

Organ donation and transplantation from donors with a diagnosis of COVID-19

The COVID-19 pandemic has had a significant impact on rates of organ transplantation in Australia and around the world^{1,2}. In Australia and New Zealand, the non-acceptance of organs from potential donors who are infected with SARS-CoV-2 at the time of planned procurement or who have recovered from SARS-CoV-2 infection has not been a major contributing factor to reduced transplant activity to date, due to the comparatively lower incidence of COVID-19 for much of the pandemic. The prevalence of potential donors who are either currently or previously infected with SARS-CoV-2 continues to increase as due to ongoing, high levels of community transmission. In order maximise organ utilisation and prevent unnecessary non-acceptance of otherwise suitable organs, donors must be carefully assessed for active SARS-CoV-2 infection or recent, known SARS-CoV-2 exposure.

Transmission of SARS-CoV-2 during solid organ transplantation has been a theoretical concern, based on the observations that; low level viremia occurs during respiratory infection³; angiotensin-converting enzyme 2 receptors, required for SARS-CoV-2 binding, are present in various organs throughout the body^{4,5}; and SARS-CoV-2 has been detected in several bodily secretions and multiple tissue types, albeit often without histopathologic evidence of associated viral lesions^{6,7}. Despite biologic plausibility, there have not been any documented cases of transmission of SARS-CoV-2 via extra-pulmonary donated organ or blood products that contain PCR-detectable virus. The use of extra-pulmonary organs from donors with a current positive SARS-CoV-2 PCR test is an area of active research and the decision to transplant these organs needs to be balanced with the risk of morbidity and mortality for waitlisted individuals.

There is mounting evidence that it may be safe to transplant extra-pulmonary organs (liver, kidney, heart) from living and deceased donors with a history of COVID-19, who have a positive nasopharyngeal (NP) swab at the time of organ procurement^{8–13}. In the largest study to date, Gupta et al. analysed the United States Organ Procurement and Transplantation Network database to report on use of organs from COVID-19 infected donors. In this study, 150 donors donated 276 organs to 262 recipients (193 kidneys, 5 pancreases, 18 hearts, 3 lungs, 57 livers, 0 intestine). 72.4% of transplanted organs were from donors who were positive on PCR for SARS-CoV-2 within seven days of organ recovery. The median duration of follow up varied from 62 to 144 days, depending on the organ(s) transplanted. Graft loss was seen only in kidney transplants (n=3, 1.6%) of which two were due to thrombosis on the day of surgery. There were five deaths including one from sepsis and one from respiratory failure. This study did not report on the donor's stage of or complications from COVID-19 and if the recipients received any prophylactic therapy¹⁴. In addition, several cases have been reported of transplantation of non-lung organs from deceased donors who tested positive for SARS-CoV-2 on PCR of nasopharyngeal swab at the time of organ procurement without SARS-CoV-2 transmission to recipients with and without evidence of immunity at the time of transplant^{11,13,15,16}. Long-term allograft outcomes are not yet known.

Given the respiratory tract is the primary site of SARS-CoV-2 inoculation and infection with high levels of virus and viral damage detected post-mortem in patients who die from COVID-19^{17,18}, one would expect higher risk of SARS-CoV-2 transmission to lung recipients. Indeed, donor-derived transmission of SARS-CoV-2 has been reported in lung recipients in instances where upper respiratory tract PCR was negative





and lower respiratory tract testing was not undertaken prior to organ procurement, but lower respiratory tract PCR was positive when retrospectively tested after transplantation ^{19,20}. Concerns have also been raised about the transplantation of small bowel from donors who test positive for SARS-CoV-2, given the high concentration of lymphoid tissue and the high immunosuppression requirement post-transplant, relative to other organs²¹.

