

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}. The prevalence of potential donors who are either currently or previously infected with SARS-CoV-2 fluctuates relative to the level of community prevalence. In order to 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 procurement⁸⁻¹³. 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 may expect higher risk of SARS-CoV-2 transmission to lung recipients. Indeed, in early 2020, 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}. However more recently there are case series reporting no donor-to-recipient transmission of SARS-CoV-2 from lung donors incidentally SARS-CoV-2 positive with PCR CT values > 35 cycles (Upper or Lower Respiratory Tract Specimen)²¹⁻²³.

It may be suitable to transplant lungs from a donor who tests positive for SARS-CoV-2 on PCR from the upper respiratory tract. Australian and New Zealand lung transplant centres recommend that this would be safest when the following conditions are met:

- Donor has a negative lower respiratory SARS-CoV-2 PCR test
- Donor lung CT chest is available and does not demonstrate any sequelae of COVID-19
- SARS-CoV-2 infection is assessed as historic rather than an acute infection, which may be evidenced by.
 1. Stable, high CT values on serial (at least two, 24 hours apart) upper respiratory tract SARS-CoV-2 PCRs

OR

 2. Definite evidence (positive SARS-CoV-2 PCR) of onset of SARS-CoV-2 infection >20 days prior to procurement. If SARS-CoV-2 infection was >28 days prior to procurement, criteria 1 must be fulfilled, as re-infection may have occurred.
- Otherwise suitable donor lung performance

Additional measures of protection, as recommended by Australian and New Zealand lung transplant centres, may include:

- Ensuring recipients are vaccinated
- Consideration of pre-emptive remdesivir for the recipient

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 organs²⁴. Only two cases of intestine transplantation from a SARS-CoV-2 PCR positive donor have been reported²¹, thus it is not possible to assure the safety of using these organs and each case should be assessed on a case-by-case basis.

Deceased donors with a diagnosis of COVID-19

- See flowchart

Living donors with a diagnosis of COVID-19

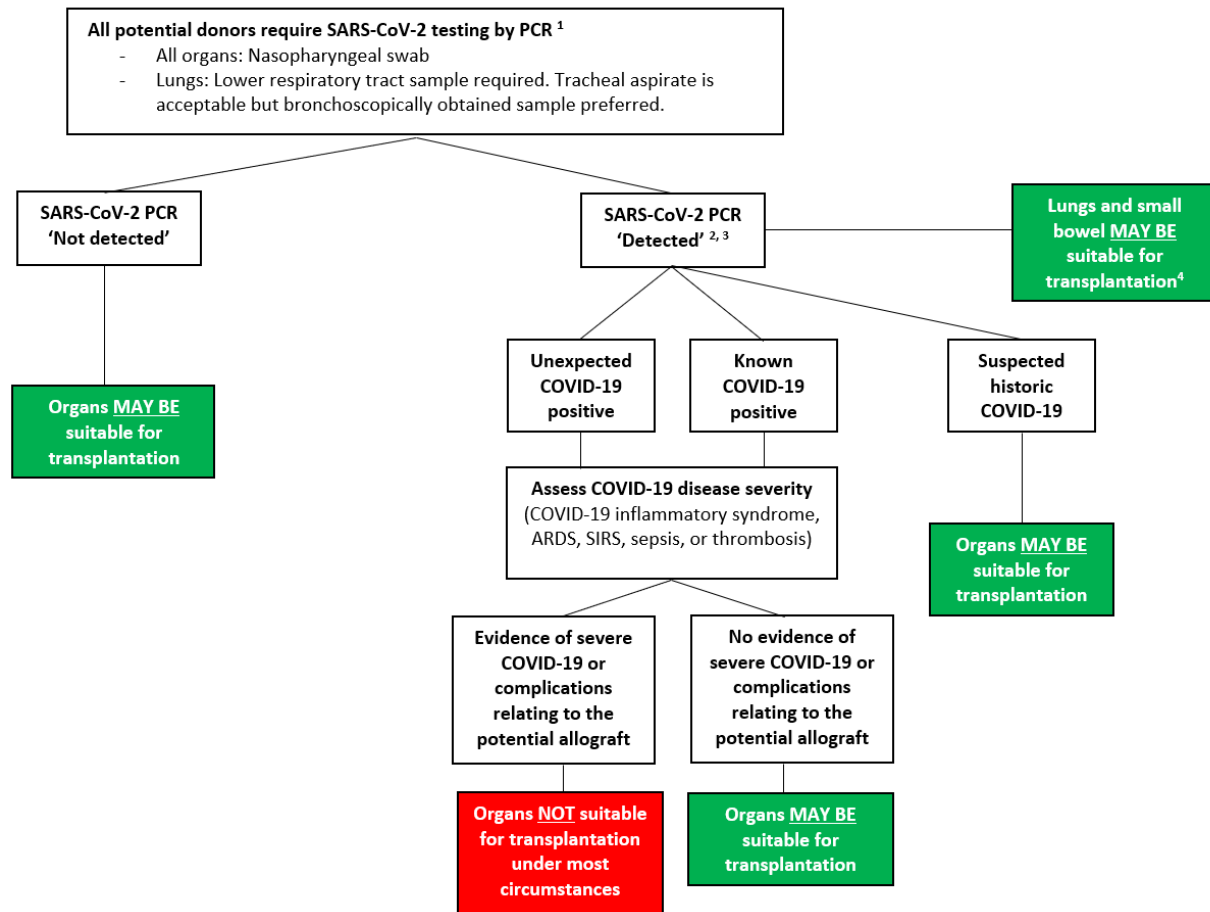
- Defer transplant until the donor has resolution of acute COVID-19 symptoms and at least 7 weeks since the onset of COVID-19 symptoms or first positive SARS-CoV-2 PCR if asymptomatic²⁵
 - o This recommendation is based on the potential risk for the donor undergoing major surgery during an acute infection 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 See text. The decision to transplant lung and small bowel allografts from donors testing positive for SARS-CoV-2 requires a case-by-case discussion that takes into consideration; the timing from SARS-CoV-2 onset (if known); the trajectory of the SARS-CoV-2 PCR CT values; CT imaging (lungs); and the urgency of transplantation. Remdesivir may be considered in the recipients.

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

1. 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 population-based 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. Rimmelink 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.0000000000003609
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.0000000000003750
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, Kundrotaitė 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. Goldman JD, Jett CT, Pouch SM, et al. Transplant of organs from donors with positive SARS-CoV-2 nucleic acid testing : A report from the organ procurement and transplantation network ad hoc disease transmission advisory committee. 2023;(September 2022):1-11. doi:10.1111/tid.14013
22. Eichenberger EM, Coniglio AC, Milano C, et al. Transplanting thoracic COVID-19 positive donors : An institutional protocol and report of the first 14 cases. *J Hear Lung Transplant.* Published online 2022. doi:10.1016/j.healun.2022.06.018
23. Hwang J, Yuen A, Rhoades J, et al. Real-time Transcription Polymerase Chain Reaction Cycle Threshold Values as Criteria for Utilization of Incidental COVID-19 Positive Lung Donors. *J Hear Lung Transplant.* Published online 2022. doi:10.1016/j.healun.2022.12.016
24. 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
25. 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