COVID-19 and the Response of Transplant Centers: the Global Response with an Emphasis on the Kidney Recipient

Yorg Azzi 1,2 · Abigail Brooks 1,2 · Hillary Yaffe 1,2 · Stuart Greenstein 1,2

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Abstract

Purpose of the Review In response to the COVID-19 pandemic, vulnerable populations, such as transplant patients, were at greater risk than the regular population. In order to protect these populations, transplant centers enacted new guidelines. We approach this review by looking at how different transplant regions responded to COVID-19 and analyze the unifying themes that have proven invaluable in the subsequent waves.

Recent Findings We noticed that most elective surgeries including living donor transplant operations were suspended in most countries. The response to deceased donor transplants varied between countries: in some deceased donor transplants continued with modified donor and recipient criteria, while in other countries this surgery was suspended. There was a general trend of decreasing or holding antimetabolites, treating the virus with hydroxychloroquine and/or azithromycin, and converting outpatient clinics to virtual clinics.

Summary We learned how to carefully select donors and recipients, tailor immunosuppressant regimens, and implement telemedicine. The kidney recipient population can be effectively managed in times of crisis with appropriate accommodations and measures. This review can be a model for the transplant community for future pandemics.

Keywords Transplant response to COVID-19 · Kidney recipients and COVID-19 · Review of transplant response to COVID-19 · COVID-19 in the transplant community

Introduction

In the winter of 2020, the first wave of SARS-CoV-2, the virus that causes coronavirus-19 (COVID-19) infection emerged from Wuhan, China. This virus spread rapidly throughout the world in an unprecedented way that has yet to abate. As the COVID-19 global pandemic erupted, the care of vulnerable populations was one of the primary challenges. Among them are the solid organ transplant patients, on account of their immunosuppressed status. In particular, the T cell response is significantly suppressed in this population [1, 2, 3, 4]. At the outset of the pandemic, when the natural history of COVID-19 infection could only be conjectured, there was bona fide concern that immunosuppressed patients would be at increased risk for infection with SARS-CoV-2 and would experience unacceptably high mortality rates [3–7]. Faced with this hypothesis, solid organ transplant programs needed to make important decisions about very practical matters [7, 8]. Is the inpatient transplant unit sufficiently physically distant from the COVID-19 unit? Should post-operative patients be seen in the outpatient clinic? How should the medical personnel be protected? Should induction immunosuppression not include lymphocyte depleting agents? Should only some transplants be performed? Should any transplants be performed?

Around the world, transplant centers made individualized decisions about the conduct of their programs, though several themes were mostly consistent: pre-operative testing of recipients and donors for COVID-19 infection, minimizing immunosuppression, rigorous limited recipient selection, and the use of telemedicine in the outpatient setting when possible [1, 3, 5, 8, 9]. In this paper, we explore the variations on these management strategies, to demonstrate that the
transplant center response to the COVID-19 pandemic developed to address the individual needs of the centers, but ultimately reflected the desire to protect patients from any modifiable excessive harm.

We reviewed the published global literature for transplant centers’ COVID-19 responses. The detailed findings are summarized in Table 1.

Transplant Centers’ Responses by Region

North America—the USA and Canada

Our center—Montefiore Medical Center in the Bronx, New York—halted all kidney transplants starting March 22, 2020, including new evaluations of both recipients and donors. Only emergent liver, heart, and lung transplants were performed. We started doing new donor and recipient evaluations for kidney transplant via telemedicine in May 2020. With the pandemic surge winding down around June 2020 in New York City, we performed our first living donor kidney transplant in the first week of June, followed by two deceased donor kidney transplants in the same week. Currently, we are still performing both living and deceased donor kidney transplants with careful selection of recipients and donors and tailoring immunosuppression and induction to immunological risk, the psychosocial needs and living situation of the recipient, and infectious risk.

All other transplant centers in the USA discontinued living donor kidney transplants, except those on the West Coast since they were not initially as hard hit with cases as the East Coast. While some centers continued doing deceased donor transplants on a case-by-case basis, considering the level of emergency of the transplant, some centers only continued to transplant those with a lower risk of delayed graft function.

Our center initially reported a mortality rate of 28% among our kidney transplant recipients with COVID-19 [10••]. In a subsequent report, we reported an overall mortality of 20% and in-hospital mortality of 38% [11••]. Other centers in New York reported similar mortality. For immunosuppression management, the antimitabolite dose was reduced or held for most patients. Hydroxychloroquine and/or azithromycin dominated the therapeutic arsenal used. All outpatient management was switched to virtual visits via telemedicine. The handling of transplants in Canada during the pandemic mirrored that of the USA.

Asia—China

Wuhan, China, closed on January 23, 2020, due to the impending threat of COVID-19. However, the impact of COVID-19 in organ transplant recipients was minor in the Hubei Province. There were only 22 confirmed cases in organ transplant recipients (19 liver and 2 kidney) [1••]. The difference in infection rate in the transplant community compared to the rest of the community at large was credited to years of effective transplant recipient education, including practicing effective self-protection with mask compliance, hand washing, and social distancing. In response to the overwhelming healthcare demands, all organ donation stopped on January 23, 2020.

Due to the lockdown of the surrounding areas, transplant outpatient management was converted to remote follow-up. Online consultation was implemented and labs collected from home were sent to transplant centers for interpretation, including dose adjustments of calcineurin inhibitors (CNI).

COVID-19-positive transplant patients were treated by a reduction or discontinuation of immunosuppression along with supportive treatment (often with low-dose methylprednisolone) based on the severity of the lung lesions. The mortality rate was low for COVID-19-positive transplant recipients, with one death among the 22 patients. In the single-center study from Tongji Hospital, Zhu et al. describe pneumonia in COVID-19-positive renal transplant recipients and assess their center’s treatment. They managed patients by discontinuing antimitobolites and CNIs and adding on antiviral medications [2].

On May 25, 2020, organ transplantation resumed as the risk of COVID-19 dwindled and healthcare systems had sufficient resources.

Asia—Hong Kong

COVID-19 first emerged in Hong Kong in January 2020 after the Chinese New Year. Resource utilization shifted to treat the influx of COVID-19 cases, so the liver transplant department at Queen Mary Hospital reduced living donor liver transplant (LDLT) cases in half [1••]. However, LDLT for urgent conditions was permitted, and the center found itself utilizing LDLT grafts for fulminant cases, who ordinarily would have received deceased donor grafts, actually doubling the LDLT rate of the prior year. There was a vast change in deceased donor liver transplantation (DDLT), with only 2 DDLT occurring in the month of February [1••].

The center required that both potential living donors and recipients were screened for COVID-19 infection if they had symptoms or a history of recent travel. For deceased donors, screening was only performed in the presence of clinical symptoms or a recent travel history [1••].

