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.

ELSEVIER

The Journal of
Heart and Lung
Transplantation

http://www.jhltonline.org

CASE ANECDOTE, COMMENTS AND OPINIONS

Ethical considerations of thoracic transplant and circulatory support during the COVID-19 pandemic: A closer look at pulmonary vascular disease

Elisa A. Bradley, MD,[a] Athénaïs Boucly, MD,[b,c] and Raymond L. Benza, MD[a]

From the [a]Division of Cardiovascular Medicine, Department of Internal Medicine, The Ohio State University Wexner Medical Center, Columbus, Ohio; [b]Faculté de Medecine, Université Paris-Saclay, Le Kremlin-Bicêtre, France; and the [c]Assistance publique – Hôpitaux de Paris, Hôpital Bicêtre, Service de Pneumologie et Soins Intensifs Respiratoires, Hôpital Bicêtre, Le Kremlin-Bicêtre, INSERM UMR_S 999, Hôpital Marie Lannelongue, Le Plessis Robinson, France.

The global consequences of severe acute respiratory syndrome coronavirus 2 infection have impacted hospital resources, including the availability of medical personnel, general and intensive care beds, and personal protective equipment, to name a few. In an effort to preserve personal protective equipment, personnel, and inpatient beds, nonemergent procedures and surgeries have largely been electively postponed in many centers. Therefore, it is important to consider the ethical consequences regarding thoracic transplant and circulatory support during the coronavirus disease 2019 (COVID-19) pandemic. These consequences extend to all cardiovascular and pulmonary disease processes that may ultimately be refractory to medical therapy and culminate in end-stage heart failure or respiratory failure, and this includes severe pulmonary vascular disease (pulmonary arterial hypertension [PAH]).

The International Society for Heart and Lung Transplantation COVID-19 Task Force publication by Holm et al[1] outlines proposed stages of the pandemic with respect to healthcare system utilization and considers ethical principles that should be evaluated during the pandemic as set forth by the Organ Procurement and Transplantation Network, inclusive of utility, justice, and respect for persons. Here, we propose that perhaps there are some carve-out groups, such as PAH, who require unique consideration during the pandemic. The Organ Procurement and Transplantation Network has proposed that the major ethical principles applicable to the promotion of equitable outcomes in organ allocation and transplant should include utility, justice, and respect for persons.[2] In the broadest sense, utility takes into account the amount and probability of benefit and risk because it relates to the overall potential population impact, in this case, related to specialized PAH testing and therapy as well as thoracic organ transplantation. In contrast, justice describes the objective (fair) dissemination of these resources and/or thoracic organ transplants. Here, we review the specific principles and effects in a patient with PAH first, as they relate to the availability of specialized testing and treatment and second, with respect to organ allocation and transplantation during the pandemic.

In the face of the current pandemic, one of the challenges that arise in the care of patients with PAH is the ability to admit those requiring invasive hemodynamic testing, which includes those with either (1) a new diagnosis of PAH or (2) declining functional capacity. This is critically important because these patients derive significant benefit (utility) from early initiation and/or titration of PAH-specific medication. Given that delaying initiation or titration of PAH therapy leads to increased morbidity and mortality, in the currently proposed stages of the pandemic, it is likely that invasive hemodynamic testing in patients with suspected new or worsening PAH should not be restricted. It is worth mentioning that these procedures may be done either outpatient or inpatient, depending on the individual degree of illness. Importantly, it would be rare that hospitalization of patients with PAH requiring invasive hemodynamic testing would compromise intensive care beds, which are best conserved for patients with active COVID-19 infection thus avoiding any competition between the patient with PAH requiring this evaluation and those needing COVID-19 care, therefore complying with just allocation of testing/treatment resources. Timely initiation of PAH therapy and/or medication titration may theoretically reduce the future need for intensive care in this group; therefore, prioritization of this workup may be particularly important when resources such as intensive care beds are scarce. Consultation with an expert and specialized pulmonary hypertension team would be useful to help determine which patients would benefit from this approach.

Advanced resource allocation for the patient with PAH, including mechanical support and organ transplant, has been questioned with respect to the principle of utility. This is largely driven by the concern that patients with PAH are high-risk and have increased potential for post-transplant graft dysfunction and increased resource utilization.[3]

However, some studies have demonstrated that up-front risk stratification of patients with PAH according to estimates of 1-year mortality can correctly identify which

1053-2498/$ - see front matter
https://doi.org/10.1016/j.healun.2020.05.014

subset of patients with PAH may benefit most while minimizing overall risk and resource utilization.[4–6] It will be crucially important to identify those patients with PAH that have a reasonable perspective for recovery. One way to assess this is to determine which patients with PAH have low-to-intermediate calculated 1-year mortality (such as using the Registry to Evaluate Early and Long-Term PAH Disease Management 2.0 score (≤8 is favorable). Perhaps, this small subset of patients with PAH should continue to be considered for mechanical support and/or transplant, irrespective of PAH itself, however noting that this will require ongoing input and assessment from the advanced transplant team, weighing risks/benefits and considering similar parameters in other individuals concurrently listed, to identify those patients with the best chance for a full recovery and least resource utilization (utility).

