Received: 25 April 2020 | Revised: 23 June 2020 | Accepted: 27 June 2020

DOI: 10.1111/ctr.14029

ORIGNAL ARTICLE

Clinical TRANSPLANTATION
The Journal of Clinical and Translational Research
WILEY

Heart transplantation in the era of the SARS-CoV-2 pandemic: Is it safe and feasible?

Gabriel Esmailian[1] | Jon A. Kobashigawa[2] | Keith Nishihara[2] | Jignesh K. Patel[2] | Lawrence Czer[2] | Dominick Megna[2] | Dominic Emerson[2] | Danny Ramzy[2] | Alfredo Trento[2] | Joanna Chikwe[2] | Fardad Esmailian[2]

[1]The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, USA

[2]Cedars-Sinai Smidt Heart Institute, Los Angeles, California, USA

Correspondence
Fardad Esmailian MD, Cedars-Sinai Smidt Heart Institute, 127 S San Vicente Blvd, 90048 CA.
Email: fardad.esmailian@cshs.org

Abstract

As the SARS-CoV-2–pandemic continues to unfold, the number of heart transplants completed in the United States has been declining steadily. The current case series examines the immediate short-term outcomes of seven heart transplant recipients transplanted during the SARS-CoV-2 pandemic. We hope to illustrate that with proper preparation, planning, and testing, heart transplantation can be continued during a pandemic. We assessed 7 patients transplanted from March 4, 2020, to April 15, 2020. The following endpoints were noted: in-hospital survival, in-hospital freedom from rejection, in-hospital nonfatal major cardiac adverse events (NF-MACE), severe primary graft dysfunction, hospital length of stay, and ICU length of stay. There were no expirations throughout the hospital admission. In addition, there were no patients with NF-MACE or treated rejection, and 1 patient developed severe primary graft dysfunction. Average length of stay was 17.2 days with a standard deviation of 5.9 days. ICU length of stay was 7.7 days with a standard deviation of 2.3 days. Despite the decreasing trend in completed heart transplants due to SARS-CoV-2, heart transplantation appears to be feasible in the immediate short term. Further follow-up is needed, however, to assess the impact of SARS-CoV-2 on post–heart transplant outcomes months after transplantation.

KEYWORDS

COVID-19, donors and donation, heart transplantation, infection and infectious agents, pandemic, patient survival, SARS-CoV-2, viral

1 | INTRODUCTION

Heart transplantation continues to be an optimal treatment for select patients with end-stage heart failure. However, throughout its 52-year history, heart transplantation has not faced the impact of a pandemic near the scope of SARS-CoV-2. In the wake of the current SARS-CoV-2 pandemic, there has understandably been concern regarding solid organ transplantation given the highly immunosuppressed state of post–transplant recipients.[1] These patients are at increased susceptibility for viral and bacterial infections with possible risk of graft rejection as immunosuppression dosages are slowly lowered to fight the infection.[2]

Despite the continuation of transplant surgeries, the impact of SARS-CoV-2 on the transplant community is already apparent. Starting February 23, 2020, and continuing into the middle of April, there was a decline in the number of heart transplant waitlist

additions in the United States. From March 15 to April 11, the rate of inactivation exceeded that of additions with an overwhelming majority of inactivation being noted as SARS-CoV-2 precaution.[3] Moreover, between March 8 and May 2, there was a 24.1% decrease in donors recovered and a 23.8% decrease in completed heart transplants when compared to approximately 2 months prior to the pandemic.[3] As more states maintain efforts to control the spread of the virus, the current downward trend in heart transplants completed will surely continue.

To help combat the spread of the virus and limit resource usage, many centers around the nation, including ours, have suspended elective surgeries during the pandemic or "lockdown." However, our center decided to continue with heart transplantation for a select group of high urgency-listed patients given the possible increased waitlist mortality should these surgeries be put on hold.

Throughout the ongoing SARS-CoV-2 pandemic, short-term outcomes of heart transplant recipients have yet to be assessed at a high-volume transplant center. Thus, the purpose of the current case series was to show that heart transplantation continues to be a feasible and effective therapy for select patients despite the current SARS-CoV-2 pandemic.