Asia—Japan

Japan’s response to organ transplantation was based on the urgency of the transplant. Heart, lung, and emergent liver transplantation continued, while kidney, pancreas, and small bowel transplantation was stopped [1••].
| Region  | Country   | Response                                                                 |
|---------|-----------|---------------------------------------------------------------------------|
| Asia    | China     | 1/23/20 Suspended all organ transplantation and resumed transplantation on 5/25/20 [1**](#) |

### Clinical study

**Coronavirus disease 2019 pneumonia in immunosuppressed renal transplant recipients: a summary of 10 confirmed cases in Wuhan, China**

- **Zhu et al. [2]**
- **Wuhan, China (Tongji Hospital)**

**Patient number:** 10 patients

**Clinical outcomes:**
- Mortality 1/10 (10%)
- Hospitalized 10/10 (100%)
- AKI 5/10 (50%)
- Discharged 8/10 (80%)

**Inpatient treatment:**
- Discontinued MMF 9/10 (90%)
- Discontinued CNI 7/10 (70%)
- Reduced dose of CNI 8/10 (80%)
- IVIG 7/10 (70%)
- Antiviral therapy 10/10 (100%)

**Outpatient management:**
- Online consultation

### Region Asia

**Country Hong Kong**

- 50% reduction in LDLT (continues in urgent conditions)
- Decreased DDLT
- Increased LDLT for liver failure [1**](#)

### Region Asia

**Country Japan**

- Continues life-saving transplantation for status 1 liver recipients
- Suspended all kidney, pancreas, and bowel transplants [1**](#)

### Region Asia

**Country South Korea**

- Partial suspension of LDKT (especially if desensitization for ABO or HLA incompatibility)
- Continued urgent LDKT and DDKT [1**](#)

### Region Asia

**Country Mongolia**

- 3/20 suspended living donor transplantation except 1 patient [1**](#)

### Region Asia

**Country Singapore**

- Discontinued LDKT except 1 patient who needed who was unable to get dialysis access
- Discontinued DDKT except those on priority waitlist for failing dialysis access or pure red cell aplasia
- Liver transplantation if meet criteria for medical urgency [1**](#)

### Region Asia

**Country India**

- LDKT and LDLT suspended in Mumbai and outside Mumbai at the discretion of the hospital
- DDKT suspended in Mumbai and the region
- Continued DDLT [1**](#)

### Region Middle East

**Country Turkey**

- Postponed all transplantation except urgent cases (acute liver failure) [3]

### Clinical study

**COVID-19 in kidney transplant recipients: a multicenter experience in Istanbul**

- **Demir et al. [4]**
- **Istanbul, Turkey (Istanbul University)**

**Patient number:** 40 patients

**Clinical outcomes:**
- Mortality 5/40 (12.5%)
- Hospitalized 39/40 (98%)
- ICU stay 7/40 (18%)
- AKI 14/40 (35%)
- Graft failure 0/40 (0%)

**Inpatient treatment:**
- Discontinued antimetabolites 40/40 (100%)
- Discontinued mTOR-I s 4/40 (10%)
- Discontinued CNI Is 11/40 (27.5%)
- Favipiravir 18/40 (45%)
- Tocilizumab 5/40 (12.5%)
- Anakinra 3/40 (7.5%)
- Antibiotics 24/40 (60%)

**Outpatient management:**
- In-person if local, otherwise telehealth
### Table 1 (continued)

| Country         | Response                                                                                       |
|-----------------|----------------------------------------------------------------------------------------------|
| Saudi Arabia    | Continued DDRT and LDRT, but discontinued LDRT when 3 kidney recipients presented symptomatically. Continued only urgent LDLT (defined as MELD > 25, HCC beyond. Milan Criteria but within UCSF criteria, acute fulminant liver failure, and recurrent decompensations) Discontinued non-urgent LDLT [3] |

| Clinical study                                                                 | Patient number | Clinical outcomes                                                                 | Inpatient treatment                                                                 | Outpatient management |
|-----------------------------------------------------------------------------|----------------|----------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|-----------------------|
| Coronavirus disease-19: disease severity and outcomes of solid organ transplant recipients: different spectrums of disease in different populations? Ali et al. [5] Riyadh, Saudi Arabia (King Faisal Specialist Hospital & Research Center) | 67 patients    | Hospitalized 47/67 (70%); ICU admission 7/47 (15%); AKI 9/47 (19%)                | Discontinued antimetabolites 47/47 (100%); Hydroxychloroquine 39/47 (83%); Azithromycin 42/47 (89%); Tocilizumab 11/47 (23%); Dexamethasone 9/47 (19%) | N/A                   |

| Region          | Country                  | Clinical outcomes                                                                 | Inpatient treatment                                                                 | Outpatient management |
|-----------------|--------------------------|----------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|-----------------------|
| Middle East     | Egypt                    |                                                                                  |                                                                                     |                       |
| Discontinued majority of transplantation [3]                             |              |                                                                                  |                                                                                     |                       |

| Region          | Country                  | Clinical outcomes                                                                 | Inpatient treatment                                                                 | Outpatient management |
|-----------------|--------------------------|----------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|-----------------------|
| Middle East     | Kuwait                   |                                                                                  |                                                                                     |                       |
| Discontinued LDRT and LDLT transplants except to avoid dialysis [3]       |              |                                                                                  |                                                                                     |                       |

| Region          | Country                  | Clinical outcomes                                                                 | Inpatient treatment                                                                 | Outpatient management |
|-----------------|--------------------------|----------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|-----------------------|
| Middle East     | Iran                     |                                                                                  |                                                                                     |                       |

| Clinical study                                                                 | Patient number | Clinical outcomes                                                                 | Inpatient treatment                                                                 | Outpatient management |
|-----------------------------------------------------------------------------|----------------|----------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|-----------------------|
| A report of 85 cases of COVID-19 and abdominal transplantation from a single center: what are the associated factors with death among organ transplantation patients Malekhosseini et al. [6] Shiraz, Iran (Abu Ali Sina Hospital) | 85 patients    | Mortality 17/85 (20%); Hospitalized 56/85 (66%); ICU admission 19/56 (34%)      | Hydroxychloroquine 30/85 (35%); Lopinavir–ritonavir 4/85 (5%); Tavanex 4/85 (5%); Tamiflu 2/85 (2%); Azithromycin 23/85 (27%); Imipenem 4/85 (27%); Cotrimoxazole 3/85 (4%); Fluconazole 2/85 (2%); Vancomycin 2/85 (2%); Salbutamol 1/85 (1%) | N/A                   |

| Region          | Country                  |                                                        |                                                                                     |                       |
|-----------------|--------------------------|-------------------------------------------------------|-------------------------------------------------------------------------------------|-----------------------|
| Europe          | Denmark                  |                                                        |                                                                                     |                       |
Table 1 (continued)

| Region | Country | Response | Clinical study | Patient number | Clinical outcomes | Inpatient treatment | Outpatient management |
|--------|---------|----------|----------------|----------------|------------------|---------------------|-----------------------|
| Europe | Sweden  | N/A      | DDKT and DDLT continued | 53 patients | Mortality rate 5/53 (9.4%) | Discontinued or reduced MMF 23/35 (66%) | N/A |
|        |         |          | LDKT continued in some centers and suspended in others |                 | In-hospital mortality rate 5/37 (14%) | Reduced CNI 11/53 (21%) |          |
|        |         |          |                 | 51 kidney/5 lung/5 heart/8 liver/4 dual organs | Hospitalized 37/52 (70%) | Hydroxychloroquine + tocilizumab 1/37 (3%) | |
|        |         |          |                 |                 | ICU admission 8/37 (22%) | LMWH 27/37 (73%) |          |
|        |         |          |                 |                 | Dialysis 12/37 (32%) | Apixaban 1/37 (3%) |          |
|        |         |          |                 |                 | Severe COVID-19 disease 12/37 (32%) | Supplemental O2 21/37 (57%) |          |
|        |         |          |                 |                 | Mechanical ventilation 7/37 (19%) |               |          |

