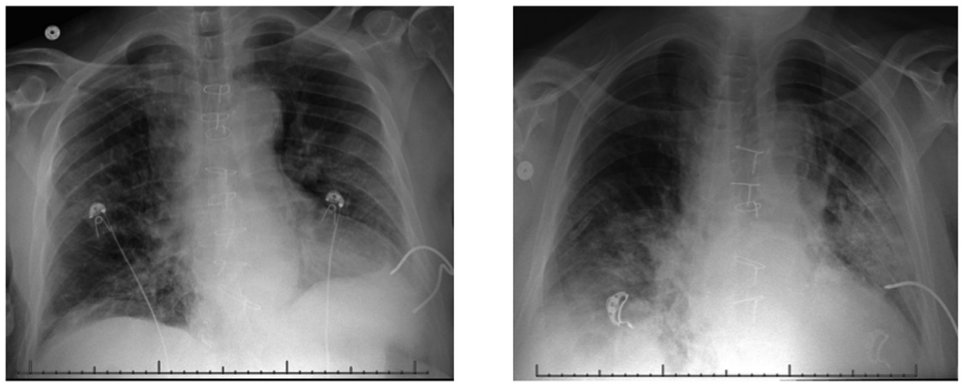

Figure 1 Radiographic assessment of the patient**.** (a) Admission chest X-ray showing bilateral multifocal patchy opacities. (b) Chest X-ray on hospital Day 4 showing bilateral worsening airspace opacities and pleural effusions.

reduced (700 /μl; reference range: 1,300−3,600 /μl). C-reactive protein was elevated (15.8 mg/liter; reference range: 0−5 mg/liter). The initial chest X-ray revealed multifocal pneumonia (Figure 1a). The patient was started empirically on vancomycin, piperacillin−tazobactam, and azithromycin. The baseline immunosuppression was reduced: prednisone was held, and tacrolimus dose was decreased to a lower goal level of 6−8 ng/ml. Prophylaxis for opportunistic infection was continued with ganciclovir and atovaquone. Oropharyngeal and nasopharyngeal swabs were sent for severe acute respiratory syndrome coronavirus 2 reverse transcriptase−polymerase chain reaction testing, and the patient was admitted to an airborne isolation bed. On hospital Day 4, the patient remained clinically stable with blood oxygen saturation ~95% on room air, but radiographic worsening was noted (Figure 1b). His severe acute respiratory syndrome coronavirus 2 reverse transcriptase−polymerase chain reaction test returned positive, and he was started on lopinavir/ritonavir 400/100 mg every 12 hours and nitazoxanide 500 mg every 12 hours for 7 days. He was also given 1 dose of 40 g intravenous immunoglobulin. Tacrolimus levels were followed daily, and given the known drug−drug interaction with ritonavir, a decreased tacrolimus clearance was observed, and no tacrolimus dose was administered or required for a week. Anti-bacterial therapy was discontinued. The patient improved and by hospital Day 14, experienced only intermittent cough with scant sputum production. His C-reactive protein decreased to 8.1 mg/liter. He was discharged home to self-care.

This patient with COVID-19 exhibited a relatively mild form of the disease, remained afebrile, and maintained good oxygen saturation throughout his hospital course. His presentation was similar to that reported in non-immunosuppressed patients, and similar presentations were reported in 2 and 3 COVID-19−positive heart transplant recipients from China[1] and Italy, respectively. Because respiratory viral illness represents a significant cause of morbidity and mortality in the aging and immunocompromised transplant populations,[2] these patients would likely benefit from early screening and aggressive treatment wherever possible. Currently, there is no proven targeted therapy available for COVID-19. The regimen of lopinavir/ritonavir, nitazoxanide, and intravenous immunoglobulin was chosen for our patient with a history of dual organ transplantation and COVID-19 on the basis of in vitro data,[3] limited clinical data,[4] and drug availability at our institution at the time of this patient's diagnosis. A recent randomized, controlled assessment of lopinavir/ritonavir in adults hospitalized with severe COVID-19 reported no significant benefit.[5] However, it should be emphasized that the patients in this study had relatively few comorbidities and may have received treatment relatively late in the disease process. It is unclear whether these findings can be extrapolated to the transplant population. An important challenge and consideration for use of lopinavir/ritonavir in transplant recipients is significant drug−drug interactions with tacrolimus. There have been limited data supporting the use of the anti-protozoal agent nitazoxanide as an anti-viral drug and immunomodulator, with several case series reporting positive outcomes in transplant patients with a viral illness.[6] In addition, small studies suggest a benefit for using intravenous immunoglobulin replacement in transplant recipients with low-level immunoglobulin and severe infections (our patient's IgG levels were at the lower limit of normal).[7] Prospective evaluation of potential therapies will be important for tailoring treatment for the COVID-19−positive transplant population as the pandemic continues to grow.

References

1. Li F, Cai J, Dong N. First cases of COVID-19 in heart transplantation from China [e-pub ahead of print]. J Heart Lung Transplant. doi: 10.1016/j.healun.2020.03.006, accessed 29 March 2020.
2. Law N, Kumar D. Post-transplant viral respiratory infections in the older patient: epidemiology, diagnosis and management. Drugs Aging 2017;34:743-54.
3. Wang M, Cao R, Zhang L, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res 2020;30:269-71.
4. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054-62.