Deceased donors with a diagnosis of COVID-19

- See flowchart

Living donors with a diagnosis of COVID-19

- Defer transplant until the donor has resolution of acute COVID-19 symptoms <u>and</u> at least 7 weeks since the onset of COVID-19 symptoms or first positive SARS-CoV-2 PCR if asymptomatic²²
 - This recommendation is based on the potential risk for the donor undergoing major surgery during an acute infection and risk of nosocomial transmission.
- Earlier donation may be considered under extenuating circumstances where the donor had asymptomatic/mild COVID-19 and the recipient has urgent need for transplantation.

Potential recipients of an organ from a donor with a diagnosis COVID-19

- The potential recipient should give informed consent to accept the organ(s) given the theoretical risk of SARS-CoV-2 transmission
- Given the lack of evidence of transmissible virus in non-pulmonary organs, alteration in recipient immunosuppression and COVID-19 prophylaxis (e.g., antivirals, COVID-19 monoclonal antibodies) are not routinely recommended.



Flow chart – assessment of potential deceased donors



¹ Rapid antigen tests are not appropriate for testing potential organ donors

² All potential donors who test positive for COVID-19 should be discussed with an infectious diseases physician

³ Surrogates for viral quantification (i.e. cycle threshold 'CT' values) should not be used as the sole indicator to assess COVID-19 disease activity due to variation based on specimen quality and lack of standardization between tests. Routine serologic testing is not recommended.

⁴ Donors with SARS-CoV-2' not detected on PCR may have been classified as a COVID-19 'close contact' within the 7 days prior to donation. This is inconsequential when considering acceptance of non-lung organs. The risk of transmission of SARS-CoV-2 via lung allografts in the setting where the donor is in the 'eclipse period' (time between infection and test positivity) is of theoretical concern but thought to be very low and should be considered on a case-by-case basis.

⁵ Pancreas transplantation includes transplantation of a small portion of duodenum. The risk of SARS-CoV-2 transmission and/or adverse graft outcomes from SARS-CoV-2 positive donors is unclear. Each



donor-recipient pair should be assessed on a case-by-case basis. Avoid transplanting organs from donors with severe COVID-19 as per other non-lung allografts

Further information in relation to organ donation and transplantation and COVID-19 is available on the TSANZ website, including:

- Routine testing for coronavirus (SARS-CoV-2) causing COVID-19: Information for donation and transplant professionals
- Organ Donation and Transplantation from Patients with COVID-19 Vaccine Induced Thrombosis with Thrombocytopenia Syndrome (TTS)