| Region | Country | Response | Clinical study | Patient number | Clinical outcomes | Inpatient treatment | Outpatient management |
|--------|---------|----------|----------------|----------------|------------------|---------------------|-----------------------|
| Europe | UK      | Routine transplantation continued | Outcomes of renal transplant recipients with SARS-CoV-2 infection in the eye of the storm: a comparative study with waitlisted patients | 28 patients | Mortality 9/28 (32%) | Discontinued MMF 19/21 (90%) | Virtual clinics |
|        |         |          | Mohamed et al. [8] |                 | Hospitalized 25/28 (89%) | Halved MMF 1/21 (5%) | Medications sent via mail |
|        |         |          | London, UK (Barts Health NHS Trust) |                 | ICU stay 5/25 (20%) | Discontinued AZA 3/3 (100%) | 24 h online support |
|        |         |          |                 |                 | AKI 14/25 (56%) | No change in antimetabolite 3/24 (12.5%) |          |
|        |         |          |                 |                 |               | Steroid increased 12/27 (44%) |          |
|        |         |          |                 |                 |               | Hydrocortisone 1/28 (4%) |          |

| Region | Country | Response | Clinical study | Patient number | Clinical outcomes | Inpatient treatment | Outpatient management |
|--------|---------|----------|----------------|----------------|------------------|---------------------|-----------------------|
| Europe | France (Paris) | Continued organ procurement including DCD donors | COVID-19 infection in kidney transplant recipients: disease incidence and clinical outcomes | 66 patients | Mortality 16/66 (24%) | Discontinued only MMF/MPA/AZA 38/61 (62%) | Cancellation of all follow-up appointments for liver transplant recipients |
|        |         |          |                 |                 | Hospitalized 60/66 (91%) | Discontinued only CNI 2/57 (4%) | Telehealth clinics for kidney |
|        |         |          |                 |                 | ICU stay 15/66 (22%) | Belatacept infusion postponed 1/6 (17%) | |
|        |         |          |                 |                 | AKI 28/66 (42%) | No change in immunosuppression 24/66 (36%) | |
|        |         |          |                 |                 | RRT 7/28 (25%) | Discontinued all immunosuppression 1/66 (2%) | |
| Clinical study | Patient number | Clinical outcomes | Inpatient treatment | Outpatient management |
|----------------|----------------|-------------------|---------------------|-----------------------|
| An initial report from the French SOT COVID Registry suggests high mortality due to COVID-19 in recipients of kidney transplants Caillard et al. [10••] | 279 patients | Mortality at 30 days (23%) | CNI discontinued 58/202 (29%) | Canceled all f/u appointments for liver Telehealth clinics for kidney |
| | | Hospitalized 243/279 (87%) | Antimetabolite discontinued 136/192 (71%) | |
| | | Ventilated 72/243 (30%) | mTOR-I discontinued 18/29 (62%) | |
| | | O2 therapy 152/210 (72%) | Belatacept discontinued 7/15 (47%) | |
| | | ICU stay 88/243 (36%) | Azithromycin 71/243 (29%) | |
| | | AKI 106/243 (44%) | Other antibiotics 153/243 (63%) | |
| | | RRT 27/243 (11%) | Antifungal drugs 6/243 (2.5%) | |
| | | Graft loss 9/243 (4%) | Remdesivir 2/243 (1%) | |
| | | | Lopinavir/ritonavir 11/243 (4.5%) | |
| | | | Oseltamivir 6/243 (2.5%) | |
| | | | Hydroxychloroquine 60/243 (25%) | |
| | | | Tocilizumab 12/243 (5%) | |
| | | | | |
| Biomarkers of cytokine release syndrome predict disease severity and mortality Benotmane et al. [11••] | 49 patients | Mortality 9/49 (19.5%) | Discontinued MMF/MMPA 35/35 (100%) | Canceled all f/u appointments for liver Telehealth clinics for kidney |
| | | Hospitalized 41/49 (84%) | Discontinued mTOR-I 6/6 (100%) | |
| | | ICU stay 14/41 (34%) | Belatacept postponed ½ (50%) | |
| | | AKI 31/41 (76%) | Discontinued CNI 15/36 (42%) | |
| Kidney transplant patients with SARS-CoV-2 infection: the Brescia Renal COVID Task Force experience Bossini et al. [12] | 53 patients | Mortality 15/45 (33%) | Hydroxychloroquine 15/41 (37%) | |
| | | Hospitalized 45/45 (100%) | Azithromycin 26/41 (65%) | |
| | | ICU stay 10/45 (22%) | Lopinavir-ritonavir 5/41 (12%) | |
| | | AKI 15/45 (33%) | High dose corticosteroids 14/41 (34%) | |
| | | RRT 3/15 (20%) | Tocilizumab 4/41 (10%) | |
| | | Discharged 27/45 (60%) | | |
| | | ARDS 27/45 (60%) | | |
| A single center observational study of the clinical characteristics and short-term | 20 patients | Mortality 5/20 (25%) | Discontinued immunosuppression 20/20 (100%) | N/A |
| | | Hospitalized 20/20 (100%) | Initiated methylprednisolone 16 mg/day 20/20 (100%) | |
| Clinical study | Patient number | Clinical outcomes | Inpatient treatment | Outpatient management |
|----------------|----------------|-------------------|--------------------|-----------------------|
| Respiratory and GI COVID-19 phenotypes in kidney transplant recipients | 414 patients | Hospitalized 380/414 (92%) | Hydroxychloroquine 369/414 (89%) | Cancelled all non-urgent appointments, lab tests, and procedures |
| COVID-19 in solid organ transplantation: a matched retrospective cohort study and evaluation of immunosuppression management | 46 patients | Hospitalized 46/46 (100%) | Discontinued tacrolimus 22/36 (61%) | N/A |
| COVID-19 in Elderly Kidney transplant recipients | 16 patients | Mortality 8/16 (50%) | mTOR-I discontinued 4/5 (80%) | Canceled all non-urgent appointments, lab tests, and procedures |

| Outcome of 20 kidney transplant patients admitted for SARS-CoV2 pneumonia in Brescia, Italy (Spedali Civili Hospital) | ICU stay 4/20 (20%) | Antiviral therapy + hydroxychloroquine 19/20 (95%) | Telehealth |
|---|---|---|---|
| AKI 6/20 (30%) | Lopinavir/ritonavir 3/20 (15%) | |
| RRT 1/6 (17%) | Darunavir + ritonavir 8/20 (40%) | |
| Discharged 3/20 (15%) | Tocilizumab 6/12 (50%) | |

| Region | Country | Response |
|---|---|---|
| Europe | Germany | Suspended most LDKT, Continued DDKT, High urgency pediatric liver transplantation, DDLT in lower urgent situations on case-by-case basis, Transport of organs across country borders continues with some restrictions [1,••] |
| Region | Country | Response |
|---|---|---|
| Europe | Netherlands | 3/13/20 Suspended LDKT and DDKT at the largest transplant center (including patients scheduled to undergo blood group ABO-incompatible kidney transplantation already treated with alemtuzumab before the decision to stop acute kidney transplants) 3/23/20 Continued DDKT at smaller centers, Liver transplantation continued [1,••] |
| Region | Country | Response |
|---|---|---|
| Europe | Spain | Postponed all LD transplantation [1,••] |