5. Cao B, Wang Y, Wen D, et al. A trial of lopinavir-ritonavir in adults hospitalized with severe Covid-19 [e-pub ahead of print]. N Engl J Med. doi: 10.1056/NEJMoa2001282, accessed 29 March 2020.
6. Avery RK, Lonze BE, Kraus ES, Marr KA, Montgomery RA. Severe chronic norovirus diarrheal disease in transplant recipients: clinical features of an under-recognized syndrome [e-pub ahead of print]. Transpl Infect Dis. doi: 10.1111/tid.12674, accessed 29 March 2020.
7. Carbone J, Sarmiento E, Del Pozo N, et al. Restoration of humoral immunity after intravenous immunoglobulin replacement therapy in heart transplant recipients with post-transplant antibody deficiency and severe infections. Clin Transpl 2012;26:E277-83.

COVID-19 and transplant research from China: An ethical dilemma

Wendy A. Rogers, BM.BS, BA Hons, PhD, MRCGP, FRACGP,[a,b] and Jacob Lavee, MD[c,d]

From the [a]Department of Philosophy, Macquarie University, Sydney, New South Wales, Australia; [b]Department of Clinical Medicine, Macquarie University, Sydney, New South Wales, Australia; [c]Heart Transplantation Unit, Sheba Medical Center, Ramat Gan, Israel; and the [d]Tel Aviv University Faculty of Medicine, Tel Aviv, Israel.

The Journal of Heart and Lung Transplantation (JHLT) has maintained a policy of not publishing papers that do not comply with the 2007 ethics statement of the International Society for Heart and Lung Transplantation (ISHLT), which states: "Obtaining organs for transplantation from the bodies of executed prisoners contravenes the principle of voluntary donation."[1] Authors are required to indicate that their research complies with the ISHLT policy. The clause pertaining to executed prisoners is particularly significant for Chinese authors, as China is the only country where widespread, state-sanctioned procurement of organs from prisoners has occurred and may still be occurring.[2,3]

The JHLT recently published a paper related to the coronavirus disease 2019 (COVID-19) pandemic that does not conform to the guidance,[4] describing the outcomes of 2 heart transplant recipients in China who were infected with COVID-19. One patient received their allograft in 2003, a time when the vast majority of organs came from executed prisoners.[3] The second patient received their transplant in 2017. It is claimed that since January 2015, all organs in China have been procured from volunteers. Recent investigations, however, have found that data about volunteer donor programs may be unreliable,[3] and there is no conclusive evidence that forced organ removal from prisoners has ceased.[2]

Owing to the lack of compliance with the ISHLT ethical guidance, should this paper have been published? The argument in favor of the publication of research of questionable ethics rests on the potential benefit of the research in terms of scientific value and the potential to save lives or decrease suffering in other patients. According to this argument, the greater the value of the research, the greater the imperative to publish, notwithstanding ethical breaches. This argument supports publication of this paper as it provides the first, and therefore unique, information about COVID-19–infected heart transplant recipients. Against this, we must consider the potential damage done by publishing unethical research, as publication may serve to minimize ethical breaches involved. Taking organs from non-consenting prisoners who may have been killed and their organs recovered is a terrible wrong that goes to the core of transplant ethics, violating the dead donor rule and the imperative for voluntary consent for organ donation. Publishing the paper may implicitly sanction the underlying practice. In addition, such publication makes those who use the results of that research morally complicit by becoming entangled in the underlying ethical breaches.[5] We assume that the JHLT valued the information in this paper to the extent that they felt it outweighed the harms of publication. Recognizing the tension, the Editor agreed to include a note about the ethical breach, as follows:

> Editor's Note: The article published from China may include patients transplanted at a time when concerns existed with unethical procurement of organ donors, and therefore may represent a violation of the publication policy. However, the editors have chosen to override this aspect due to the critical importance of the information provided in such a paper for the benefit and help of our patients while recognizing the dignity of those from whom the unethical organs were most probably obtained.

The note appears on the journal webpage dedicated to COVID-19 and cardiothoracic transplant[6] and also in the published version of these papers.

In our view, the standard for publishing research that involves organs taken from executed prisoners should be exceptionally high. We can expect to see multiple papers from China reporting on various transplant-related aspects of COVID-19,[7] requiring Editors to be alert to potential ethical breaches. However, this scrutiny is not evident. For example, *Transplantation* published a Global Transplantation COVID Report that fails to note that data from China almost certainly includes that derived from unethical transplantations.[8] Opening up prestigious publication platforms such as this journal to papers that are in breach of the ISHLT ethical statement sends a strong message that the journal's ethical standards are open to exceptions (albeit during distinctly unique times). We must beware of turning an ethical blind eye to obtain apparently unique knowledge and seek ways of sharing knowledge that does not confer the prestige of publication on authors involved in ethical breaches.

References

1. International Society for Heart and Lung Transplantation. ISHLT Statement on Transplant Ethics. Available at: https://ishlt.org/publications-resources/professional-resources/standards-guidelines/health-policy-guidance-documents.
2. China Tribunal. Judgment. Available at: https://chinatribunal.com/final-judgment-report/.
3. Robertson MP, Hinde RL, Lavee J. Analysis of official deceased organ donation data casts doubt on the credibility of China's organ transplant reform. BMC Med Eth 2019;20:79. Available at: https://bmcmedethics.biomedcentral.com/articles/10.1186/s12910-019-0406-6.