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BRIEF COMMUNICATION

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Heart transplantation in the early phase of the COVID-19 pandemic: A single-center case series

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Abstract

The infectious disease coronavirus disease 2019 (COVID-19) was declared a pandemic by the World Health Organization in March 2020. The impact of COVID-19 on solid organ transplantations, including heart transplantation, is currently unclear. Many transplant programs have been forced to swiftly re-evaluate and adapt their practices, leading to a marked decrease in transplants performed. This trend has been due to various factors, including increased donor COVID-19 screening scrutiny and recipient waiting list management in anticipation of COVID-19 critical care surge capacity planning. In the face of these unknown variables, determining when and how to proceed with transplantation in our population of patients with end-stage cardiomyopathies is challenging. Here, we describe our center's experience with orthotopic heart transplantation (OHT) in one of the country's pandemic epicenters, where we performed eight OHTs in the first 2 months after community spread began in late February 2020.

KEYWORDS

coronavirus, COVID-19, heart transplantation, pandemic, SARS-CoV-2

1 | INTRODUCTION

On February 26, 2020, the first case of community spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the United States (US) was confirmed.[1] SARS-CoV-2 causes coronavirus disease 2019 (COVID-19), and on March 11, the World Health Organization declared COVID-19 a global pandemic. By May 27, 2020, SARS-CoV-2 had infected over 1.6 million people in the United States, resulting in over 100 000 deaths.[2]

The ongoing pandemic has presented a challenging predicament for organ transplantation programs. The combination of a protracted asymptomatic incubation period of SARS-CoV-2 and the lack of capacity for rapid testing of potential donors to avoid transmission of SARS-CoV-2 were challenges to transplant programs.[3] Further, the effects of SARS-CoV-2 in highly immunosuppressed patients in the early post-transplant period are currently unclear. Nonetheless, it has been assumed that any significant viral infection in this patient cohort would be detrimental, which has been demonstrated in early reports.[4] In addition, cardiovascular disease has emerged as a risk factor for mortality with COVID-19.[5] Indeed, the number of patients inactivated on the heart transplant waitlist more than doubled between the weeks of March 8 and

TABLE 1 Summary of clinical parameters of heart transplant recipients in COVID-19 pandemic

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8
Age (years)	51	48	56	51	63	56	53	65
Sex	Female	Female	Male	Male	Male	Male	Male	Male
Medical history	LVAD	Inotrope	Impella 5.0, inotrope	Inotrope	Home inotrope	Home inotrope	Inotrope	Inotrope
Blood type	B+	O−	O+	O+	O+	A+	O+	B+
Listing status on transplant	Status 3	Status 3	Status 2	Status 3	Status 4	Status 4	Status 3E	Status 3
Donor testing for SARS-CoV-2	None	None	PCR NP and BAL	PCR BAL	PCR BAL	PCR NP and BAL	PCR NP and BAL	PCR NP and BAL
Recipient testing for SARS-CoV-2	None	None	PCR NP	PCR NP	PCR NP	PCR NP	PCR NP	PCR NP
Induction immunosuppression	None	None	Basiliximab	None	None	None	Basiliximab	Basiliximab
Immunosuppression regimen	Tacrolimus, mycophenolate mofetil, corticosteroids	Tacrolimus, mycophenolate mofetil, corticosteroids	Tacrolimus, mycophenolate mofetil, corticosteroids	Tacrolimus, mycophenolate mofetil, corticosteroids	Tacrolimus, mycophenolate mofetil, corticosteroids	Tacrolimus, mycophenolate mofetil, corticosteroids	Tacrolimus, mycophenolate mofetil, corticosteroids	Tacrolimus, mycophenolate mofetil, corticosteroids
Length of stay (days after transplant)	12	8	13	12	13	7	28	8
Readmitted? (time after discharge, reason for admission)	Yes: 60 d, volume overload	Yes: 20 d, hyperglycemia	No	Yes: 3 d, volume overload	No	No	No	No
New DSA?	No	No	No	No	No	No	No	No
COVID-19–related complications?	No	No	No	No	No	No	No	No

Abbreviations: BAL, bronchoalveolar lavage;COVID-19, coronavirus disease 2019; DSA, donor-specific antibodies; LVAD, left ventricular assist device; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

March 15 in the United States, and the number of weekly orthotopic heart transplantation (OHT) procedures decreased from 76 to 50 during the same time span according to the United Network for Organ Sharing.[6] These trends persisted through the week of April 5, when only 43 OHTs were performed, but by mid-May, returned to pre-pandemic levels.