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|----------------|----------------|-------------------|--------------------|-----------------------|
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| Region | Country | Response |
|---|---|---|
| Europe | Spain | Postponed all LD transplantation [1,••] |
| Clinical study | Patient number | Clinical outcomes | Outpatient management |
|----------------|----------------|-------------------|----------------------|
| Clinical characteristics and risk factors for severe COVID-19 in hospitalized kidney transplant recipients: a multicentric cohort study | 104 patients | Mortality 28/104 (27%) Hospitalized 104/104 (100%) ICU stay 24/104 (23%) AKI 47/100 (47%) ARDS 47/104 (55%) | Discontinued at least one immunosuppressive agent 95/104 (91.3%) IV steroids 55/104 (53%) Hydroxychloroquine 101/104 (97%) Lopinavir/ritonavir 50/104 (48%) Azithromycin 67/104 (64%) |
| Region | Europe | Switzerland | 3/3/20 |
| Response | | | 6-stage plan: |
| | | | 1. Discontinued all LD transplantation |
| | | | 2. Discontinued all DDPT and islet transplants, discontinue all DCD donors |
| | | | 3. Discontinued DDKT |
| | | | 4. Liver, lung, and heart based on urgent status |
| | | | 5. Only urgent transplants |
| | | | 6. Discontinue all transplants |
| | | | 3/2/20 |
| | | | Discontinued all transplant and procurements except urgent cases like fulminant hepatitis [1••] |
| Region | Oceania | | |
| Country | Australia | | Suspended LDKT |
| Response | | | Suspended DDKT [1] |
| Region | Oceania | | |
| Country | New Zealand | | Continued DDKT at 2/3 transplant centers |
| Response | | | Discontinued LDKT [1••] |
| Region | Africa | | |
| Country | South Africa | | Discontinued LDKT and DDKT in government hospitals |
| Response | | | Continued DDKT in private hospitals |
| | | | Discontinued LDKT in private hospitals [1••] |
| Region | North America | | |
| Country | Canada | | Montreal: Suspended LDKT |
| Response | | | Suspended DDKT except recipients > 70 and highly sensitized |
| | | | Toronto: 3/16/20 Suspended LDKT |
| | | | Suspended DDKT except active patients on the waiting list medically urgent or cPRA > 99% [1••] |
| Region | North America | | |
| Country | USA | | |
| Clinical study | Patient number | Clinical outcomes | Inpatient treatment | Outpatient management |
|----------------|----------------|-------------------|---------------------|-----------------------|
| Kidney allograft recipients, immunosuppression, and coronavirus disease-2019: a report of consecutive cases from a New York City transplant center | NY: Continued transplantation (considered emergency) [1••] | 54 patients | Mortality rate 7/54 (13%) | Tacrolimus reduction 17/54 (33%) |
| Lubetzky M, et al. [18•] NY, USA (Weill Cornell Medicine) | | | Hospitalized 39/54 (72%) | MMF 50% reduction 15/54 (28%) |
| | | | AKI 21/54 (39%) | MMF discontinuation 24/54 (44%) |
| | | | Graft failure 6/54 (11%) | Azithromycin 12/54 (22%) |
| | | | Discharged 37/39 (95%) | Doxycycline 8/54 (17%) |
| | | | | Hydroxychloroquine 32/54 (62%) |
| | | | | Remdesivir 2/54 (4%) |
| | | | | IL-6 Inhibitor 2/54 (4%) |
| | | | | Convalescent plasma 1/54 (2%) |
| Outpatient management of kidney transplant recipients with suspected COVID-19—single-center experience during the New York City surge | | 44 patients | Mortality rate 6/44 (14%) | Discontinued antimetabolites 26/33 (78.8%) |
| Mehta S, et al. [19] NY, USA (NYU Langone) | | | Hospitalized 34/44 (77%) | Reduced dose of antimetabolites by 50-75% 6/33 (18.2%) |
| | | | AKI 18/34 (53%) | Hydroxychloroquine 33/34 (97%) |
| | | | Discharged 27/34 (79%) | Azithromycin 27/34 (79%) |
| COVID-19 and kidney transplant | | 36 patients | Mortality 10/36 (28%) | Clazakizumab or tocilizumab 9/34 (26.5%) |
| Akalin et al. [20] NY, USA (Montefiore Medical Center) | | | Hospitalized 28/36 (78%) | |
| | | | Viral PNA 27/28 (96%) | |
| | | | Intubation 11/28 (39%) | |
| | | | RRT 6/28 (21%) | |
| | | | Discharged 10/28 (36%) | |
| COVID-19 in kidney transplant recipients | | 10 patients | Mortality 3/10 (30%) | Discontinued antimetabolite 24/28 (86%) |
| Nair et al. [21••] NY, USA (Hofstra/Northwell Health) | | | Hospitalized 9/10 (90%) | Discontinued tacrolimus 6/28 (21%) |
| | | | ICU stay 5/10 (50%) | Hydroxychloroquine 24/28 (86%) |
| | | | AKI 5/10 (50%) | Apixaban if D-dimer levels higher than 3.0 micrograms/mL |
| | | | Discharged 7/10 (70%) | Leronlimab (CCR5-I) 6/28 (21%) |
| Early outcomes of outpatient management of kidney transplant recipients with coronavirus disease 2019 | | 41 patients | Mortality 3/10 (30%) | Tocilizumab (IL-6R antagonist) 2/28 (7%) |
| Husain et al. [22] NY, USA (Columbia University College of Physicians and Surgeons and New York Presbyterian Hospital) | | | Hospitalized 9/10 (90%) | |
| | | | ICU stay 5/10 (50%) | |
| | | | AKI 5/10 (50%) | |
| | | | Discharged 7/10 (70%) | |
| | | | Mortality rate 13/41 (32%) | Discontinued antimetabolite (MMF/MPA) 9/10 (90%) |
| | | | Hospitalized 26/41 (63%) reduction in immunosuppression | Discontinued CNI 2/9 (22%) |
| | | | | Discontinued Sirolimus 1/1 (100%) |
| | | | | Hydroxychloroquine + azithromycin 9/10 (90%) | Discontinued antimetabolite (MMF/MPA) 9/10 (90%) |
| | | | | Discontinued CNI 2/9 (22%) |
| | | | | Discontinued Sirolimus 1/1 (100%) |
| | | | | Hydroxychloroquine + azithromycin 9/10 (90%) | Discontinued antimetabolite (MMF/MPA) 9/10 (90%) |
### Table 1 (continued)

