Summary of Current Evidence and Information– Donor SARS-CoV-2 Testing & Organ Recovery from Donors with a History of COVID-19

Aim

This document is a summary of evidence and information regarding donor screening for SARS-CoV-2 and considerations for organ acceptance from donors with a history of COVID-19. It is based on peer-reviewed literature, and Organ Procurement and Transplantation Network (OPTN) and Centers for Disease Control and Prevention (CDC) data to date. This resource is subject to revision as new data accumulate. It will be reviewed annually or as needed for currency. The overarching objective of this document is to compile the latest information known for minimizing the risk of donor derived COVID-19 while maximizing donor utilization.

Terms to know

- **Nucleic Acid Test (NAT):** Nucleic acid tests are laboratory tests that detect viral genetic material. These include nucleic acid amplification tests (NAAT), RNA tests, and Polymerase Chain Reaction (PCR) tests
- **Upper respiratory tract (URT) specimen:** A sample taken from the respiratory system above the glottis that includes a nasopharyngeal (NP) swab, NP wash or NP aspirate, nasal wash or nasal aspirate, mid-turbinate (MT) swab, anterior nasal swab, or oropharyngeal (OP) swab sample.
- **Lower respiratory tract (LRT) specimen:** A sample taken from the respiratory system from below the glottis that includes a sputum, tracheal aspirate, bronchial suction or wash, bronchoalveolar lavage (BAL), and lung biopsy.

- **Cycle threshold (Ct) value:** Cycle threshold values indicate the number of amplification cycles needed to achieve a positive result from a PCR test.
- **Date of disease onset:** In this document will refer to the date of onset of COVID-19 symptoms or the initial date of test positivity if onset of symptoms cannot be confirmed or if asymptomatic.
- **Asymptomatic COVID-19 Infection:** Detection of SARS-CoV-2 in a respiratory sample without current or past symptoms compatible with COVID-19. If a donor date of onset of symptoms or symptoms are unknown, this person should not be considered asymptomatic.
- **Mild COVID-19:** Detection of SARS-CoV-2 in a respiratory sample in patients with symptoms consistent with COVID-19 infection who did not require oxygen supplementation or inpatient hospitalization for COVID-19.
- **Severe COVID-19:** Detection of SARS-CoV-2 in a respiratory sample in patients with symptoms consistent with COVID-19 infection who required oxygen supplementation or inpatient hospitalization for COVID-19.
- **Resolved COVID-19:** A donor with a history of confirmed COVID-19, with resolution of symptoms and more than 21 days from the date of onset of symptoms.

Methods

The OPTN Ad Hoc Disease Transmission Advisory Committee (DTAC) and relevant stakeholders from the Centers for Disease Control and Prevention (CDC), American Society of Transplantation (AST), American Society of Transplant Surgeons (ASTS), Association of Organ Procurement Organizations (AOPO), and Health Resources & Services Administration (HRSA) reviewed published literature and data reported to the OPTN during the time period corresponding to the COVID-19 pandemic (from March 2020 to July 2022). Specifically, DTAC and relevant stakeholders assessed the available evidence as it relates to living and deceased donor evaluation and testing and recovery of organs from living or deceased donors with a history of resolved or active COVID-19.

Discussion

Omicron Sublineages

The Omicron variant of concern is the dominant circulating SARS-CoV-2 variant globally and is comprised of several sublineages, including XBB.1.5, BQ.1.1, and BQ.1. Data suggest that XBB.1.5 exhibits higher transmissibility than previous Omicron sublineages, and reinfection with XBB.1.5 following infection with another Omicron sublineage has been reported.

SARS-CoV-2 Deceased Donor Evaluation and Testing

1. OPOs and transplant teams should adhere to CDC Infection Prevention and Control Recommendations for Health Care Personnel during the Coronavirus Disease 2019 (COVID-19) pandemic to minimize the risk of disease transmission to the procurement and transplant teams.
    - The CDC recommends that healthcare workers caring for patients with confirmed or suspected SARS-CoV-2 infection use a NIOSH-approved N95 or equivalent or higher-level respirator, gown, gloves, and eye protection.
    - The CDC recommends the use of eye protection and NIOSH-approved N95 or equivalent or higher-level respirator for the following procedures, even if SARS-CoV-2 infection is not suspected:
        - All aerosol-generating procedures, including extubation
        - All surgical procedures that may pose a higher risk for transmission if the patient were to have COVID-19, including those which could generate aerosols or involve the nose, throat, or respiratory tract
    - The CDC recommends COVID-19 vaccination for all healthcare workers.
2. The Food and Drug Administration (FDA) provides information about the impact of viral mutations on COVID-19 tests, recommendations for clinical laboratory staff and health care providers, and information about certain tests for which the FDA has identified potential impacts on performance due to SARS-CoV-2 genetic mutations.
    - Antigen tests are generally less sensitive and less likely to pick up