References

- Chadban SJ, McDonald M, Wyburn K, Opdam H, Barry L, Coates PT. Significant impact of COVID-19 on organ donation and transplantation in a low-prevalence country: Australia. *Kidney Int*. 2020;98(6):1616-1618. doi:10.1016/j.kint.2020.10.007
- 2. Aubert O, Yoo D, Zielinski D, et al. COVID-19 pandemic and worldwide organ transplantation: a populationbased study. *Lancet Public Heal*. 2021;2667(21). doi:10.1016/s2468-2667(21)00200-0
- 3. Cappy P, Candotti D, Sauvage V, et al. No evidence of SARS-CoV-2 transfusion transmission despite RNA detection in blood donors showing symptoms after donation. *Blood*. 2020;136(16):1888-1891. doi:10.1113/JP279694.20.
- 4. Dong M, Zhang J, Ma X, Al. E. ACE2, TMPRSS2 distribution and extrapulmonary organ injury in patients with COVID-19. *Biomed Pharmacother*. 2020;131(110678).
- 5. Hamming I, Timens W, Bulthuis M. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. *J Pathol*. 2004;203:631-637.
- 6. Remmelink M, De Mendonça R, D'Haene N, et al. Unspecific post-mortem findings despite multiorgan viral spread in COVID-19 patients. *Crit Care*. 2020;24(1):1-10. doi:10.1186/s13054-020-03218-5
- 7. Wang W, Xu Y, Gao R, et al. Detection of SARS-CoV-2 in Different Types of Clinical Specimens. *JAMA*. (PG-10.1001/jama.2020.3786):10.1001/jama.2020.3786. doi:10.1001/jama.2020.3786
- 8. de la Villa S, Valerio M, Salcedo M, et al. Heart and liver transplant recipients from donor with positive SARS-CoV-2 RT-PCR at time of transplantation. *Transpl Infect Dis*. 2021;(May):1-3. doi:10.1111/tid.13664
- 9. Kute VB, Godara S, Guleria S, et al. Is it Safe to Be Transplanted from Living Donors Who Recovered from COVID-19? Experience of 31 Kidney Transplants in a Multicenter Cohort Study from India. *Transplantation*. 2021;105(4):842-850. doi:10.1097/TP.000000000003609
- 10. Malleeswaran S, Mohanka R, Yalakanti RB, et al. Living Donor Hepatectomy After Proven SARS-CoV-2 Infection: First Report of 9 Cases From 3 Centers. *Transplantation*. 2021;105(7):e70-e71. doi:10.1097/TP.00000000003750
- 11. Koval CE, Poggio ED, Lin YC, Kerr H, Eltemamy M, Wee A. Early success transplanting kidneys from donors with new SARS-CoV-2 RNA positivity: A report of 10 cases. *Am J Transplant*. Published online 2021. doi:10.1111/ajt.16765
- 12. Vazquez L. Antifungal Prophylaxis in Immunocompromised Patients. *Mediterr J Hematol Infect Dis*. 2016;8(1):e2016040. doi:10.4084/MJHID.2016.040
- 13. Romagnoli R, Gruttadauria S, Tisone G, et al. Liver transplantation from active COVID- 19 donors : A lifesaving opportunity worth grasping ? *Am J Transpl*. 2021;Online Ahe. doi:10.1111/ajt.16823
- 14. Gupta G, Azhar A, Gungor A, Molnar MZ. Early Data on Utilization and Discard of Organs From COVID-19 infected Donors : A US National Registry Analysis. 2022;00(00):19-21. doi:10.1097/TP.0000000000004091
- 15. Puodziukaite L, Serpytis M, Kundrotaite A, et al. Kidney transplantation from a SARS-CoV-2-positive donor for the recipients with immunity after COVID-19. *Transpl Infect Dis.* 2021;(June). doi:10.1111/tid.13666
- 16. Frattaroli P, Anjan S, Coro A, et al. Is it safe to perform abdominal transplantation from SARS-CoV-2 polymerase chain reaction positive donors? *Transpl Infect Dis*. 2021;(June):3-5. doi:10.1111/tid.13688
- 17. Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med*. (PG-). doi:10.1056/NEJMoa2001017
- 18. Skok K, Stelzl E, Trauner M, Kessler HH, Lax SF. Post-mortem viral dynamics and tropism in COVID-19 patients in correlation with organ damage. *Virchows Arch*. 2021;478(2):343-353. doi:10.1007/s00428-020-02903-8
- 19. Kumar D, Humar A, Keshavjee S, Cypel M. A call to routinely test lower respiratory tract samples for SARS-CoV-2 in lung donors. *Am J Transplant*. Published online 2021:1-2. doi:10.1111/ajt.16576



- 20. Kaul DR, Valesano AL, Petrie JG, et al. Donor to recipient transmission of SARS-CoV-2 by lung transplantation despite negative donor upper respiratory tract testing. *Am J Transplant*. 2021;21(8):2885-2889. doi:10.1111/ajt.16532
- 21. Natori Y, Anjan S, Simkins J, et al. Small bowel transplantation from SARS-CoV-2 respiratory PCR positive donors: Is it safe? *Transpl Infect Dis*. Published online 2021. doi:doi.org/10.1111/tid.13752
- 22. COVIDSurgCollaborative, CollaborativeGlobalSurge. Timing of surgery following SARS-CoV-2 infection: an international prospective cohort study. *Anaesthesia*. 2021;76(6):748-758. doi:10.1111/anae.15458