| Clinical study | Patient number | Clinical outcomes | Outpatient management |
|----------------|----------------|-------------------|-----------------------|
| Early description of coronavirus 2019 disease in kidney transplant recipients in New York | 15 patients | Mortality 2/15 (13%) | Discontinued all immunosuppression 2/15 (14%) Virtual |
| Mohan et al. [23] NY, USA (Columbia University College of Physicians and Surgeons and New York Presbyterian Hospital) | | Hospitalized 15/15 (100%) | Discontinued only MMF/MPA/AZA/leflunomide 10/14 (71%) |
| | | Intubation 4/15 (27%) | Reduced prednisone 1/10 (10%) |
| | | AKI 6/15 (40%) | Belatacept infusion postponed ½ (50%) |
| | | RRT 2/15 (13%) | Replaced tacrolimus and MMF with prednisone 1/15 (7%) |
| | | Discharged 8/15 (53%) | Hydroxychloroquine w/o azithromycin 4/15 (27%) |
| | | | Hydroxychloroquine + azithromycin 9/15 (60%) |
| | | | Tocilizumab 1/15 (7%) |
| Clinical study | 18 patients | Clinical outcomes | Outpatient management |
| Evidence of potent humoral immune activity in COVID-19-infected kidney transplant recipients | | Mortality 7/18 (39%) | Discontinued MMF/MPA 5/18 (28%) Virtual |
| Hartzell et al. [24] NY, USA (Icahn School of Medicine at Mount Sinai) | | Hospitalized 18/18 (100%) | Discontinued all immunosuppressive meds 1/18 (5%) |
| | | ICU stay 11/18 (61%) | Reduced dose MMF/MPA 13/18 |
| | | AKI 16/18 (89%) | Started on steroids (not previously on for antirejection) 2/18 (11%) |
| | | Discharged 11/18 (61%) | |
| Clinical study | 90 patients | Clinical outcomes | Outpatient management |
| COVID-19 in solid organ transplant recipients: initial report from the US epicenter | 46 kidney/17 lung/13 liver/9 heart/5 dual organs | Mortality rate 16/90 (18%) | |
| Pereira et al. [25] NY, USA (Columbia University College of Physicians and Surgeons and New York Presbyterian Hospital) | | In-hospital mortality rate 16/68 (24%) | |
| | | Hospitalized 68/90 (76%) | |
| | | Mechanical ventilation 2/68 (35%) | |
| | | ICU admission 23/68 (34%) | |
| Clinical study/hospital response | 229 patients | Clinical outcomes | |
| COVID-19 infection in kidney transplant recipients at the epicenter of pandemics | | Mortality rate 47/229 (21%) | |
| Azzi et al. [26] NY, USA (Montefiore Medical Center) | | In-hospital mortality rate 42/229 (19%) | |
| | | Hospitalized 229/229 (100%) | |
| | | Mechanical ventilation 42/229 (19%) | |
| | | ICU admission 229/229 (100%) | |
| Region | North America | | |
| Country | USA (Northeast) | | |
| Response | Northeast: Only life-saving transplantation (kidney transplants with 100% PRA 0 Ag mismatch, to avoid dialysis, vascular access failure and pediatric patients, liver transplants with high MELD, heart transplant with high HAS, lung transplant with high LAS) [1] [•] | | |

### Clinical study/hospital response

| Clinical study/hospital response | Patient number | Clinical outcomes | Outpatient management |
| COVID-19 in solid organ transplant recipients: dynamics of disease | 52 patients | Mortality rate 8/52 (16%) | |
| | | Azathioprine/MMF halved 7/24 (29%) | |

### Clinical outcomes

- **Mortality**: The percentage of patients who did not survive during the hospital stay.
- **Hospitalized**: The percentage of patients who required hospitalization.
- **Intubation**: The percentage of patients who required intubation.
- **AKI**: The percentage of patients who developed acute kidney injury.
- **RRT**: The percentage of patients who required renal replacement therapy.
- **Discharged**: The percentage of patients who were discharged from the hospital.
- **Discontinued all immunosuppression**: The percentage of patients who had all immunosuppressive medications discontinued.
- **Discontinued MMF/MPA/AZA/leflunomide**: The percentage of patients who had MMF/MPA/AZA/leflunomide discontinued.
- **Reduced prednisone**: The percentage of patients who had their prednisone dosage reduced.
- **Belatacept infusion postponed**: The percentage of patients whose belatacept infusion was postponed.
- **Replaced tacrolimus and MMF with prednisone**: The percentage of patients who had tacrolimus and MMF replaced with prednisone.
- **Hydroxychloroquine w/o azithromycin**: The percentage of patients who received hydroxychloroquine without azithromycin.
- **Hydroxychloroquine + azithromycin**: The percentage of patients who received hydroxychloroquine with azithromycin.
- **Tocilizumab**: The percentage of patients who received tocilizumab.
### Table 1 (continued)

| Region          | Country          | Response                                                                 |
|-----------------|------------------|--------------------------------------------------------------------------|
| North America   | USA (Midwest)    | Discontinued all living donor transplants                                 |
|                 |                  | Continued deceased donor on case-by-case basis                            |
|                 |                  | Discontinued new donor and recipient evaluations                          |
|                 |                  | Continued organ procurements                                              |

#### Clinical study

**COVID-19 outcomes among solid organ transplant recipients: a case-control study**

**Sharma et al. [28]**

**MI, USA (University of Michigan)**

| Patient number | Clinical outcomes | Inpatient treatment | Outpatient management |
|----------------|-------------------|---------------------|-----------------------|
| 41 patients    | Mortality rate 6/41 (14.6%) | Hydroxychloroquine 12/41 (29%) | N/A                   |
| 16 kidney/3 lung/9 heart/8 liver/5 dual organs | In-hospital mortality rate 6/36 (17%) | IL-6 1 11/41 (27%) | Vasopressors 6/41 (17%) |

#### Clinical study

**Clinical characteristics and outcomes of COVID-19 in solid organ transplant recipients: a cohort study**

**Chauhdry et al. [29]**

**MI, USA (Henry Ford Hospital)**

| Patient number | Clinical outcomes | Inpatient treatment | Outpatient management |
|----------------|-------------------|---------------------|-----------------------|
| 47 patients    | Mortality rate 8/47 (17%) | Discontinuation or reduction of antimetabolite 27/32 (84%) | N/A                   |
| 38 kidney/4 lung/5 heart/1 liver/1 pancreas | In-hospital mortality rate 8/35 (23%) | Discontinuation or reduction of CNIs 53/33 (15%) | Vasopressors 7/35 (20%) |
|                | Hospitalized 35/47 (74%) | Discontinuation or reduction of mTOR-I 11/35 (3%) | Corticosteroid 3/35 (66%) |
|                | ARDS 12/35 (35.5%) | Discontinuation or reduction of belatacept 1/35 (3%) | Tocilizumab 3/35 (9%) |
### Table 1 (continued)

| Clinical study | Patient number | Clinical outcomes | Inpatient treatment | Outpatient management |
|----------------|----------------|-------------------|---------------------|-----------------------|
| Early Experience with COVID-19 and Solid Organ Transplantation at a U.S. High-volume Transplant Center Yi SG, et al. [30] TX, USA (Houston Methodist Hospital) | 21 patients | Hospitalization 14/21 (67%) ICU 7/14 (50%) Intubation 5/14 (36%) AKI 11/14 (69%) Discharged 8/14 (57%) | Discontinued antimetabolite 12/14 (86%) Reduced CNI 3/14 (14%) Increased baseline steroids 3/14 (5%) Antiviral therapy 12/21 (575) Hydroxychloroquine + azithromycin 7/12 (58%) Hydroxychloroquine only 2/12 (17%) Azithromycin only 2/12 (17%) Convalescent plasma 1/12 (8%) Ribavirin 6/12 (50%) Remdesivir 1/12 (8%) Immunomodulating therapy 4/21 (19%) Tocilizumab 4/4 (100%) Nebulized interferon alpha-2b 1/4 (25%) Anakinra 1/4 (25%) | Telehealth |
| Region | North America | Country USA (West Coast) | Response Continued LDLT, DDLT, LDKT, and DDKT | Discontinued pancreas transplants [1••] |
| Region | Global | Country Global | Response N/A |
| Clinical study | Patient number | Clinical outcomes | Inpatient treatment | Outpatient management |
| COVID-19 and kidney transplantation: results from the Tango International Transplant Consortium Cravedi et al. [31] (USA, Italy, Spain) | 144 patients | Mortality rate 39/98 (40%) Hospitalized 98/98 (100%) ARDS 73/98 (74%) AKI requiring dialysis 36/98 (37%) New infection 24/98 (24%) ICU admission 98/98 (100%) Mechanical ventilation 55/98 (56%) | Discontinued tacrolimus 32/144 (22.9%) Discontinued CNI 33/144 (23%) Hydroxychloroquine 102/144 (71%) Antibiotics 107/144 (74%) Tocilizumab 19/144 (13%) Antivirals 20/144 (14%) | N/A |
| Clinical study | Patient number | Clinical outcomes | Inpatient treatment | Outpatient management |
| Outcomes of critically ill solid organ transplant patients with COVID-19 in the United States Molnar et al. [32] Multicenter USA | 98 patients | Mortality rate 39/98 (40%) Hospitalized 98/98 (100%) ARDS 73/98 (74%) AKI requiring dialysis 36/98 (37%) New infection 24/98 (24%) ICU admission 98/98 (100%) Mechanical ventilation 55/98 (56%) | Chloroquine 2/98 (2%) Hydroxychloroquine 62/98 (63%) Azithromycin 49/98 (50%) Hydroxychloroquine + azithromycin 74/98 (76%) Remdesivir 6/98 (6%) Lopinavir–ritonavir 3/98 (3%) Anticoagulation 46/98 (47%) Corticosteroids 64/98 (65%) Statin 40/98 (41%) Tocilizumab 23/98 (23%) IL-6 inhibitor 1/98 (1%) Vitamin C 4/98 (4%) Convalescent plasma 5/98 (5%) | N/A |
Screening for COVID-19 in donors and recipients was recommended for those with significant exposure to COVID-19, travel history to high-risk countries, or for patients with fever and respiratory symptoms. It was recommended that living donors for kidney, lung, and liver transplant stay at home or isolated in the hospital for 14 days before donation to avoid unnecessary exposure. In communities with available testing, it was recommended at 14 days and at 1 day before transplantation in both donors and recipients. Chest CT scans were also recommended before transplantation in donors and recipients [1••].

