

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

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.





Navigating Kidney Transplantation in the Early Phase of Coronavirus Disease 2019: Screening Patients With Reverse Transcriptase Polymerase Chain Reaction and Low-Radiation-Dose Chest Computed Tomography

Fauzia K. Butta, Kathleen Julian, Zakiyah Kadry, and Ashokkumar Jain

^aDepartment of Surgery, Division of Transplantation, Penn State Health Milton S. Hershey Medical Center, Hershey, Pennsylvania; and ^bDepartment of Medicine, Division of Infectious Diseases, Penn State Health Milton S. Hershey Medical Center, Hershey, Pennsylvania

ABSTRACT

Background. The coronavirus disease 2019 (COVID-19) pandemic of 2020 changed organ transplantation. All elective cases at our institution were postponed for approximately 3 months. Centers for Medicare and Medicaid Services considers organ transplant surgery a Tier 3b case, along with other high acuity procedures, recommending no postponement. Our transplant program collaborated with our transplant infectious disease colleagues to create a protocol that would ensure both patient and staff safety during these unprecedented times.

Methods. The living donor program was electively placed on hold until we had the proper protocols in place. Preoperative COVID-19 testing was required for all recipients and living donors. All patients underwent a rapid nasopharyngeal swab test. After testing negative by nasopharyngeal swab, recipients also underwent a low-radiation-dose computed tomography scan to rule out any radiographic changes suggestive of a COVID-19 infection.

Results. We performed 8 living donor and 9 deceased donor kidney transplants. In comparison, we performed 10 living donor and 4 deceased donor transplants during the same time period in the previous year. Our testing protocol enabled efficient use of all suitable organs offered during the viral pandemic. No recipients or living donors tested positive or developed COVID-19.

Conclusions. Creation of a viral testing protocol, developed in conjunction with our infectious disease team, permitted kidney transplantation to be performed safely, and the number of deceased donor transplants increased considerably without adversely affecting our outcomes.

THE CORONAVIRUS disease 2019 (COVID-19) pandemic of 2020 changed the world in countless ways. However, little is known about how organ transplantation was affected and the multiple challenges faced by programs in performing transplants in a manner that was safe for all involved [1]. Our aim was to examine how we handled these challenges at our own center while maintaining the safety of our patients and staff, yet using all suitable organs for transplantation. All elective cases at our institution were postponed for approximately 3 months. The Centers for

Medicare and Medicaid Services considers organ transplant surgery to be a Tier 3b case, along with other high acuity procedures, such as trauma, limb-threatening vascular surgery, and cardiac surgery for symptomatic patients, and

*Address correspondence to Fauzia K. Butt, Department of Surgery, Division of Transplantation, Penn State Health Milton S. Hershey Medical Center, 500 University Dr, PO Box 850, Hershey, PA 17033. Tel: 717-531-5921; Fax: 717-531-5851. E-mail: fbutt@pennstatehealth.psu.edu

© 2021 Elsevier Inc. All rights reserved. 230 Park Avenue, New York, NY 10169 0041-1345/21 https://doi.org/10.1016/j.transproceed.2021.01.001 1170 BUTT, JULIAN, KADRY ET AL

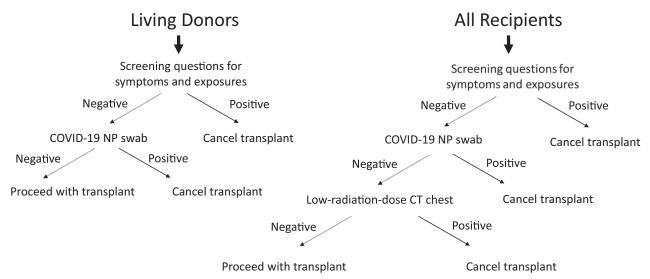


Fig 1. COVID-19 testing protocol for living doors and all recipients. COVID-19, coronavirus disease 2019; CT, computed tomography; NP, nasopharyngeal.

recommends continuation during the COVID-19 pandemic [2]. Our transplant program collaborated with our transplant infectious disease colleagues to create a protocol that would ensure patient and staff safety during these unprecedented times.