very early infections compared to molecular tests. In following the FDA's long-standing rapid test recommendations, if a person tests negative with an antigen test (immunoassays that detect the presence of a specific viral antigen) but is suspected of having COVID-19, such as experiencing symptoms or having a high likelihood of infection due to exposure, follow-up molecular testing (polymerase chain reaction (PCR) and other nucleic acid amplification tests (NAATs) tests, which detect genetic material called RNA from the virus) is important for determining a COVID-19 infection.

- The FDA's analysis to date has identified certain EUA-authorized molecular tests whose performance may be impacted by mutations in the SARS-CoV-2 omicron variant. Some molecular tests are expected to *fail* to detect some SARS-CoV-2 omicron variants, and the FDA is collaborating with government partners and test developers to evaluate the impact of the Omicron variant and subvariants on SARS-CoV-2 diagnostic tests.

3. Available evidence indicates that testing deceased donors for SARS-CoV-2 by NAT from a respiratory sample within 72 hours of organ procurement, but ideally as close as possible to organ recovery, could decrease the risk of unrecognized infection.

4. When lungs will be recovered for transplantation, testing for SARS-CoV-2 by NAT in a lower respiratory sample is anticipated to significantly decrease the risk of unrecognized infection.
    - The CDC has investigated all potential donor-derived COVID-19 events reported to DTAC. Between March 2020–March 2021, there were three donor-derived SARS-CoV-2 transmissions documented to lung recipients. In these events, the donor tested negative for SARS-CoV-2 in an URT specimen but retrospectively tested positive in a LRT specimen. Prospective testing of a LRT sample would have informed the lung programs and recipients of the risk of transmission.
    - Effective May 27, 2021, OPTN policy requires OPOs to perform LRT

SARS-CoV-2 testing on all potential lung donors and have test results available prior to transplant of the lungs. Between May 27, 2021 and February 28, 2022, 93 donors were identified as having negative URT but positive LRT SARS-CoV-2 tests. The only confirmed donor-derived transmissions have been through the airway; demonstration of non-airway transmission has not been confirmed at this time.

- The United Kingdom National Health Service Blood and Transplant mandates testing for SARS-CoV-2 RNA in URT and LRT specimens in all potential deceased donors. As of January 2021, 987 deceased donors with negative upper and lower respiratory tract testing enabled 2469 transplants of which 75 were lung transplants. There was no evidence of donor derived COVID-19, suggesting that this strategy minimizes the risk of SARS-CoV-2 transmission to lung transplant recipients.
- The Food and Drug Administration (FDA) under Emergency Use Authorization (EUA) provides validated specimen types for all SARS-CoV-2 assays. There are over 80 tests currently validated for lower respiratory tract specimens.

5. The FDA has issued notification of potential false positive and false negative results associated with certain SARS-CoV-2 testing platforms. These notifications can inform selection of testing platforms to minimize the possibility of donor deferral due to false test results.

6. In December 2020, the FDA permitted laboratory reporting of cycle threshold (Ct) values for authorized molecular diagnostic SARS-CoV-2 tests.
    - A Ct value indicates the number of amplification cycles needed to achieve a positive result from a real-time PCR test. Low Ct values are generally considered to reflect a higher viral load, and high Ct values are generally considered to reflect a lower viral load.
    - Higher Ct values tend to correlate with culture negativity. The CDC reported that attempts to recover SARS-CoV-2 in culture of upper airway samples was generally unsuccessful when their assay Ct values were >35. However, due to the multiple factors known to

impact Ct values (testing platform, specimen collection and storage), caution is advised when applying published correlations of Ct values with the presence of infectious virus detectable in culture, and hence as a predictor of transmissibility.

- The CDC and FDA currently recommend against the use of Ct values for assessment of an individual's degree of infectivity or risk for disease severity.