Outpatient follow-up was converted to telemedicine and extended periods between visits. Additionally, to prepare patients for the lockdown, a stockpile of additional immunosuppressants was distributed to patients.

Asia—South Korea

The response to organ transplantation was mixed. Some living donor kidney transplants were postponed, especially if undergoing desensitization for ABO or human leukocyte antigen incompatibility, but urgent living donor kidney transplantation and deceased donor programs continued [1••].

Screening for COVID-19 involved testing all deceased donors, while living donors were screened based on the center’s decision. On March 13, 2020, the Korean Society for Transplantation released a guideline recommending routine COVID-19 screening of both donor and recipient [1••]. There was one report of a living liver donor who tested positive for COVID-19 after liver donation to her mother, but neither the donor nor the recipient developed symptoms.

Asia—Singapore

In response to the pandemic, all living kidney transplants were cancelled except for one patient who had no other access options. For this case, a nasopharyngeal swab for COVID-19 was performed for both the recipient and the living donor on day 15 and day 2 before surgery [1••]. Additionally, chest x-ray was performed on admission and on day 2 before surgery to assess for pneumonia. Deceased donor kidney transplantation had also been cancelled except for priority waitlisted patients with failing dialysis access or pure red cell aplasia. Liver, heart, and lung transplantations were permitted if medically urgent. One combined lung–liver was performed from a single deceased donor who underwent PCR testing for COVID-19 three times in addition to a CT thorax to exclude COVID-19 infection. These recipients were reported to be doing well.

Hospital transplant teams were divided into smaller groups working separately in different areas. They set up an acute respiratory tract infection ward where renal patients, including kidney transplant recipients, with respiratory complaints were
admitted for COVID-19 screening, with bedside access to dialysis. Patients in the acute respiratory tract infection ward had to have two negative COVID-19 swabs before being transferred to the general ward. Due to case reports of transplant recipients presenting with gastroenteritis, transplant recipients with gastroenteritis were required to be screened by COVID-19 PCR.

Outpatient management included virtual clinics with remote monitoring and home delivery of medications.

**Asia—India**

In Mumbai, all living donor transplants stopped. Outside of Mumbai organ transplants continued at the discretion of each hospital. Deceased donor kidney transplants were suspended in Mumbai and the surrounding region. Neither the National Organ & Tissue Transplant Organization nor the Regional Organ & Tissue Transplant Organization issued edicts to stop deceased donor liver and heart transplants [1••].

Outpatient follow-up was encouraged to be performed via phone and video call. If transplant patients required in-person follow-up, then they were scheduled to come into the clinic at intervals such that there would be no wait time nor contact with other patients. It was recommended that all transplant patients had a minimum of 1 month of immunosuppressants in stock [1••].

**Middle East—Turkey**

All elective procedures and surgeries were postponed across Turkey. Beginning on March 20, 2020, all private hospitals were denoted as COVID-19-only hospitals. From February 1 to April 1, 2020, in Ankara and Istanbul, only 21 liver and 23 kidney transplants were performed.

In describing a multi-center experience in Istanbul, Demir et al. found that 5 out of 40 renal transplant patients infected with COVID-19 died [12]. Inpatient management of transplant patients with COVID-19 was as follows: discontinuation of antimetabolites (both mycophenolate mofetil and azathioprine) and continuation of CNIs, except if patients required ventilation with a severe pneumonia. The interleukin-6 inhibitor, tocilizumab, was considered to treat severe cytokine release symptoms [9••].

Outpatient follow-up was mostly via telemedicine.

**Middle East—Saudi Arabia**

The Saudi Center for Organ Transplant (SCOT) addressed the dilemmas facing the transplant community during the pandemic and issued a position statement that provided guidelines and recommendations for deceased and living donation. All deceased donors were to be screened for COVID-19 with PCR from bronchoalveolar lavage or tracheal aspirate. All positive donors were declined. COVID-19-negative donors were considered on a case-by-case basis according to the level of risk.

Only urgent liver transplants (e.g., HCC meeting UCSF criteria, acute fulminant liver failure, recurrent decompensations, MELD > 25) continued. Donor and recipients in high-risk groups were tested for COVID-19 on the day of admission. In the case of COVID-19 positivity, the transplant was cancelled. In the circumstance of a first negative COVID-19 test, a second was performed before surgery. Low-risk patients required one negative PCR test at admission. Between February 1 and April 15, 2020, 33 liver transplants including 25 from living donors were performed without COVID-19 complications.

Outpatient management involved a switch to telemedicine, blood work in the nearest laboratory with results discussed via phone, and medications delivered to the home. Only patients recently transplanted were seen in clinic. Only one post-liver transplant patient from 2016 presented positive for COVID-19; no modifications were made to his medications.

Only 40 kidney transplants were performed from February 1 to April 2020; 7 of those were from deceased donors. There were no reported COVID-19 complications. Three kidney recipients presented with fever, cough, and fatigue and tested positive for COVID-19. Inpatient management consisted of azithromycin, hydroxychloroquine, and ceftriaxone and maintenance doses of low levels of tacrolimus and steroids. The living donor kidney program suspended all transplants from March until the first week of May [9••].

**Middle East—Egypt**

Transplant activities in Egypt were limited to live donor liver and kidney surgeries. Most governmental and university centers suspended transplant activities based on too great a risk to the donor and an unknown impact of COVID-19 on the recipient. The proposed precautions adopted for those undergoing transplant were home isolation for both the donor and recipient for 2 weeks before the transplant, to perform COVID-19 PCR twice at 48-h intervals before transplant, and to admit the recipient 3 days and donors 1 day before transplant.

Outpatient management involved telemedicine and in-person follow-up only for patients recently transplanted and those with abnormal laboratory or radiographic findings [9••].