MATERIALS AND METHODS Deceased Donor Kidney Transplants

For deceased donor recipients, we made several changes to the admissions process, including a preliminary telephonic screening for symptoms of an ongoing viral infection. Screening questions included the presence of fevers, respiratory symptoms, recent travel, and contact with an infected person or close contact with undiagnosed acute respiratory illnesses. After passing the initial screening process, recipients were admitted and tested for COVID-19 infection with a nasopharyngeal (NP) swab. Early in the pandemic, several relatively asymptomatic, nontransplant COVID-19 cases were recognized by computed tomography (CT) scan findings alone. We also experienced several cases of false-negative severe acute respiratory syndrome coronavirus 2 polymerase chain reaction. We developed a 2-step testing process (Fig 1). After a negative NP swab result, recipients proceeded to have a low-radiation-dose CT (LDCT) of the chest without contrast to ensure that there was no evidence of a COVID-19 infection indicated by radiographic changes. We felt that this confirmatory testing was essential in all recipients because of the lower sensitivity of NP swab testing alone [3-6]. The time required to perform testing and obtain results was considered before the acceptance of any deceased donor organ offers.

Our center also changed the way in which we screened deceased donor offers during this viral pandemic. All deceased donors were required to have a negative COVID-19 NP swab. A bronchoalveolar lavage for COVID-19 was also required in the presence of any radiographic changes on chest radiography or CT scan that were consistent with infection, including ground-glass opacities, infiltrates, or consolidation. Any deceased donors who tested positive for COVID-19 or had strong radiographic

evidence of infection were not used by our institution for transplantation.

Living Donor Kidney Transplants

Initially, there was much uncertainty regarding our elective living donor kidney transplant cases. While these cases technically fell under the Centers for Medicare and Medicaid Services Tier 3b category designation, they were also elective and involved a healthy donor undergoing surgery who would now have the added risk of developing an infection with COVID-19. In addition, there was a risk of donor-derived severe acute respiratory syndrome coronavirus 2 infection for the recipient. Resource allocation was another consideration because all recipients are admitted to the intensive care unit (ICU) at our institution. As a program, we electively chose to postpone all living donor cases until there was a better understanding of the viral pandemic and the hospital infrastructure was ready to support resumption of our caseload. Protocols needed to be in place to ensure the safety of donors, recipients, and hospital staff, including residents and medical students. Our living donor program ended its voluntary suspension on May 14, 2020, resulting in about a 2.5-month postponement of living donor cases. The institution, as a whole, resumed nontransplant elective surgical cases on May 26, 2020.

When we resumed our living donor cases, living donors and their recipients were both admitted the day before the scheduled procedure after passing an initial telephonic screening for symptoms and exposures. This was a departure from our standard process because patients were typically admitted in the early morning on the day of surgery. Both living donors and recipients were tested with a COVID-19 NP swab after admission (Fig 1), which usually ended up being sometime in the afternoon because of bed availability. Living donor recipients then proceeded with LDCT of the chest (Fig 1) after testing negative with the NP swab to rule out any radiographic changes indicative of a COVID-19 infection. We felt that this confirmatory testing was essential because of the lower sensitivity of NP swab testing alone [3–6]. This new admission protocol was developed with the assistance of our transplant infectious disease team to ensure that there would be adequate time

provided for COVID-19 testing and that the patients would not risk exposure to the virus after initially testing negative. When elective procedures resumed at our institution, patients were required to have a negative COVID-19 NP swab test as an outpatient through a contracted reference laboratory, which had a turnaround time of 2 to 3 days. We did not feel that this was adequate for patients receiving immunosuppression and we did not want to risk exposure to COVID-19 before their scheduled procedure. We developed a protocol to conduct in-house testing with a 2- to 4-hour turnaround time, to be completed within 24 hours of the planned transplant operation.

Recipient Education

Our transplant program created a special consent form regarding COVID-19 and the possibility of acquiring this viral infection. In general, this consent informed the recipients that despite our testing protocols, they could be infected at any time, before, during, or after transplantation. It also stated that the risk of acquiring the infection is reduced if guidelines are followed, including mask wearing, social distancing, hand washing, etc. These guidelines were reinforced by the staff during education prior to discharge.

RESULTS

During this period, specifically from March 1, 2020, through June 30, 2020, we performed a total of 17 kidney transplants: 8 living donors and 9 deceased donors. In comparison, during the same 4 months the previous year, we performed 14 transplants: 10 living donors and 4 deceased donors.