2 | METHODS

In total, seven patients transplanted from California's declaration of a State of Emergency on March 4, 2020, to April 15, 2020, were assessed retrospectively at a single center. Informed consent was obtained, and our institutional review board approved the study.

Demographics were noted, and the patients were assessed on the following endpoints: in-hospital survival, in-hospital freedom from rejection (acute cellular, antibody-mediated, and hyperacute), in-hospital nonfatal major cardiac adverse events (NF-MACE: myocardial infarction, new congestive heart failure, percutaneous coronary intervention, implantable cardioverter-defibrillator/pacemaker implant, stroke), severe primary graft dysfunction (PGD), hospital length of stay, and ICU length of stay.

TABLE 1 Demographics for the recipients transplanted from March 4, 2020, to April 15, 2020

Demographics	Transplanted 3/4/2020-4/15/2020 (n = 7)
Mean recipient age, years ± SD	54.3 ± 13.9
Mean donor age, years ± SD	36.7 ± 12.9
Body mass index ± SD	26.2 ± 4.6
Female, n (%)	2 (29)
Previous pregnancy in females, n (%)	2 (100)
Mean ischemic time, mins ± SD	171.3 ± 43.6
Status at transplant	
2	5 (71.4)
3	1 (14.3)
4	1 (14.3)
Cytomegalovirus mismatch, n (%)	2 (29.3)
Diabetes mellitus, n (%)	3 (42.9)
Treated hypertension, n (%)	5 (71.4)
Durable MCS, n (%)	0
Prior blood transfusion, n (%)	2 (29.3)
Peak pre-transplant PRA ≥10%, n (%)	1 (14.3)
Pre-transplant creatinine, mean ± SD	2.2 ± 1.9
Durable LVAD	0
Temporary MCS	5 (71.4)
Donor cause of death, n (%)	
Gunshot wound to head	2 (29.3)
Blunt injury to head	1 (14.3)
Anoxia	4 (57.1)
Diagnoses, n (%)	
Dilated cardiomyopathy	4 (57.1)
Ischemic cardiomyopathy	1 (14.3)
Amyloid	1 (14.3)
Recurrent AMR post–heart transplant	1 (14.3)
Redo sternotomy	1 (14.3)
Combined heart–kidney transplant	3 (42.9)

3 | RESULTS

Table 1 depicts the full demographics for the seven patients transplanted after March 4, 2020. Mean recipient age was 54.3 years with a standard deviation of 13.9 years. Mean donor age was 36.7 with a standard deviation of 12.9 years. There were two female recipients and five male recipients. Of the two females, both had previous pregnancies. Mean ischemic time was 171.3 minutes with a standard deviation of 43.6 minutes. Five patients were listed as status 2 prior to transplant. In addition, one patient was status 3 and one patient was status 4 prior to transplant. None of the patients had durable mechanical circulatory support (MCS) devices, and five had temporary MCS devices. Diagnoses prior to heart transplant included five patients with dilated cardiomyopathy, one patient with ischemic cardiomyopathy, one patient with amyloid, and one patient with recurrent antibody-mediated rejection post-transplant. Lastly, three patients received combined heart-kidney transplants, and one patient had a redo sternotomy.

Table 2 depicts the in-hospital admission endpoints for the same seven recipients. Of these patients, there were no expirations throughout the hospital admission. In addition, there were no in-hospital NF-MACE events or treated rejection. One patient developed severe primary graft dysfunction. Average length of stay was 17.2 days with a standard deviation of 5.9 days. ICU length of stay was 7.7 days with a standard deviation of 2.3 days.