7. Currently there is insufficient evidence to support the use of SARS-CoV- 2 antibody donor testing as a marker for assessing safety or potential transmission risk to recipients.
8. NAT testing of non-respiratory samples is not standardized, and there is insufficient evidence to support its use for clinical evaluation of donors at this time.
9. While evidence supports the use of chest computed tomography (CT) and chest x-ray in conjunction with other testing methods for SARS-CoV-2 infection, it does not currently support radiographic imaging as the sole diagnostic method for SARS-CoV-2 infection.
10. Available evidence supports an assessment for potential end-organ dysfunction if a donor has a history of COVID-19.
11. OPOs collecting a history and timeline of COVID-19 exposure and COVID-19 symptoms in a potential donor could contextualize SARS-CoV-2 test results and lower the risk of undetected infection and maximize organ utilization.

Recovery of Organs from Deceased Donors given SARS-CoV-2 Test Results

1. Prior guidance stratified risk to all recipients based on the recency of positive testing in the donor. Current guidance stratifies lung and non-lung donation separately as transmission from donor to lung recipient is known to occur, yet no proven transmission to non-lung recipients has been documented to date.

Deceased Donors for Non-lung Transplants:

1. SARS-CoV-2 NAT negative non-lung donors, even if exposed, are generally considered safe.
2. SARS-CoV-2 NAT positive non-lung donors are unlikely to transmit infection and should be considered, provided no evidence of end-organ dysfunction or thrombosis and considering limited long-term outcome data at this time.
3. Emerging evidence suggests that short-term outcomes are similar between non-lung recipients receiving SARS-CoV-2 NAT recently positive within 21 days and SARS-CoV-2 NAT negative organs.
    - A report from DTAC showed similar 30-day outcomes of death and graft loss between non-lung recipients of SARS-CoV-2 NAT+ and NAT- donors. Limitations to these data include the short time horizon, univariate analyses, and uncertainty about other potentially relevant outcomes, such as thrombotic complications.
    - A multivariate, matched analysis on a smaller dataset with longer follow-up time showed similar mortality experience between non-lung recipients of SARS-CoV-2 NAT+ and NAT- donors.
    - A single center retrospective study of >100 transplants from donors recently testing SARS-CoV-2 NAT+ included those who died from symptomatic COVID-19, included those with active infections. This study noted similar rates of delayed graft function, rejection, graft failure, and mortality. Allograft function was lower in those with cause of death as COVID-19, but was similar to NAT- in those NAT+ with other cause of death.
4. It is likely that donors were selected for either high organ quality, low risk of active disease or both in the early experience with the use of SARS-CoV-2 NAT+ organs. Thus, it is uncertain whether SARS-CoV-2 can be transmitted to non-lung transplant recipients, though the risk of this possibility seems extremely low. Use of organs from donors with very recent (within 10 days) infection and signs of active COVID-19 preceding death should be weighed carefully against the risk for remaining on the waitlist. Donors in the study by Koval et al (cited above) had evidence of recent infection, though these are initial findings which should be replicated. Additional uncertainty exists as to potential for unintended consequences that have not been reported, including endothelial or other thrombotic complications of non-respiratory transmission.

5. There is not currently enough experience to comment on the safety of intestinal transplant from donors who are SARS-CoV-2 NAT+ within 21 days. It is noted that the gastrointestinal tract is thought to be a reservoir of persistence of SARS-CoV-2.

Deceased Donors for Lung Transplants:

1. Transmission from donor to lung recipient has been documented in cases where the donor was SARS-CoV-2 NAT negative on an upper respiratory track (LRT) specimen, but testing of a specimen from the lower respiratory track was not performed. Since implementation of the policy requiring LRT testing for lung donors, no transmission events have been reviewed by DTAC.
2. There are two approaches to the use of SARS-CoV-2 NAT + donors. The first is to recover lungs from SARS-CoV-2 NAT positive donors only when symptom onset or test positivity occurred >20 days prior. The second is to recover all organs from SARS-CoV-2 NAT positive donors who never experienced symptoms of COVID-19, stratifying the risk of disease transmission using the Ct value. The former emphasizes safety while the latter maximizes organ utilization at the expense of a higher risk of disease transmission given limitation of Ct values to determine infectivity.
    a. A case series described the use of two SARS-CoV-2 URT NAT + LRT NAT donors – with a history of asymptomatic SARS-CoV-2 infection more than 20 days after the onset of symptoms. The donors had no evidence of terminal illness complicated by hypercoagulability or hyperinflammatory syndrome. One of the recipients had 3 doses of an mRNA vaccine and the other 2 doses and a prior history of COVID-19; there was no evidence of disease transmission.
    b. A second case series described the use of eight SARS-CoV-2 URT NAT + (Ct value >35) donors with a LRT NAT that was either negative or positive with a Ct value >35. The donors were asymptomatic and had no known history of COVID-19. There was no evidence of disease transmission, and all recipients were alive at a median time of 161 days.
3. The risk of donor-derived SARS-CoV-2 transmission from SARS-CoV-2 NAT+ donors remains unclear as does the optimal approach to mitigating

this risk. A careful evaluation weighing the risk of pre-transplant mortality with the risk of disease transmission is required. Unless the mortality on the waitlist is high, the risk of disease transmission may not be justified.