The results of the transplants performed are summarized in Table 1. Ages of recipients ranged from 17 to 68 years, with a median of 52 years. The Kidney Donor Profile Index for deceased donors ranged from 2% to 82%, with a mean value of 32%. The ages of the deceased donors ranged from 19 to 53 years, with a mean of 35 years. There were 4 donation after cardiac death (DCD) donor kidneys accepted; 2 kidneys came from the same DCD donor. Two deceased donors were categorized as increased risk, and 1 DCD donor was an increased risk and hepatitis C-positive donor. Interestingly, there were 2 deceased donors from whom we received both kidneys, which is an unusual occurrence. The sequence numbers ranged from #1, in a recipient with 100% calculated panel-reactive antibodies, to 223, with a median of 30. The cold ischemia time for the deceased donors ranged from 603 minutes (10 hours and 3 minutes) to 1380 minutes (23 hours), with a median of 1001 minutes (16 hours and 41 minutes).

To date, no recipient or living donor outlined in Table 1 has contracted COVID-19, and they are all doing well. All of the deceased donor recipients have stable allograft function.

DISCUSSION Challenges

We experienced several challenges with the COVID-19 testing. A designated COVID swab team was only available between the hours of 7 AM to 11 PM. Patients

admitted after 11 PM could not be tested until 7 AM the following morning. Recognition of these delays sometimes mandated passing on DCD donors or other offers with a time constraint present. Occasionally, these testing limitations also required us to decline the admission of recipients who were backing up a multiorgan recipient because we could not obtain the NP swab testing in an expedient and timely manner. Eventually, the COVID-19 swab team was disbanded and charge nurses were individually trained to perform this testing, which was much more accommodating for our patients. Our laboratory ran the COVID-19 samples as a priority for these patients and produced results in 2 hours, enabling us to accept offers and perform transplants in an expedient manner.

The COVID-19 testing and admission protocol for living donors and their recipients caused some delays when we were involved in a swap or a transplant chain through the National Kidney Registry (NKR). NKR required test results by 3 PM the day before a scheduled transplant, and occasionally the hospital was at a capacity where beds were not immediately available. Admission and subsequent testing were occasionally delayed beyond the 3 PM deadline, much to the dismay of our living donor coordinator and NKR.

Our program's medical students were prohibited from being in the hospital during this 3-month period. Surgical residents were reduced to a skeleton crew with 2 weeks on and 2 weeks off, in case they needed to be guarantined for a suspected COVID-19 infection. Without a surgical resident team specifically assigned to the transplant service, the chief resident would make assignments for individual operative cases daily. Occasionally, 2 attending surgeons would scrub on a case because there were no residents available because of the staffing shortage. Resident participation in deceased donor recovery procedures was limited because they were only allowed to participate in cases at our own institution. The local organ procurement organization (OPO) also requested local surgeons to recover organs for teams outside of our immediate area. When we recovered organs for the OPO at nearby hospitals outside of our system, residents were not allowed to participate and an OPO staff member served as a surgical assistant.

Screening With Low-Radiation-Dose Chest CT

LDCT has been recommended by the US Preventive Services Task Force for lung cancer screening since 2013 [7]. Several groups have applied LDCT during the viral pandemic to assist with diagnosis, especially when reverse transcriptase polymerase chain reaction (RT-PCR) may not be readily available. Bahrami-Motlagh et al evaluated the diagnostic efficacy of LDCT compared with RT-PCR and found that LDCT had a sensitivity of 96.6% and negative predictive value of 90% [8]. They concluded that LDCT is a suitable alternative to standard-dose CT in epidemic areas when RT-PCR may not be readily available. Dangis et al compared LDCT with RT-PCR and concluded that LDCT demonstrated excellent sensitivity (86.7%), specificity