The potential risks of OHT in this setting need to be weighed against the well-established risk of mortality on the waitlist in patients with advanced heart failure (HF). In this context, we describe our center's OHT experience in this early phase of the pandemic. Located in one of the country's epicenters (Los Angeles, California), our program performed eight OHTs in the first two months since community spread began. As detailed below, there have been no COVID-19–related complications thus far.

2 | CASES

From early March 2020 to late April 2020, our program performed eight OHTs, and the details of each case are summarized in Table 1. Patient ages ranged from 48 to 65 years, with three male and two female patients transplanted during this period. One patient was transplanted after Status 2 listing, given the need for percutaneous temporary left ventricular assist device (LVAD) support. Five patients were transplanted after Status 3 listing, and two patients were transplanted after outpatient Status 4 listing. One patient (Case 7) underwent dual-organ (heart-kidney) transplantation.

Per our program protocol, all eight patients were maintained on a triple immunosuppression regimen post-transplant—tacrolimus (target trough 10-15 ng/mL), mycophenolate mofetil (1 gram orally twice daily), and high-dose corticosteroids. Three of the eight patients received induction immunosuppression with basiliximab. The decisions of whether or not to use basiliximab in each case were based on our program's routine protocol, and they were not influenced by concern of the developing pandemic.

For Cases 1 and 2, neither the donors nor recipients were tested for SARS-CoV-2; at that time, testing was not available nor required by our program. Starting with Case 3, with increased testing capacity, our heart transplant program had instituted a policy requiring reverse-transcriptase polymerase chain reaction (RT-PCR) testing of both the donor (bronchoalveolar lavage [BAL] sample) and the recipient (nasopharyngeal [NP] or BAL sample) for SARS-CoV-2. Negative tests from both donors and recipients were required within 48 hours of the transplant procedure.

Over the course of these eight cases, our program had transitioned our post-transplant education to a hybrid in-person and telehealth approach to minimize the potential risk of viral transmission to patients and other team members. Patients received explicit education on the importance of hand hygiene, face mask use, and practice of social distancing. Our transplant coordinator, nutritionist, and pharmacist delivered sessions with the patients and their caregivers via a secure telehealth platform.

Three of the eight patients were readmitted to the hospital during this period: two for worsening volume overload and one for severe hyperglycemia. There have been no COVID-19–related complications in any of the eight patients thus far.

3 | DISCUSSION

The COVID-19 pandemic poses complex challenges for organ transplant programs around the world, particularly in epicenters,[7] forcing many programs to re-evaluate their practices. These decisions must weigh the known benefit of OHT against the potential risk of nosocomial spread of SARS-CoV-2, the undetermined effect of the pandemic on the donor pool and wait time, the possibility of acquiring COVID-19 from a donor in the setting of limited testing capabilities, and the unclear impact of SARS-CoV-2 infection in the early post-transplant period, among other risks. Accordingly, after COVID-19 was declared a pandemic, the number of OHTs performed in the United States markedly dropped, largely due to a dramatic increase in the number of inactivated patients on the waitlist due to COVID-19 concerns.[6]

While located in a COVID-19 epicenter in the United States, our hospital is a quaternary care center that prepared itself to accommodate a surge in patients with COVID-19. As cases of COVID-19 rose in our hospital, our surge planning protocol triggered the formation of designated intensive care units (ICUs) for the care of critically ill patients with COVID-19. These COVID-19–designated ICUs were physically separated from the ICUs where our patients are roomed pre- and post-transplantation. Fortunately, during the period described, we did not near reaching our hospital's ICU bed capacity. Further, our hospital is a specialized extracorporeal membrane oxygenation (ECMO) center, and during the period described in this report, we managed two patients with COVID-19 who required veno-venous ECMO.