SARS-CoV-2 Living Donor Testing and other precautions to minimize the risk of Donor-Derived COVID-19

1. CDC recommendations on infection control can help living donors reduce the risk of SARS-CoV-2 infection prior to donation and during recovery.
2. COVID-19 vaccination including up-to-date boosters are strongly encouraged for living donors, preferably with vaccine completion at least 2 weeks prior to anticipation of donation
3. Testing for SARS-CoV-2 with NAT in an upper respiratory sample as close to organ recovery as possible but within 72 hours prior to recovery, is recommended to reduce the risk of undetected infection. The exact timing should be guided by institutional polices but the result should be made available prior to surgery.
4. The FDA has identified certain EUA-authorized molecular tests whose performance is potentially impacted by mutations in the SARS-CoV-2 Omicron variant and Omicron sub-variants. Some molecular tests are expected to fail to detect the SARS-CoV-2 Omicron variant and its sub-variants.

Recovery of Organs from Living Donors with a History of Resolved COVID-19

Evidence suggests the decision to recover and transplant organs from living donors with resolved COVID-19 include the following:

1. Consideration of emerging data on peri-operative mortality in relation to diagnosis of COVID-19. It should be noted that current guidelines regarding the timing of surgery in relation to COVID-19 diagnosis pre-date the emergence of the Omicron variant and COVID-vaccine availability. Key points from old and newer studies are summarized below.

2. Current guidelines are based on data published by the COVIDSurg Collaborative, which looked at the timing of surgery in relation to pre-operative diagnosis of COVID-19 and impact on early post-operative mortality. Their analysis showed increased 30-day post-operative mortality among patients with COVID-19 diagnosed ≤ 6 weeks preceding surgery. For surgeries performed ≥7 weeks from COVID-19 diagnosis, the post-operative mortality was similar to the baseline mortality among patients who were asymptomatic. It was, however, higher than baseline mortality among those who had ongoing symptomatic SARS-CoV-2 infection at that time point.

3. Recently published retrospective cohort study of patients who underwent elective surgery between January 1st 2018 and February 28th 2022, evaluated the association between post-surgical complications and timing of surgery after pre-operative COVID-19 diagnosis, and the impact of vaccination on this association. The investigators found that in comparison to patients without pre-operative COVID-19, among fully vaccinated patients who underwent surgery as early as 0-4 weeks of COVID-19 diagnosis had a similar risk of perioperative complications in comparison to patients without pre-operative COVID-19.

4. COVIDSurg-3 is an ongoing study which will be looking at surgical outcomes in relation to the current landscape of the COVID-19 pandemic and will provide information on the impact of predominant global SARS CoV-2 variants and vaccinations.

5. Current additional considerations based on gaps in knowledge and risk/benefit balance:
    a. Currently unknown long-term effects, including the possibility of thrombotic events, of COVID-19 infection for the living donor
    b. Living donors with resolved COVID-19 are unlikely to transmit infection.
    c. There is unclear evidence on the need for a negative SARS-CoV-2 NAT for living donors with a history of COVID-19 prior to donation within 90 days of disease onset. It is always important to follow local infection prevention and control policies.

d. Living Donors with resolved COVID-19 and a positive SARS-CoV-2 NAT more than 90 days after the date of disease onset may reflect reinfection.
e. The candidate risk of mortality or further complications while delaying transplantation and remaining on the waiting list.
f. The estimated risk of donor-derived COVID-19 transmission to the recipient
g. Currently unknown long-term outcomes, including the possibility of thrombotic events, of recipients of organs from living donors with resolved COVID-19

6. Infectious diseases experts can offer subject matter epertise when accepting organs from these donors.

Timing of Transplant for Recipients with a History of COVID-19

Although emerging data shows an increased risk of peri-operative mortality in the first 6 weeks after the diagnosis of COVID-19, the survival benefit of transplantation may offset this risk.