**Middle East—Kuwait**

Living donor transplants were suspended on February 19, 2020, with one exception to prevent the need for dialysis. Deceased donor transplants continued, but with a rapid decline in number. From February 1 to April 1, 2020, there were no liver transplants and only 12 kidney transplants. Screening involved testing all donors for COVID-19.
Outpatient management focused on distributing sufficient quantity of immunosuppressants to the transplant community [9••].

**Europe—Denmark**

National health authorities categorized transplantation as a vital surgery that should not be suspended. As a result, deceased donor kidney, liver, lung, and heart transplantations continued at all Danish centers. However, simultaneous kidney–pancreas transplantation was stopped. Organ exchange within the Scandinavian deceased donor exchange program continued. All potential deceased donors were tested for SARS-CoV-2. Already scheduled living donor transplantation was at the discretion of the transplant center (some centers cancelled and some centers continued). However, no new living donor kidney transplantations were scheduled [1••].

Outpatient management was converted to telemedicine.

**Europe—the UK**

Patients with acute liver failure continued to be listed and transplanted. Pediatric liver transplantation continued. All LDLTs were cancelled. All procurement activity resumed as normal.

The UK government issued guidelines for transplant patients recommending 12 weeks of self-isolation due to the high risk of COVID-19 in a particularly vulnerable population. All transplant patients had 24-h online support.

In the single-center study in London at Barts Health NHS Trust, Mohamed et al. analyzed outcomes of COVID-19 infection in renal transplant recipients. Twenty-five of the 28 patients were hospitalized, with five patients requiring intensive care unit (ICU) admission. Nine patients died. Inpatient management involved discontinuation of mycophenolate mofetil and azathioprine and increased steroid doses [3].

Outpatient management involved cancelling all regular transplant assessments, with the implementation of virtual clinics. Medications were mailed to each patient’s home.

**Europe—France**

Living and deceased donor kidney transplantation was halted. Any transplant patient suspected of having COVID-19 infection was seen in the infectious disease unit, tested by PCR, and then allocated to a COVID-19-positive hospital. Inpatient management involved discontinuation of mycophenolate mofetil and mammalian target of rapamycin (mTOR) inhibitors. In patients with acute respiratory distress syndrome, tacrolimus was discontinued as well. Each positive patient was called daily to monitor his/her progress [1••].

In the single-center study at Saint Louis Hospital in Paris, Elias et al. described the clinical outcomes of COVID-19-positive renal transplant recipients. Sixty of the 66 patients were hospitalized, with 15 requiring ICU care. Sixteen of the patients died. Inpatient management involved discontinuation of antimetabolites and the addition of hydroxychloroquine and monoclonal antibodies (tocilizumab and eculizumab) in a few severe cases [7].

In the multi-center study in France, Calliard et al. analyzed the outcomes of solid abdominal organ recipients with COVID-19 in a larger cohort. Of the 279 patients, 243 were hospitalized, with 88 requiring ICU care. Inpatient management was similar to the Elias et al. study cohort, with the additional use of azithromycin in 71 patients, remdesivir in 2 patients, lopinavir–ritonavir in 11 patients, antifungal drugs in 6 patients, and oseltamivir in 6 patients [13].

Outpatient care was converted to telemedicine clinics with the creation of comprehensive file of 2300 follow-up patients to reach out to about care [1••].

**Europe—Italy**

In the multi-center study in Brescia, Italy, Bossini et al. described kidney transplant recipients infected with COVID-19. The hospitalization rate was 45 of 53 patients, with 10 requiring ICU admission. Fifteen patients died. Inpatient management consisted of adjustments to immunosuppressive medications. A reduction in steroids and CNIs occurred in the majority of patients. Antiviral medications included lopinavir–ritonavir, darunavir–ritonavir, and hydroxychloroquine [14].

In the observational study from Spedali Civili Hospital in Brescia, Italy, Alberici et al. similarly described clinical outcomes of kidney transplant recipients who tested positive for COVID-19. Out of the 20 hospitalized patients, 4 were admitted to the ICU. Inpatient management involved a discontinuation of immunosuppression in 100% of the patients and high-dose steroid initiation. Antiviral medication included hydroxychloroquine, lopinavir–ritonavir, darunavir–ritonavir, and tocilizumab [15].

**Europe—Germany**

Throughout Germany, living kidney donor transplant surgeries were mostly suspended, while deceased donor transplantation continued. All deceased donors were screened for COVID-19; however, the test results did not change whether the organ was transplanted [1••].

Outpatient management consisted of prolonging the period between visits and saving in-person visits only for those recently transplanted or with an urgent need. Tele- and video-medicine were instituted [1••].

Liver transplantation followed different policies than renal transplantation. High urgency children were still eligible for
both deceased and living transplantation. Deceased donor liver transplants were performed in lower urgency situations if the COVID-19 risk was low [1••].

Transport of organs across country borders remained active with only limited restrictions.

**Europe—Netherlands**

The largest kidney transplant center stopped all activity on March 13, 2020. All living donor transplants were suspended, even patients scheduled to undergo ABO-incompatible kidney transplantation who had been treated with alemtuzumab [1••]. The decision to stop transplantation was based on the risk of immunosuppressed patients acquiring a more severe version of COVID-19. The other six transplant centers stopped all living donor transplantation, but continued deceased donor transplantation.

Two renal transplant patients were admitted due to severe COVID-19 infection. Inpatient management consisted of not altering the maintenance immunosuppressive regimen unless life-threatening complications occurred. The liver, lung, and heart transplant programs remained active [1••].

Outpatient management consisted of postponing appointments and a conversion to consultations via telemedicine or email [1••].

**Europe—Spain**

Elective and living donor transplantation was suspended with only emergency life-saving transplants allowed to proceed [1••].

In the multi-center study from Spain, Crespo et al. found that 380 of the 414 COVID-19-positive renal transplant recipients required hospitalization, with 50 requiring ICU admission. Inpatient management consisted of hydroxychloroquine, azithromycin, glucocorticoids, lopinavir–ritonavir, and a small percentage received tocilizumab [16].

In another multi-center study from Spain, Crespo et al. analyzed the effect of COVID-19 in elderly transplant recipients. Fifteen of 16 patients were hospitalized with only two patients being admitted to the ICU. The mortality rate was eight out of 16 patients, with a higher frequency in more obese and frail patients and those with underlying heart disease. Additionally, it was found that patients who died had abnormal complete blood counts and inflammatory markers that reflected more anemia, lymphopenia, higher D-dimer, C-reactive protein, and IL-6 on admission. The study concluded that COVID-19 in the elderly population of kidney transplant recipients is correlated with an early and a high mortality rate. Similar inpatient management was used with discontinuation of mTOR-Is, antimetabolites, and CNIs [17].

Telemedicine was implemented to decrease the risk of COVID-19 transmission to the transplant community. Outpatient follow-up was cancelled including all non-urgent laboratory testing and procedures [1••].

**Europe—Switzerland**

Together, Swisstransplant and the Federal Office of Public Health coordinated a national response to the pandemic between the six transplant centers [1••]. The plan’s stages were (1) stop all live donor transplantation activities; (2) stop all deceased donor pancreas and islet cell transplants; (3) stop all deceased donor kidney transplants; (4) select and tailor approach to urgent status for liver, lung, and heart transplants; (5) only urgent transplants were to be performed; and (6) stop all transplant activities [1••].

On March 22, 2020, the last stage was reached and all transplant activities were stopped due to the limited hospital resources. The only exceptions were urgent cases, such as fulminant hepatitis [1••].

Outpatient clinics were converted to telemedicine unless there was an urgent need for inpatient visit.