We must also consider the effects of COVID-19 on the patient with PAH more specifically. It is not entirely clear whether patients with underlying pulmonary disease and PAH do worse with COVID-19.[7] Therefore, it is not likely fair (justice) to impart resource restriction to the patient with PAH listed for transplant during the pandemic on the basis of disease process alone. Reflecting further on PAH, one must consider the unique pathophysiologic consequences inflicted upon the cardiovascular and pulmonary systems in those infected with COVID-19. Indeed, both the disease itself and subsequent treatment (ventilation and positive end-expiratory pressure) have profound adverse effects on the right ventricle, which in many cases is already adversely remodeled in PAH. Thus, it would be anticipated that patients with PAH with COVID-19 would not fare well and that resource allocation might be best utilized for others. Conversely, given that significant endothelial dysfunction and vascular complications are implicated in COVID-19, theoretically, PAH-specific medications may be beneficial as they target endothelial function and offload the right ventricle.[4,5] In addition, several PAH-specific therapies may also impart direct anti-Coronaviridae viral effects.[8,9]

In summary, operational ethical principles applied to the overarching cardiovascular and pulmonary transplant groups should equally extend to those with an underlying diagnosis of pulmonary vascular disease. It is important to maintain accessibility to invasive hemodynamic testing in those patients with new and/or suspected worsening of PAH despite the stage of the current pandemic. Finally, advanced resources such as mechanical circulatory support and organ transplant may be considered in a small subset of patients with PAH identified as having a reasonable perspective of recovery and if overall vetted risk among other recipients remains relatively low.

References

1. Holm AM, Mehra MR, Courtwright A, et al. Ethical considerations regarding heart and lung transplantation and mechanical circulatory support during the COVID-19 pandemic: an ISHLT COVID-19 task-force statement [e-pub ahead of print]. J Heart Lung Transplant doi: 10.1016/j.healun.2020.04.019, accessed April 26, 2020.
2. Organ Procurement and Transplantation Network>2015 ethical principles to be considered in the allocation of human organs. Available at: https://optn.transplant.hrsa.gov/resources/ethics/ethical-principles-in-the-allocation-of-human-organs/.
3. Diamond JM, Lee JC, Kawut SM, et al. Clinical risk factors for primary graft dysfunction after lung transplantation. Am J Respir Crit Care Med 2013;187:527-34.
4. Galiè N, Humbert M, Vachiery JL, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: the Joint Task Force for the diagnosis and treatment of pulmonary hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT) [published correction appears in Eur Respir J 2015;46:1855-6]. Eur Respir J 2015;46:903−75.
5. Benza RL, Gomberg-Maitland M, Elliott CG, et al. Predicting survival in patients with pulmonary arterial hypertension: the REVEAL risk score Calculator 2.0 and comparison with ESC/ERS-based risk assessment strategies. Chest 2019;156:323-37.
6. Hoeper MM, Benza RL, Corris P, et al. Intensive care, right ventricular support and lung transplantation in patients with pulmonary hypertension. Eur Respir J 2019;53:1801906.
7. The Lancet Respiratory Medicine. Time to wake the giant of obstructive sleep apnoea. Lancet Respir Med 2020;8:1.
8. Akerström S, Mousavi-Jazi M, Klingström J, Leijon M, Lundkvist A, Mirazimi A. Nitric oxide inhibits the replication cycle of severe acute respiratory syndrome coronavirus. J Virol 2005;79:1966-9.
9. Keyaerts E, Vijgen L, Chen L, Maes P, Hedenstierna G, Van Ranst M. Inhibition of SARS-coronavirus infection in vitro by S-nitroso-N-acetylpenicillamine, a nitric oxide donor compound. Int J Infect Dis 2004;8:223-6.

COVID-19 leading to acute encephalopathy in a patient with heart transplant

Kristine Jang, DO,[a] Akshay Khatri, MBBS, MD,[b] and David T. Majure, MD, MPH[a,c]

From the [a]Department of Cardiology, North Shore University Hospital, Manhasset, New York; [b]Division of Infectious Disease, Department of Medicine, North Shore University Hospital, Northwell Health, Manhasset, New York; and the [c]Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, New York.

There is increasing evidence that severe acute respiratory syndrome coronavirus (CoV) 2 (SARS-CoV-2) impacts the neurologic system.[1–3] However, how the immunosuppressed state modifies neurologic involvement and clinical course remains uncertain.[4] We describe a patient with heart transplant who developed prolonged symptoms of encephalopathy late in CoV disease 2019 (COVID-19) illness.

A 67-year-old man was admitted with fever, cough, nasal congestion, sore throat, and diarrhea 20 months after an uneventful heart transplantation. He was not hypoxic. Chest computed tomography (CT) showed bilateral multifocal peripheral ground-glass opacities (GGOs). White blood cell count was 4,720/μl with lymphocyte count of 1,040/μl. Blood cultures and cytomegalovirus polymerase chain reaction (PCR) were unremarkable. C-reactive protein (CRP) was 0.55 mg/dl. Nasopharyngeal PCR for SARS-CoV-2 was positive, consistent with COVID-19 illness. Immunosuppression included 500 mg mycophenolate