Themes

- COVID-19
- SARS-CoV-2 donor testing

Bibliography

Abbasi J. “Researchers Investigate What COVID-19 Does to the Heart.” JAMA. 2021;325(9):808–811. doi:10.1001/jama.2021.0107

Abdullah F. Myers J. et al. “Decreased severity of disease during the first global omicron variant covid-19 outbreak in a large hospital in Tshwane, south Africa.” Int J Infect Dis. 2021 Dec 28;S1201-9712(21)01256-X. doi: 10.1016/j.ijid.2021.12.357.

“American Society of Anesthesiologists and Anesthesia Patient Safety ...,” Updated February 22, 2022. https://www.apsf.org/wp-content/uploads/news-updates/2022/ASA-APSF-Joint-Statement-Elective-Surgery-2022-02-22.pdf.

Andersson M, Arancibia - Carcamo CV, Auckland K, et al. “SARS-CoV-2 RNA detected in blood samples from patients with COVID-19 is not associated with infectious virus.” medRxiv. 2020:2020.05.21.20105486. doi:10.1101/2020.05.21.20105486.

Arons MM, Hatfield KM, Reddy SC, Kimball A, James A, Jacobs JR, et al. “Presymptomatic SARS-CoV-2 infections and transmission in a skilled nursing facility.” N Engl J Med 2020 May 28; 382(22): 2081-2090.

Aydillo T, Gonzalez-Reiche AS, Aslam S, et al. “Shedding of viable SARS-CoV-2 after immunosuppressive therapy for cancer.” N Engl J Med 2020 Dec1. doi: 10.1056/NEJMc2031670. Online ahead of print.

Bock MJ, Vaughn GR, Chau P, Berumen JA, Nigro JJ, Ingulli EG. Organ transplantation using COVID-19-positive deceased donors. Am J Transplant. 2022 Sep;22(9):2203-2216. doi: 10.1111/ajt.17145. Epub 2022 Jul 25. PMID: 35822320; PMCID: PMC9349433.

Boyarsky BJ, Po-Yu Chiang T, Werbel WA, et al. “Early impact of COVID-19 on transplant center practices and policies in the United States.” Am J Transplant. 07 2020;20(7):1809-1818. doi:10.1111/ajt.15915.

Bradley BT, Maioli H, Johnston R, et al. “Histopathology and ultrastructural findings of fatal COVID-19 infections in Washington State: a case series.” Lancet. 08 2020;396(10247):320-332. doi:10.1016/S0140-6736(20)31305-2.

Bulfamante GP, Perrucci GL, Falleni M, et al. « Evidence of SARS-CoV-2 Transcriptional Activity in Cardiomyocytes of COVID-19 Patients without Clinical Signs of Cardiac Involvement.” Biomedicines. Dec 2020;8(12) doi:10.3390/biomedicines8120626.

Bullard J, Durst K, Funk D, et al. “Predicting infectious SARS-CoV-2 from diagnostic samples.” Clin Infect Dis 2020 May 22. doi: 10.1093/cid/ciaa638.

Centers for Disease Control and Prevention. “CDC Covid Data Tracker.” Updated January 30, 2023. https://covid.cdc.gov/covid-data-tracker/#variant-proportions.

Centers for Disease Control and Prevention. “Clinical Questions about COVID-19: Questions and Answered.” Accessed January 12, 2022. https://www.cdc.gov/coronavirus/2019-ncov/hcp/faq.html#Infection-Control

Centers for Disease Control and Prevention. “COVID Data Tracker.” Accessed January 12, 2022. https://covid.cdc.gov/covid-data-tracker/#variant-proportion

Centers for Disease Control and Prevention. “Covid-19 Vaccination Clinical and Professional Resources.”, May 13, 2022. https://www.cdc.gov/vaccines/covid-19/.

Centers for Disease Control and Prevention. “COVID-19 vaccines for healthcare personnel.” Accessed August 22, 2021. https://www.cdc.gov/coronavirus/2019- ncov/vaccines/recommendations/hcp.html.

Centers for Disease Control and Prevention. “Delta Variant: What We Know About the Science.” Accessed August 2021. https://www.cdc.gov/coronavirus/2019-ncov/variants/delta- variant.html

Centers for Disease Control and Prevention. “Duration of isolation and precautions for adults with COVID-19.” October 19, 2020. www.cdc.gov/coronavirus/2019-ncov/hcp/duration- isolation.html.