**Oceania—Australia and New Zealand**

Throughout Australia, transplantation was greatly reduced. Living donor and deceased donor kidney transplantation was stopped due to limited intensive care unit beds and personal protective equipment, and their being too great a risk for recipients on high-dose immunosuppression in times of a worldwide pandemic. Screening for transplantation required COVID-19 testing for all deceased donors [1••].

Outpatient management transitioned to telemedicine and “apps” for consultations. Laboratory tests converted to separate labs outside of the hospital [1••].

During the first wave of COVID-19 in New Zealand, deceased donor kidney transplantation continued at two of the three transplant centers. Due to the travel restrictions, living donor renal transplantation was stopped [1••].

Outpatient follow-up was transformed by the use of telemedicine and remote monitoring. Only urgent patients were seen in the clinic [1••].

**Africa—South Africa**

The healthcare system within South Africa has disproportionately distributed resources, with 85% of the population reliant on the state for medical care, but the resources are mostly situated in the private sector [1••]. The transplantation resources are also limited by a lack of specialty surgeons. In response to the strain on the healthcare system of South Africa, transplantation was stopped in the state sector. However, within the private sector, deceased donor transplantation continued, but was greatly limited by very few potential deceased donors [1••]. All living donation was halted.
Ethics

The COVID-19 pandemic has highlighted many ethical issues in transplantation. The purpose of this section of the paper is not to give definitive statements. We have all learned that the transplant community is very vulnerable to outside forces and necessitates more resources than the ordinary patient population. The pandemic has heightened our awareness. It is not our role to decide for individual programs what is right or wrong. It is our duty to raise some of these questions, so that we begin to think and formulate strategies with potential answers when faced with this type of problem in the future.

These are some of the ethical questions that we have had to face during the pandemic; some of which may come back even sooner than we think:

1. How do we allocate scarce resources of hospital beds including ICU beds as well as staffing? Do we curtail activity in heavily affected regions?
2. Do we not perform living donor operations in regions which are heavily affected by COVID-19? Do we not expose living donors to risks in the hospital?
3. Do we transplant high-risk or low-risk recipients?
4. Do we not transplant kidney patients, but only do liver, heart, and lung as these patients have no alternative to staying alive?
5. Do we not transplant patients who cannot quarantine properly post-transplant?
6. Do we not utilize beds for potential deceased donors as resources are needed for COVID-19 patients?
7. Do we not send teams to regions where COVID-19 is rampant and do we not accept organs from these regions?
8. Do we tell patients that our program is unwilling to take the risk and that they should look to other programs that may not be as risk averse?

These are some of the questions that we as leaders in the transplant community have to consider now and potentially in the future [18•, 19, 20•].

Vaccines

Currently, there are no proven therapeutics that work against SARS-CoV-2 virus; therefore, vaccination emerged as a crucial strategy to potentially decrease the number of infections and curtail the pandemic.

Two mRNA vaccines were given Emergency Use Authorization by the US Food and Drug Administration on December 11, 2020. Two additional ones using adenovirus as the vector for the spike protein are currently in the pipeline for approval (Table 2).

Kidney transplant recipients are known to develop low antibody response to vaccination due to the fact that they are on immunosuppression. It is unclear how they will respond to the vaccine.

mRNA vaccines have been shown to stimulate CD4 and CD8, cells which are reportedly decreased in patients infected with COVID-19, particularly those who are also kidney transplant recipients. Therefore, mRNA vaccines are an attractive option for kidney transplant recipients. Evaluating their response to the vaccine is to be determined in future studies [21••, 22–24, 25•].

Global Trends in the Kidney Transplant Response

In this review, we analyzed how different transplant centers around the world responded to the COVID-19 crisis. We noticed global trends in the varied responses to the COVID-19 pandemic. We focused on looking at transplant centers’ responses to transplantation policies, the inpatient management of transplant patients infected with COVID-19, and the outpatient management of transplant recipients.

Overall, we noticed a trend of transplant centers to halt all transplantation (living and deceased donor) during peak infection times to save hospital resources and protect the vulnerable patient population. The exceptions were mostly for emergent surgery, such as kidney recipients who had exhausted all access options. It was a trend for centers to close the living donor programs first and then the deceased donor programs subsequently. However, the response to deceased donor transplants varied between countries more so than the living donor programs. In some countries, deceased donor transplants continued with modified donor and recipient criteria, while in other countries, this surgery was suspended due to the high risk of COVID-19 infection.

We noticed a few therapeutic agents dominated the inpatient management of transplant recipients infected with COVID-19. In the spring of 2020, inpatient management of kidney recipients generally consisted of hydroxychloroquine and azithromycin. The therapeutic management began to broaden in the summer and fall of 2020 to additionally include remdesivir and tocilizumab for more severe cases.

Outpatient management and follow-up was largely converted to telemedicine with remote patient monitoring. It was encouraged for transplant patients to protect themselves from COVID-19 infection and to only follow-up in person if they were a very recent transplant recipient or had an urgent or emergent indication.

The global community can learn from one another especially in times of crisis. We feel this review can share the responses of different countries and help us to understand
| Company/organization name | Location | Vaccine type | Antigen and immunogenicity | Vaccine efficacy | Number of doses | Storage conditions | Side effects |
|---------------------------|----------|--------------|----------------------------|-----------------|----------------|------------------|--------------|
| Biotech/Pfizer/Forsun Germany [1••, 2] | Germany | Modified nucleoside mRNA | Spike receptor binding domain (RBD) Seroconversion with neutralizing antibodies and ELISA binding Higher response in higher dose group Neutralizing antibody increased on booster in 10 μg and 30 μg groups Similar results seen in a second study with the same construct Comparative study with alternative construct had equivalent immunogenicity | 95% | 2 parental injections over a 3-week period | − 80 °C | Fatigue (3.8%) Headache (2.0%) |
| Moderna [3] USA | mRNA | Stabilized spike 100% seroconversion by after second dose by ELISA and neutralization Increase in response from 25 to 100 μg dose, rough equivalence between 100 and 250 μg dose Antigen-specific T cells detectable, greater in 100 μg group than 25 μg | 94.1% | 2 parental injections over a 4-week period | − 4 °C | Fatigue (9.7%) Arthralgia (5.2%) Injection site pain (4.1%) Myalgia (8.9%) Headache (4.5%) Injection site redness (2.0%) |
| University of Oxford/AstraZeneca [4, 5] UK | Adenovirus vector vaccine Adenovirus: ChAdOx1nCov-19/AZD1222 | Spike Seroconversion with neutralizing antibodies, (91% after one dose, 100% after two doses) | 74% | 2 parenteral injection over a 4-week period | − 4 °C | Neurological (transverse myelitis) |
| Johnson and Johnson Janssen [6] USA | Non-replicating viral vector vaccine (Adenovirus vector vaccine) Adenovirus 26 | Spike Seroconversion with neutralizing antibodies | 66% | 1 parenteral injection | − 4 °C | Headache Myalgias Fever Pain at injection site |
and manage the transplant population in the midst of pandemics.

Conclusions

COVID-19 is an important cause of morbidity and mortality in transplant recipients worldwide. Tailoring transplant activity during a pandemic with careful selection of donors and recipients is crucial for optimal patient outcomes. Given that there are no proven therapeutics against COVID-19, vaccination of transplant recipients is key to decreasing morbidity and mortality and eventually curtailting the pandemic.

Declaration

Conflicts of Interest Yorg Azzi, Abigail Brooks, Hillary Yaffe, and Stuart Greenstein declare no conflict of interest.

Human and Animals Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- Of major importance

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