In this setting, our program made the decision to continue heart transplantation, and our OHT volume remained unchanged during this time. Interestingly, the number of donor organ offers our program received during the period described did not differ significantly from the number of offers seen in the prior two years. Critical to our efforts were the following adaptations:

- Frequent reassessment of our hospital and ICU bed capacity,
- Acceptance of organ offers for only our highest urgency recipients at greatest risk of waitlist mortality (Statuses 1-3, select Status 4 patients),
- Counseling actively listed patients on COVID-19 screening policies implemented by our program for potential donors and informing them of the option to inactivate their status on the waitlist,
- Strict COVID-19 screening (ie, travel history to endemic areas, possible exposures to known or suspected cases, concerning symptoms) and testing criteria for donors and recipients (RT-PCR testing negative for SARS-CoV-2 from donor BAL sample *and*

recipient NP or BAL sample within 48 hours prior to transplant procedure),

- Strict enforcement of hospital infection control policies (ie, restriction of hospital visitors),
- Effective local community infection control policies, and
- Integration of virtual telehealth platforms into post-transplant education and care.

These policies are similar to those described by other centers in high endemicity areas.[8] Central to our plan was the requirement that, once testing became available, both the donor and recipient undergo RT-PCR testing for SARS-CoV-2. UCLA developed an internal RT-PCR test with a high negative predictive value, and for donors in our local organ procurement organization, we had samples couriered to our laboratories for rapid testing (<24-hour turnaround time early in the pandemic course, improving to <4 hours later) when testing was not immediately available at the donor hospital. This protocol increased our confidence that infection was unlikely in potential donors, reducing risk to our recipients and our surgical procurement team. Indeed, our program would decline offers if the donor hospital could not provide a BAL sample for testing. Current recommendations from the International Society of Heart and Lung Transplantation (ISHLT) are for all potential donors to undergo PCR-based testing for SARS-CoV-2.[9] While ISHLT recommendations do not state a preferred specimen, they note that the tracheal aspirate and BAL samples yield higher sensitivity,[10] which factored into our decision to require BAL samples for donors.

Starting in early April 2020, with increased testing capacity available, our hospital implemented policies whereby all patients admitted to the hospital required PCR-based testing of an NP sample for SARS-CoV-2. Also, all patients undergoing procedures (including right heart catheterizations and transplant surgeries) were required to have PCR-based testing of an NP sample within 48 hours prior to the procedure. While our program did not require COVID-19 testing in order to list a transplant candidate, these measures taken together strengthened our confidence in the safety of proceeding with heart transplantation in our recipients.

Additionally, strict enforcement of our hospital's visitor policy, which restricted visitors from entering patients' rooms, and a reinforced education program on social distancing and hand hygiene were critical elements for patients who underwent transplantation. Furthermore, Los Angeles County issued "Stay at Home" orders on March 20, 2020, which may have helped to protect patients from exposure and infection after their discharge.

In our eight cases performed during the period of pandemic onset (Table 1), none have become infected with SARS-CoV-2 to