Centers for Disease Control and Prevention. “Infection Control Guidance for Healthcare Professionals about Coronavirus (COVID-19).” Accessed January 7, 2022. https://www.cdc.gov/coronavirus/2019-

ncov/hcp/infection-control.html

Centers for Disease Control and Prevention. “Frequently asked questions about coronavirus (COVID-19) for laboratories.” Accessed August 24, 2021.https://www.cdc.gov/coronavirus/2019-ncov/lab/faqs.html#Interpreting-Results-of- Diagnostic-Tests.

Centers for Disease Control and Prevention. “Interim infection prevention and control recommendations for healthcare personnel during the coronavirus disease 2019 (COVID-19) pandemic.” Accessed August 22, 2021. https://www.cdc.gov/coronavirus/2019- ncov/hcp/infection-control-recommendations.html#anchor_1604360721943.

Centers for Disease Control and Prevention. “Late Sequelae of COVID-19.” Accessed December 30th, 2020

Centers for Disease Control and Prevention. “Overview of Testing for SARS-COV-2, the Virus That Causes Covid-19. Updated September 28, 2022. https://www.cdc.gov/coronavirus/2019-ncov/hcp/testing-overview.html.

Centers for Disease Control and Prevention. “Quarantine and isolation.” Accessed August 24, 2021. https://www.cdc.gov/coronavirus/2019-ncov/your-health/quarantine-isolation.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019- ncov%2Fif-you-are-sick%2Fquarantine.html

Centers for Disease Control and Prevention. “Recommended Vaccines for Healthcare Workers.” Accessed January 12, 2022. https://www.cdc.gov/vaccines/adults/rec-vac/hcw.html

Centers for Disease Control and Prevention. “Stay up to Date with Covid-19 Vaccines Including Boosters.” Updated January 25, 2023. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html#:~:text=When%20Are%20You%20Up%20to,also%20considered%20up%20to%20date.

Centers for Disease Control and Prevention. “Symptoms of coronavirus.” Updated Dec 22, 2020. https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html.

Centers for Disease Control and Prevention. “Your Health.” Updated August 11, 2022. https://www.cdc.gov/coronavirus/2019-ncov/your-health/.

Center for Devices and Radiological Health. “SARS-COV-2 Viral Mutations: Impact on COVID-19 Tests.” U.S. Food and Drug Administration. FDA, Updated January 12, 2023. https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests.

Ceulemans LJ, Slambrouck JV, De Leyn P,et al. “Successful double-lung transplantation from a donor previously infected with SARS-CoV-2.” Lancet Respir Med. 2020 Dec 1: S2213- 2600(20)30524-5. doi: 10.1016/S2213-2600(20)30524-5. Online ahead of print.

Cevik M, Tate M, Lloyd O, et al. “SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta- analysis.” Lancet Microbe 2021; 2(10): E13-E22.

Choi B, Choudhary MC, Regan J, et al. “Persistence and evolution of SARS-CoV-2 in an

immunocompromised host." N Engl J Med 2020; 383(23): 2291-2293.

Cholankeril G, Podboy A, Alshuwaykh OS, et al. "Early Impact of COVID-19 on Solid Organ Transplantation in the United States." Transplantation. 11 2020;104(11):2221-2224.

Commissioner, Office of the. "Covid-19 Test Basics." U.S. Food and Drug Administration. FDA, January 4, 2023. https://www.fda.gov/consumers/consumer-updates/covid-19-test-basics.

Connolly, Liam. "XBB.1.5: What You Need to Know about Covid-19's 'Kraken' Variant." UC Davis Health. UC Davis, January 17, 2023. https://health.ucdavis.edu/news/headlines/xbb15-what-you-need-to-know-about-covid-19s-kraken-variant-/2023/01.

COVIDSurg Collaborative and GolbalSurg Collaborative. "Timing of Surgery Following SARS- CoV-2 Infection: an International Prospective Cohort Study." *Anaesthesia*, 2021. https://doi.org/doi:10.1111/anae.15458.