1172 BUTT, JULIAN, KADRY ET AL

Table 1. Donor and Recipient Characteristics

Patient No.	Age, y	Sex	Donor Type	UNOS Sequence No.	DCD	HCV	KDPI, %	cPRA	CIT, h	Donor Age, y	IRD
1	46	F	LURD	-	-	-	-	-	-	-	
2	39	M	Deceased	5	N	N	14	0	10.62	35	Ν
3	68	F	Deceased	1	N	N	2	100	16.68	19	Ν
4	60	F	Deceased	89	Υ	N	82	0	20.18	53	Ν
5	67	F	Deceased	223	Υ	N	82	0	23.00	53	Ν
6	37	M	Deceased	22	N	N	6	0	10.05	27	Ν
7	51	M	Deceased	30	N	N	6	0	14.18	27	Ν
8	45	F	Deceased	31	N	N	35	0	11.90	35	Υ
9	56	M	Deceased	25	Υ	N	63	0	21.23	39	Ν
10	48	F	LURD	-	-	-	-	-	-	-	-
11	57	M	LURD	-	-	-	-	-	-	-	-
12	52	M	Deceased	38	Υ	Υ	32	0	22.13	30	Υ
13	17	M	LURD	-	-	-	-	-	-	-	-
14	45	F	LURD	-	-	-	-	-	-	-	-
15	63	F	LURD	-	-	-	-	-	-	-	-
16	42	M	LRD	-	-	-	-	-	-	-	-
17	53	F	LURD	-	-	-	-	-	-	-	-
Mean	52.73			51.56			35.78		16.66	35.33	
SD	10.20			69.07			32.44		5.15	11.58	
Median	52.00			30.00			32.00		16.68	35.00	

Abbreviations: CIT, cold ischemia time; cPRA, calculated panel-reactive antibody; DCD, donation after cardiac death; HCV, hepatitis C virus; F, female; IRD, increased risk donor; KDPI, Kidney Donor Profile Index; LRD, living related donor; LURD, living unrelated donor; M, male; N, no; UNOS, United Network for Organ Sharing; Y, yes.

(93.6%), positive predictive value (91.1%), negative predictive value (90.3%), and accuracy (90.2%) for the diagnosis of COVID-19 [9]. They found that these results improved for patients with clinical symptoms \geq 48 hours to 95.6%, 93.2%, 91.5%, 96.5%, and 94.4%, respectively. In addition, the median time between CT acquisition and the reported results was 25 minutes. Fang et al compared chest CT with RT-PCR at initial patient presentation and found a sensitivity for COVID-19 infection of 98% compared with 71%, respectively [10]. Kang et al cited these findings and further recommended performing LDCT to decrease the radiation dose to one-eighth to one-ninth of the standard dose to diagnose COVID-19 [11].

The CT chest findings in a patient with an early COVID-19 infection include ground-glass opacities, bilateral/multifocal involvement, and peripheral distribution. At a later stage, these can develop into crazy paving, consolidation, and a reversed halo sign [9]. Figure 2 is an LDCT chest of one of our patients who had a negative RT-PCR on preoperative screening for a liver transplant, but CT findings were consistent with a possible COVID-19 infection, including patchy, peripheral ground-glass opacities in the anterior lungs.

Postoperative Protocols

Inpatient. Post-transplant protocols had to be created regarding the admission of recipients from the operating room. At our center pre-COVID-19, all transplant recipients were admitted to the surgical anesthesia intensive care unit (SAICU). During the viral pandemic, we made a deliberate effort to admit our patients to an

ICU that was completely separate from the SAICU, where patients infected with COVID-19 were already located. All transplant recipients were admitted to the Heart and Vascular Institute ICU, which was physically located on a different floor, yet staffed by the same anesthesia attending staff as the SAICU. This physical separation was important to prevent accidental transmission of COVID-19 to our highly immunosuppressed new transplant recipients. Anecdotally, we have heard of cases at another institution where new transplant recipients were located in the same ICU as patients infected with COVID-19, and 3 liver transplant recipients became infected with COVID-19.

Outpatient. Clinic changes took effect almost immediately, with the postponement of all surgical donor and recipient evaluations. In an effort to minimize the unnecessary potential exposure of transplant recipients to COVID-19, a weekly huddle was conducted to review all of the patients scheduled for clinic visits that week. Physical visits were reserved for patients who absolutely needed one for medical issues or for the removal of drains or staples. The majority of visits were converted to a telehealth platform. These telehealth visits presented their own challenges because initially our institution stated that any video platform was acceptable, despite the inability to protect patient's health information because patient care was the priority. That blanket approval was then revoked because certain video platforms, such as Doximity and Facetime, did not have the proper security safeguards in place. The OnDemand video platform that our institution eventually adopted also had some limitations because it was only compatible with the iPhone and not with the



Fig 2. Low-dose chest computed tomography of pretransplant patient with negative reverse transcriptase polymerase chain reaction with findings positive for coronavirus disease 2019 infection: patchy, peripheral ground-glass opacities in the anterior lungs (circled areas).

