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Successful simultaneous pancreas and kidney transplant in a patient post-COVID-19 infection

To the editor: The coronavirus disease 2019 (COVID-19) pandemic has slowed down the solid organ transplantation worldwide. Although we have heard of few solid organ transplants having been performed in patients recovered from COVID-19 infection, none has been reported yet. We present a patient who underwent a simultaneous pancreas and kidney transplantation after recovering from COVID-19 and is doing well close to 2 months post-transplantation. A 66-year-old Caucasian woman with end-stage renal disease secondary to insulin-dependent type 2 diabetes mellitus was called in to undergo simultaneous pancreas and kidney transplantation. On admission, we found that 3 months earlier she had been diagnosed with COVID-19 with fever and cough but had recovered completely while in self-quarantine at home. On her admission, she had stable vitals and physical exam was unremarkable. A COVID-19 antibody test was positive for IgG, and COVID-19 rapid polymerase chain reaction (PCR) test was negative on 2 occasions a day apart (Table 1^{1}). Other laboratory parameters were unremarkable. The chest X-ray and computed tomography scan of the lungs showed no lung abnormalities. The patient underwent simultaneous pancreas and kidney transplantation successfully from a COVID-19negative donor and had an uneventful post-transplant course. Her serum creatinine trended down to 0.8 mg/dl, and she came off insulin by day 4 post-transplant. She received 3 reduced doses of rabbit anti-thymocyte globulin (Thymoglobulin; Sanofi-Genzyme, Cambridge, MA) 1 mg/kg/d for induction along with intravenous methylprednisolone taper. She was discharged on postoperative day 5 on mycophenolate mofetil 500 mg twice a day, extended-release tacrolimus (Envarsus XR; Rottendorf Pharma GmbH, 59320 Ennigerloh, North Rhine-Westphalia, Germany) 6 mg once a day (target tacrolimus level 7-9 ng/ml), and oral prednisone taper. The patient has remained asymptomatic with no signs of repeat COVID-19 infection 7 weeks after her transplant.

Table 1 | COVID-19 PCR and antibody test results

	April 19, 2020	July 2, 2020	July 3, 2020	July 9, 2020	July 13, 2020	July 16, 2020	July 23, 2020	July 30, 2020
SARS-CoV-2 RNA by RT-PCR	Positive	Negative	Negative	Negative	Negative	Negative	Negative	
CoV-2, total index (reference range <1.0 S/C ^a)		19.3	-	-	-	22.7	31.4	26.3
CoV-2, total Ab (IgG and/or IgM)		Reactive				Reactive	Reactive	Reactive
SARS-CoV IgG Ab		Reactive		Nonreactive	Nonreactive	Nonreactive	Nonreactive	Nonreactive
SARS-CoV lgG index (<1.0 S/C ^a)		1.09		0.35	0.31	0.36	0.42	0.31

Ab, antibodies; COVID-19, coronavirus disease 2019; PCR, polymerase chain reaction; RT-PCR, reverse-transcriptase polymerase chain reaction; SARS-CoV-2; severe acute respiratory syndrome coronavirus 2.

^aS/C, signal for test sample/signal at cutoff value. VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack (Ortho-Clinical Diagnostics, Inc., Rochester, NY).¹