Danziger-Isakov L, Goldman JD, Wooley A, Pouch S, Agarwal A, Berry G, Dunn K, Ho S, Kittleson M, Lee DH, Levine D, Marboe C, Marklin G, Razonable R, Taimur S, Te H, Fox C, Jett C, Booker S, Klassen D, LaHoz R. Organs from Donors with Positive SARS-CoV-2 NAT+ Testing: A Report from the Ad Hoc Disease Transmission Advisory Committee [abstract]. Am J Transplant. 2022; 22 (suppl 3). https://atcmeetingabstracts.com/abstract/organs-from-donors- with-positive-sars-cov-2-nat-testing-a-report-from-the-ad-hoc-disease-transmission-advisory- committee/. Accessed August 15, 2022

Dhawan M, Saied AA, Emran TB, Choudhary OP. Emergence of omicron variant's sublineages BA.4 and BA.5: risks assessment and possible countermeasures. New Microbes New Infect. 2022 Jun 17;48:100997. doi: 10.1016/j.nmni.2022.100997. PMID: 35873063; PMCID: PMC9293046.

Eichenberger EM, Coniglio AC, Milano C, Schroder J, Bryner BS, Spencer PJ, Haney JC, Klapper J, Glass C, Pavlisko E, Dibernardo L, Patel CB, DeVore AD, Reynolds J, Wolfe CR. Transplanting thoracic COVID-19 positive donors: An institutional protocol and report of the first 14 cases. J Heart Lung Transplant. 2022 Oct;41(10):1376-1381. doi: 10.1016/j.healun.2022.06.018. Epub 2022 Jun 30. PMID: 35871114; PMCID: PMC9245398.

El-Boghdadly K, Cook TM, Goodacre T, et al. SARS-CoV-2 infection, COVID-19 and timing of elective surgery: a multidisciplinary consensus TABLE 3. statement on behalf of the Association of Anaesthetists, the Centre for Peri-operative Care, the Federation of Surgical Specialty Associations, the Royal College of Anaesthetists and the Royal College of Surgeons of England. Anaesthesia. 2021;76:940–946. 9. Falasca L, Nardacci R, Colombo D, et al. "Postmortem Findings in Italian Patients With COVID-19: A Descriptive Full Autopsy Study of Cases With and Without Comorbidities." J Infect Dis. 11 2020;222(11):1807-1815. doi:10.1093/infdis/jiaa578.

Farkash E, Wilson A and Jentzen J. "Ultrastructural Evidence for Direct Renal Infection with SARS-CoV-2." JASN August 2020, 31(8): 1683-1687. doi: https://doi.org/10.1681.

Free RJ, Annambhotla P, La Hoz RM, et al. "Risk of Severe Acute Respiratory Syndrome Coronavirus 2 Transmission Through Solid Organ Transplantation and Outcomes of Coronavirus Disease 2019 Among Recent Transplant Recipients"**.** Open Forum Infect Dis. 2022 May 2;9(7):ofac221.doi: 10.1093/ofid/ofac221

Food and Drug Administration. “Potential for False Positive Results with Antigen Tests for Rapid Detection of SARS-CoV-2 - Letter to Clinical Laboratory Staff and Health Care Providers.” https://www.fda.gov/medical-devices/letters-health-care-providers/potential-false- positive-results-antigen-tests-rapid-detection-sars-cov-2-letter-clinical-laboratory.

Food and Drug Administration. “COVID-19 Test Uses: FAQs on Testing for SARS-CoV-2.” Accessed August 24, 2021. https://www.fda.gov/medical-devices/coronavirus-covid-19-and- medical-devices/covid-19-test-uses-faqs-testing-sars-cov-2.

Food and Drug Administration. “SARS-CoV-2 Viral Mutations: Impact on COVID-19 Tests.” Accessed January 12, 2022. https://www.fda.gov/medical-devices/coronavirus-covid-19-and- medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests

Goff RR, Wilk AR, Toll AE, McBride MA, Klassen DK. “Navigating the COVID-19 pandemic: Initial impacts and responses of the Organ Procurement and Transplantation Network in the United States.” Am J Transplant. Nov 2020; doi:10.1111/ajt.16411.

Goldman, Jason D., Stephanie M. Pouch, Ann E. Woolley, Sarah E. Booker, Courtney T. Jett, Cole Fox, Gerald J. Berry, 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.” Transplant Infectious Disease, 2023. https://doi.org/10.1111/tid.14013.

Goldsmith CS, Miller SE, Martines RB, Bullock HA, Zaki SR. “Electron microscopy of SARS- CoV-2: a challenging task.” *Lancet*. 05 2020;395(10238):e99. doi:10.1016/S0140- 6736(20)31188-0.