Android operating system. Some of our patients had trouble registering for OnDemand, did not have reliable Wi-Fi connectivity, or lacked a smartphone. For these patients, visits had to be conducted by telephone. Other unforeseen challenges with the OnDemand video platform included the lack of webcams on the providers' desktops, and these had to be installed. Also, if our patient resided in another state, providers had to be licensed in that state to use the video platform, otherwise we were limited to performing the visit with a phone call.

CONCLUSIONS

In response to the COVID-19 pandemic, our transplant program closely collaborated with our infectious disease colleagues to develop a protocol that allowed transplantation to continue while ensuring the safety of our patients and staff. While initial challenges were experienced in performing timely testing, we were able to perform a total of 17 kidney transplants, including living donors, without the development of any COVID-19 infections. We created a screening protocol during the early phase of the viral

1174 BUTT, JULIAN, KADRY ET AL

pandemic. RT-PCR in combination with LDCT chest appears to be a safe and effective screening tool. It is unclear whether other transplant programs were being more conservative or may not yet have had their own COVID-19 protocols in place. Perhaps this played a role in receiving 4 kidneys from 2 of the deceased donors. Careful screening for all suitable deceased donor organs in a safe and timely fashion was essential to keep the program operational. Although most of the transplant support staff worked remotely from home, these staffing changes did not adversely affect our ability to continue to serve our patients. We performed more than twice the number of deceased donor kidney transplants during the same period the previous year and maintained 80% of our living donor volume, even with the temporary closure of the living donor program. Despite the limitations of the COVID-19 pandemic, we successfully maintained our transplant volumes, maintained the safety of all individuals involved, and experienced a considerable increase in the number of deceased donor transplants performed over the previous year.

REFERENCES

- [1] Esagain SM, Zioga IA, Giannis D, Hayat MH, Elaias N, Tsoulfas G. Challenges in abdominal organ transplantation during the COVID-19 pandemic. Front Med 2020;7:1–8. https://doi.org/10.3389/fmed.2020.00287.
- [2] Centers for Medicare and Medicaid Services. CMS adult elective surgery and procedures recommendations: limit all non-essential planned surgeries and procedures, including dental, until

further notice. https://www.cms.gov/files/document/covid-elective-surgery-recommendations.pdf; 2020 [accessed 20.06.16].

- [3] American Society of Transplantation. 2019-nCoV (coronavirus): recommendations and guidance for organ donor testing. https://www.myast.org/sites/default/files/COVID19% 20FAQ%20Donor%20Testing%2005.19.2020_0.pdf [accessed 20.06.29].
- [4] Wang W, Xu Y, Gao R, et al. Detection of SARS-CoV-2 in different types of clinical specimens. JAMA 2020;323:1843–4. https://doi.org/10.1001/jama.2020.3786.
- [5] Ai T, Yang Z, Hou H, et al. Correlation of chest CT and RT-PCR testing for coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. Radiology 2020;296:E32–40. https://doi.org/10.1148/radiol.2020200642.
- [6] American Society of Transplantation. Webinar COVID-19: organ donation and transplant town hall. https://www.youtube.com/watch?v=LUM8-vDH-kI [accessed 28.06.20].
- [7] Moyer VA, U.S. Preventive Services Task Force. Screening for lung cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2014;160:330–8. https://doi.org/10.7326/M13-2771.
- [8] Bahrami-Motlagh H, Abbasi S, Haghighimorad M, et al. Performance of low-dose chest CT scan for initial triage of COVID-19. Iran J Radiol 2020;17:e104950. https://doi.org/10.5812/iranjradiol.104950.
- [9] Dangis A, Gieraerts C, De Bruecker Y, et al: Accuracy and reproducibility of low-dose submillisievert chest CT for the diagnosis of COVID-19 [e-pub ahead of print]. Radiol Cardiothorac Imaging. https://doi.org/10.1148/ryct.2020200196, accessed December 30, 2020.
- [10] Fang Y, Zhang H, Xie J, et al. Sensitivity of chest CT for COVID-19: comparison to RT-PCR. Radiology 2020;296:E115–7. https://doi.org/10.1148/radiol.2020200432.
- [11] Kang Z, Li X, Zhou S. Recommendation of low-dose CT in the detection and management of COVID-19. Eur Radiol 2020;30: 4356–7. https://doi.org/10.1007/s00330-020-06809-6.