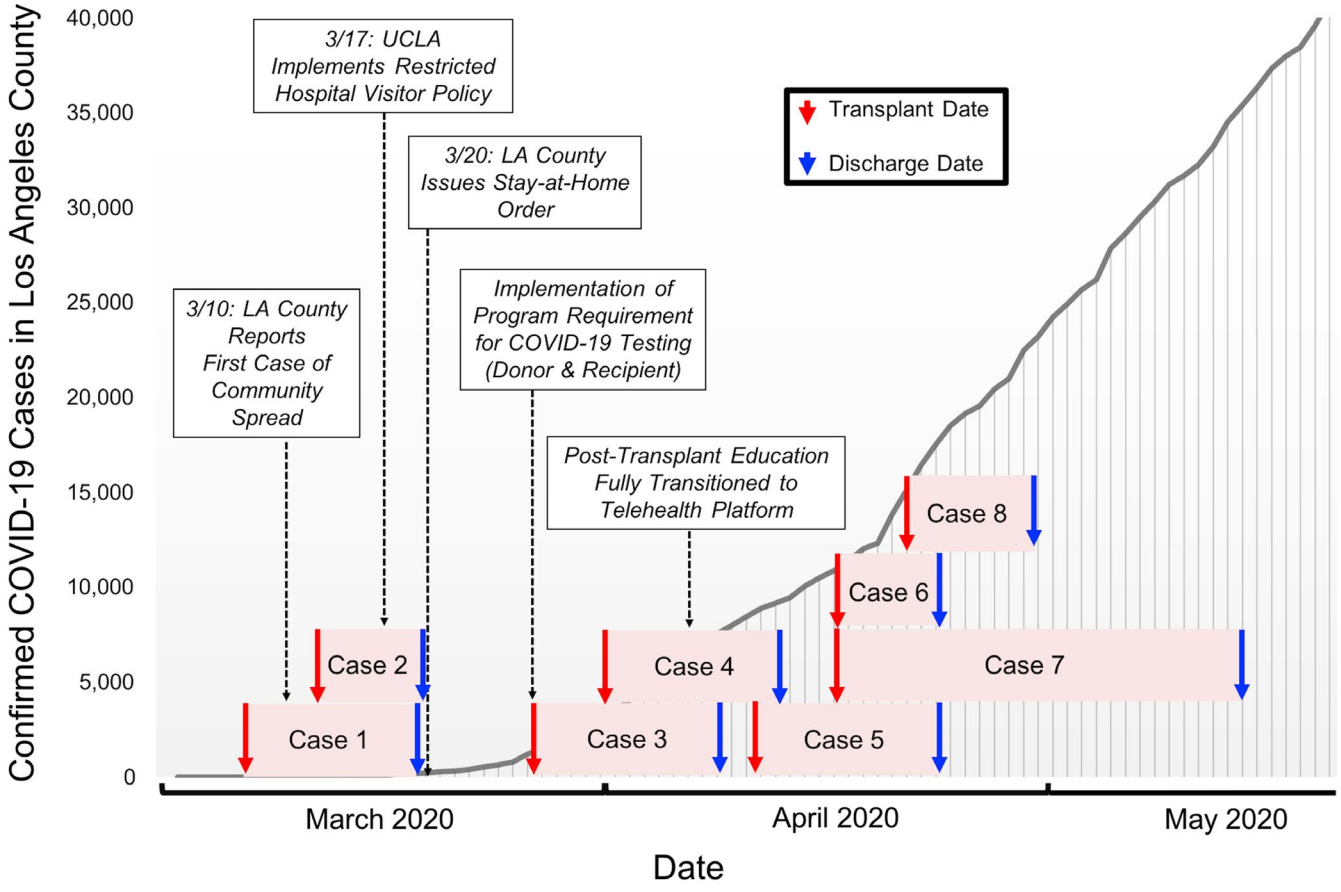

FIGURE 1 Heart transplantations at UCLA during first phase of COVID-19 pandemic in Los Angeles, California. Visual representation of the timing of heart transplantations at UCLA relative to the growth of confirmed COVID-19 cases in Los Angeles County. (Source: Los Angeles Times[15])