TABLE 2 Endpoints during hospital admission for recipients transplanted from March 4, 2020, to April 15, 2020

Endpoints during transplant hospital admission	Transplanted 3/4/2020-4/15/2020 (n = 7)
Survival, n (%)	7 (100%)
Nonfatal major cardiac adverse events , n (%)	0 (0%)
Any treated rejection, n (%)	0 (0%)
Acute cellular rejection, n (%)	0 (0%)
Antibody-mediated rejection, n (%)	0 (0%)
Hyperacute rejection, n (%)	0 (0%)
Severe PGD, n (%)	1 (14.3%)
Hospital length of stay, days ± SD	17.2 ± 5.9
ICU length of stay, days ± SD	7.7 ± 2.3

4 | DISCUSSION

Our main objective for the current case series was to illustrate that in the era of SARS-CoV-2, where the number of heart transplants has decreased since mid-March,[3] heart transplantation continues to be a safe and feasible option for select patients. Overall, there were no expirations for the seven patients transplanted during the SARS-CoV-2 pandemic. No patients experienced in-hospital rejection or NF-MACE events, and length of stay metrics was acceptable. One patient with prior sternotomy had a severe case of PGD secondary to significant amount of blood transfusion perioperatively for severe coagulopathy. He required extracorporeal membrane oxygenation support for 72 hours. However, he has fully recovered.

Several factors may have contributed to the favorable outcomes shown for these recipients. Our initial planning involved prioritizing transplanting status 1-status 3 patients due to their urgency and potential high waitlist mortality. Furthermore, status 4-status six patients were selected for transplantation on a case-by-case basis. Factors determining our selection for status 4-status six patients included restrictive cardiomyopathies such as cardiac allograft vasculopathy and amyloidosis, patients with total artificial hearts, and complications from left ventricular assist device (LVAD) placement such as infection, LVAD thrombosis, and RV dysfunction. Although none of our patients in this series had durable MCS devices, patients with durable MCS devices listed status 1-status 3 would have been considered for transplantation if a suitable donor became available. The combination of prioritizing status 1-status 3 patients for transplantation, and the limited sample size may have accounted for the lack of transplant recipients with stable durable MCS devices in this cohort. One patient underwent redo heart transplant combined with kidney transplant who was listed as status 4. The patient was transplanted due to recurrent antibody-mediated rejection refractory to medical therapy.

After discussions with organ procurement agencies, a decision was made that all the donors were to be tested for SARS-CoV-2. The donors from areas denoted as "hot spots," which had significant increases in SARS-CoV-2 incidence, were not excluded. The organs were then allocated after two negative RT-PCR tests. In addition, all the recipients were required to be tested prior to transplantation with a negative result within the 7 days prior to transplantation. In the event, there was not enough time from obtaining the results of the test and the scheduled donor operating room time, and the organ was not accepted by our center.

In addition, all status 1-status 3 patients were isolated in non–SARS-CoV-2 areas of the hospital. Only the primary caregivers, such as the attending and fellow, made daily rounds on the patients. Other healthcare providers who may have had contact with suspected or confirmed positive SARS-CoV-2 patients in the hospital, such as respiratory therapists and nursing staff, would not be assigned to pre- or post–heart transplant recipients. The entire cardiac surgery intensive care unit and coronary care unit were assigned to non–SARS-CoV-2 patients. Standard immunosuppression regimen was maintained without any changes. This included triple therapy with tacrolimus, mycophenolate mofetil, and corticosteroid. Antithymocyte globulin induction therapy was used in patients with renal insufficiency and dual-organ transplantation such as heart-kidney transplantation.

Prior to the pandemic and as part of our standard practice, all of our transplant patients were followed routinely by infectious disease doctors postoperatively. Appropriate changes to antimicrobial medications would be made as necessary. During the pandemic, no changes were made to this routine practice. In addition, no serial SARS-CoV-2 testing was done for recipients postoperatively.

To further limit possible SARS-CoV-2 exposure, our heart transplant outpatient clinic transitioned to telemedicine video visits for all patients over 1 year out post-transplant. In-person visits for new transplant recipients continued for the first 6 months post-transplantation. However, video visits were utilized on postoperative months 7, 9, and 11 during the pandemic. As part of routine surveillance for detecting early rejection prior to the pandemic, endomyocardial biopsies were obtained for the first 6 months post-transplantation. Gene expression profiling, such as AlloMap, was utilized from the 7th month post-transplantation onward. This pattern of surveillance did not change during the pandemic. Blood draws were done at home for gene expression profiling and adjustment of immunosuppressive medication. Lastly, we eliminated the early coronary angiogram during the pandemic.