There were several considerations before proceeding with her transplantation. First, had she successfully cleared the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection? The detection of COVID-19 by reverse transcriptase-PCR may yield false-negative tests.^{2,3} This uncertainty in test results is further complicated by reports of confirmed reverse transcriptase-PCR-positive COVID-19 cases who recovered from the illness, tested negative on repeat reverse transcriptase-PCR but again tested positive afterward, bringing into question whether this was a repeat infection or whether the preceding test results were, in fact, falsely negative.^{4,5} Our patient had no symptoms or signs of infection, COVID-19 PCR was negative on two occasions a day apart, and a COVID-19 antibody test was positive. Second, could she have developed a chronic COVID-19 carrier state, and if infection would relapse post-transplant? Many (nonretrovirus) RNA viruses like hepatitis C can establish "within host" persistent infections that occasionally lead to chronic or reactivated disease.⁶ Chronic COVID-19 carrier state has not been reported yet. Our patient exhibited no symptoms or signs of chronic organ dysfunction and since her transplant, multiple SARS-CoV-2 PCRs have stayed negative. Third, will positive SARS-CoV-2 antibodies protect her from repeat infection? There have been reports of prolonged coexistence of anti-SARS-CoV-2 IgG along with the positive reverse transcriptase-PCR for SARS-CoV-2, raising the possibility of variable level of immunity provided by the antibodies.⁷ In a smaller study conducted by Zhang et al.,⁸ both IgM and IgG antibodies were detected in all 39 patients infected with SARS-CoV-2 after 5 days of disease onset. In a report of 149 convalescent individuals with COVID-19 who recovered, authors found that most convalescent plasmas collected an average of 39 days after the onset of symptoms do not contain high levels of neutralizing activity.⁹ Transplant patients who are on long-term immunosuppression may have attenuated immunity, putting them at risk of atypical presentations, delayed or missed diagnoses, and higher morbidity and possible higher mortality with COVID-19 compared with the general population.^{10,11} We lowered the dose of induction and maintenance immunosuppression in our patient to retain the positive anti-SARS-CoV-2 antibodies. Although her total antibodies (IgG and IgM) have



persisted until the time of last follow-up, IgG antibodies became negative at 1-week follow-up post-transplant.

In conclusion, this case study suggests that it may be reasonable to proceed with solid organ transplant in waitlist candidates if they have recovered completely from COVID-19 with no evidence of active infection, after confirming 2 consecutively negative PCR tests, and with positive SARS-CoV-2 antibody levels. The role of SARS-CoV-2 antibodies in providing protection is unclear, and levels may fall off rapidly post-transplant probably due to immunosuppression. Patients must be advised to continue to take safety precautions post-transplant.

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Significant impact of COVID-19 on organ donation and transplantation in a low-prevalence country: Australia

To the editor: The incidence and impact of coronavirus disease 2019 (COVID-19) has varied enormously across the

globe. The pandemic has negatively impacted organ donation and transplantation in countries that have experienced high rates of infection, including the United States, France, and the United Kindgom, all reporting >50% reductions in transplant activity.^{1,2} Australia has experienced a significantly lower incidence of COVID-19 (Table 1). Despite this, the impact on organ transplantation has been significant.

Cases of COVID-19 were first detected in Australia in late January 2020 and from March 18 the incidence had exceeded 100 cases per day. Given data from China and Europe revealing exponential increases, overwhelming demand for intensive care unit beds and ventilators and rapidly rising cumulative mortality from COVID-19, Australia anticipated similar outcomes.

Australia's National Incident Room was engaged, and public health policies to support case detection, contact tracing, quarantine, social distancing, and hand hygiene were implemented nationally. Health care facilities prepared for a surge of hospital admissions to manage severe cases of COVID-19.

The Australian Organ and Tissue Authority and the Transplantation Society of Australia and New Zealand formed the National Transplantation and Donation Rapid Response Taskforce-COVID-19 (Taskforce), including experts in transplantation, organ donation, infectious diseases, and data analytics. The Taskforce was charged with devising and coordinating a national approach to transplantation and donation during the pandemic. Concerned that early posttransplant acquisition of COVID-19 may produce severe disease and mortality, and that growing case numbers in hospitals may limit capacity and compromise safety of donation and transplantation, during March, the Taskforce recommended suspension of all adult kidney transplantation. Urgent heart, lung, liver, and pediatric transplantation continued, following case-by-case assessment of risks and benefits.³ Early communication between donation and transplant clinicians was recommended to minimize futile donor work-ups. All recommendations were implemented nationally.

By mid-April, incident cases had fallen below 20 per day and intensive care unit capacity was uncompromised. The Taskforce recommended resumption of usual donation and transplantation activity on April 24, subject to precautions including donor and recipient screening for COVID-19, which was approved by all government Chief Medical Officers and implemented by all state-based health jurisdictions.

Following suppression of the initial outbreak in March and April 2020, a second wave occurred, primarily in Victoria (Figure 1). A jurisdictional response occurred, primarily addressed by public health measures including case detection, contact tracing, and containment via "lock down" border closures and strict travel restrictions. Donation and transplantation services continued but remain impacted by logistical barriers to transportation of organs, medical teams, and patients. Further isolated "outbreaks" are expected for the foreseeable future.