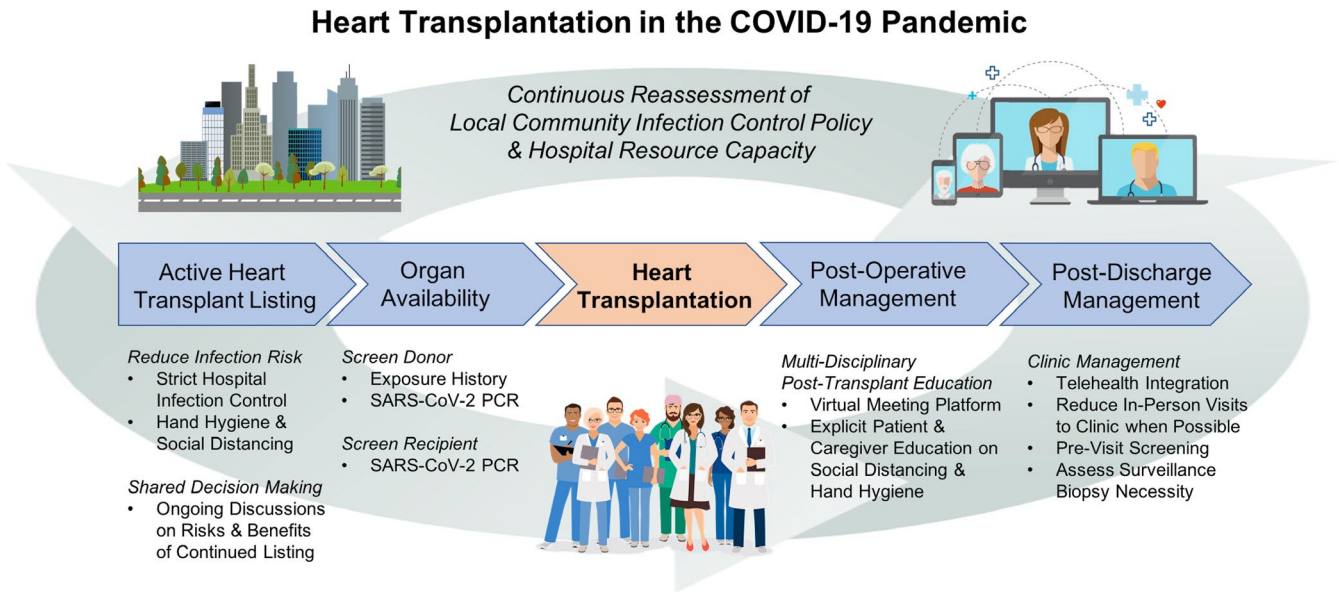

FIGURE 2 Heart transplantation in the COVID-19 pandemic

date, despite the growing number of cases in Los Angeles (Figure 1). Importantly, the first two cases did not receive either donor or recipient testing for SARS-CoV-2, as they occurred during the initial period in which testing was unavailable or greatly limited. Additionally, two of the eight cases underwent transplant after waiting at home (Status 4). The impact of social distancing and hand hygiene education that post-transplant patients receive likely played a strong role. Supporting this notion is the observation that a low rate of SARS-CoV-2 infection was seen in OHT recipients in Wuhan.[11] Importantly, we actively decided to continue performing surveillance endomyocardial biopsies per our normal protocol. However, we have required that all of our outpatients have COVID-19 testing within 48 hours before their procedure to reduce the exposure risk to team members.

We and others have reported cases of COVID-19 in longer-term OHT recipients, which had relatively benign clinical courses.[12,13] However, a recent study found a 25% case fatality rate among OHT patients,[14] and a full understanding of COVID-19 in this population remains to be determined. Similarly, the impact of SARS-CoV-2 infection in a patient with a newly transplanted cardiac graft is unclear, as to our knowledge, there have yet to be any cases reported at the time of this communication. While only 3 of our 8 patients above received induction immunosuppression therapy, we continued to make decisions on induction following our standard protocol, not solely for the purpose of infection prevention. More evidence is needed to determine the risks of SARS-CoV-2 infection in newly transplanted patients.

In summary, we describe our center's experience with 8 patients with varied paths to transplantation (Statuses 2-4) who underwent successful OHT with no COVID-19–related complications to date, with no changes in our protocols for induction, immunosuppression, and post-transplant surveillance monitoring. Their post-transplant lengths of stay were not different from our program's averages. Additional evidence is needed to more fully determine the risk profile of performing OHTs in this COVID-19 pandemic. Nonetheless, these outcomes are likely to be affected by the magnitude of COVID-19 spread in each community, and the impact of the relaxation of local "Stay at Home" orders is to be determined. Although Los Angeles was one of the earliest urban centers in the country to experience high levels of infection, early social distancing interventions slowed the infection rate; therefore, our experience may not be generalizable to other areas undergoing higher peaks of infection activity. Continuous reassessment of the local community situation relative to the pandemic, with reciprocally frequent re-evaluation of each transplant program's policies, is needed in this dynamic societal and medical landscape (Figure 2).

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CONFLICT OF INTEREST

None.

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