Although recent pandemics have not reached the magnitude of SARS-CoV-2, there have been studies examining the impact of these pandemics on the organ sharing network and transplantation. In 2010, 5 H1N1 influenza–positive donors were followed in the United Kingdom.[4] Of the 13 recipients who received organs from these donors, none contracted H1N1 influenza.[4] Another case report highlighted four recipients of organs (3 kidneys and 1 liver) from H1N1-positive donors.[5] All four recipients showed good short-term outcomes post-transplant. However, in contrast to H1N1 influenza, SARS-CoV-2 presents a greater challenge due to its severe respiratory sequelae, high transmission rate, and possible asymptomatic transmission.[6] Although the current study did not accept hearts

from SARS-CoV-2 positive donors, similar post-transplant outcomes were found compared with the previous study that examined transplanting recipients with H1N1-positive donors.[5]

4.1 | Study limitations

The current study's primary limitation included a small sample size for the patient population transplanted during the SARS-CoV-2 pandemic. The study also examined the recipients' outcomes solely throughout the in-hospital admission. Further long-term monitoring is needed to assess the impact of SARS-CoV-2 months after transplantation. In addition, only heart and combined heart-kidney transplant recipients were examined. Therefore, caution must be taken in extrapolating the data to other solid organ transplantation.

5 | CONCLUSION

Even in the era of a pandemic such as SARS-CoV-2, with proper preparation, testing, and strategic hospital space planning, heart transplantation appears to be feasible with acceptable short-term outcomes. This pattern of practice should continue to provide this therapeutic option to the patients with high waitlist mortality. Furthermore, more stable patients can potentially get transplanted as more donors are tested despite the continuing current downward trend in heart transplants during the pandemic.

CONFLICT OF INTEREST

Dr Kobashigawa serves as a consultant to CareDx. Dr Patel receives funding from Alexion Pharmaceuticals and serves as a consultant to Care Dx. The remaining authors have no disclosures to report.

AUTHORS' CONTRIBUTIONS

Gabriel Esmailian, Jignesh Patel, and Fardad Esmailian: Conceptualized or designed the study; Gabriel Esmailian: Drafted the article. Jon Kobashigawa: Critically revised the manuscript; Jon Kobashigawa and Fardad Esmailian: Approved the article; Keith Nishihara, Lawrence Czer, Dominick Megna, Dominic Emerson, Danny Ramzy, Alfredo Trento, and Joanna Chikwe: Analyzed or interpreted the data; and Keith Nishihara: Collected data.

ORCID

Gabriel Esmailian https://orcid.org/0000-0002-1820-7910
Dominic Emerson https://orcid.org/0000-0001-5728-0152

REFERENCES

1. Aslam S, Mehra MR. COVID-19: yet another coronavirus challenge in transplantation. *J Heart Lung Transplant*. 2020;39(5):408-409.
2. Vilchez RA, McCurry K, Dauber J, et al. Influenza virus infection in adult solid organ transplant recipients. *Am J Transplant*. 2002;2:287-291.
3. COVID. United network for organ sharing. https://unos.org/covid/#AnchorData. Accessed April 12, 2020.
4. Halliday N, Wilmore S, Griffiths PD, Neuberger J, Thorburn D. Risk of transmission of H1N1 influenza by solid organ transplantation in the United Kingdom. *Transplantation*. 2012;93(5):551-554.
5. Cockbain AJ, Jacob M, Ecuyer C, Hostert L, Ahmad N. Transplantation of solid organs procured from influenza A H1N1 infected donors. *Transplant Int*. 2011;24:e107-e110.
6. Bai Y, Yao L, Wei T, et al. Presumed asymptomatic carrier transmission of COVID-19. *JAMA*. 2020;323(14):1406.

How to cite this article: Esmailian G, Kobashigawa JA, Nishihara K, et al. Heart transplantation in the era of the SARS-CoV-2 pandemic: Is it safe and feasible?. *Clin Transplant*. 2020;34:e14029. https://doi.org/10.1111/ctr.14029