Haffner MR, Hai LV, Saiz AM, et al. “Postoperative In-Hospital Morbidity and Mortality of Patients with COVID-19 Infection Compared with Patients Without COVID-19 Infection.” JAMA Netw Open. April 2021; 4(4):e215697. doi:10.1001/jamanetworkopen.2021.5697

Hanley B, Naresh KN, Roufosse C, et al. “Histopathological findings and viral tropism in UK patients with severe fatal COVID-19: a post-mortem study.” Lancet Microbe. Oct 2020;1(6):e245-e253. doi:10.1016/S2666-5247(20)30115-4.

Hong HL, Kim SH, Choi DL, Kwon HH. “A case of coronavirus disease 2019-infected liver transplant donor.” Am J Transplant. 10 2020;20(10):2938-2941. doi:10.1111/ajt.15997.Huang C, Wang Y, Li X, et al. “Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China.” Lancet. 02 2020;395(10223):497-506. doi:10.1016/S0140- 6736(20)30183-5.

Hwang, Josephine, Alexander Yuen, Joshua Rhoades, Darina Barnes, Phillip Zakowski, Dominick J. Megna, Pedro Catarino, Lorenzo Zaffiri, and Reinaldo Rampolla. “Real-Time Transcription Polymerase Chain Reaction Cycle Threshold Values as Criteria for Utilization of Incidental Covid-19 Positive Lung Donors.” The Journal of Heart and Lung Transplantation. Elsevier, December 27, 2022. https://www.jhltonline.org/article/S1053-2498(22)02272-0/fulltext.

Jefferson T, Spencer EA, Brassey J, Heneghan C. Viral cultures for COVID-19 infectious potential assessment - a systematic review. Clin Infect Dis. 2020 Dec 3:ciaa1764. doi: 10.1093/cid/ciaa1764.

Jones J, Kracalik I, Rana MM, et al. SARS-CoV-2 infections among recent organ recipients, March-May 2020, United States. Emerg Infect Dis. 2020

Dec16;27(2). doi:10.3201/eid2702.204046.

Kates OS, Fisher CE, Rakita RM, Reyes JD, Limaye AP. Use of SARS-CoV-2-infected deceased organ donors: Should we always "just say no?". Am J Transplant. Jul 2020;20(7):1787-1794. doi:10.1111/ajt.16000.

Kaul, Daniel R, Andrew L Valesano, Joshua G Petrie, Rommel Sagana, Dennis Lyu, Jules Lin, Emily Stoneman, Lane M Smith, Paul Lephart, and Adam S Lauring. “Donor to Recipient Transmission of SARS-CoV-2 by Lung Transplantation Despite Negative Donor Upper Respiratory Tract Testing.” American Journal of Transplantation, February 10, 2021. https://doi.org/10.1111/ajt.16532.

Koval CE, Eltemamy M, Poggio ED, Schold JD, Wee AC. Comparative outcomes for over 100 deceased donor kidney transplants from SARS-CoV-2 positive donors: A single-center experience. Am J Transplant. 2022 Dec;22(12):2903-2911. doi: 10.1111/ajt.17203. Epub 2022 Oct 17. PMID: 36176236; PMCID: PMC9538585.

Koval CE, Poggio ED, Lin Y-C, et al. “Early success transplanting kidneys from donors with new SARS-CoV-2 RNA positivity: a reprt of 10 cases.” Am J Transplant 2021. Jul 13. doi:10.1111/ajt.16765

Kumar, Deepali, Atul Humar, Shaf Keshavjee, and Marcelo Cypel. “A Call to Routinely Test Lower Respiratory Tract Samples for SARS-CoV-2 in Lung Donors.” American Journal of Transplantation, March 23, 2021. https://doi.org/doi/10.1111/ajt.16576.

Kumar D, Manuel O, Natori Y, Egawa H, Grossi P, Han SH, Fernandez-Ruiz M, Humar A. “COVID-19: A global transplant perspective on successfully navigating a pandemic.” Am J Transplant 2020 Jul;20(7):1773-1779. doi: 10.1111/ajt.15876.

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. 2020 Dec 24; Publish Ahead of Print. doi: 10.1097/TP.0000000000003609.

La Hoz R., Mufti A., Vagefi P. “Short-term liver transplant outcomes from SARS-CoV-2 lower respiratory tract NAT positive donors.” Transpl Infect Dis. 2021 Nov 6; e13757. doi:10.1111/tid.13757

La Hoz, Ricardo M, Lara A Danziger-Isakov, David K Klassen, and Marian G Michaels. “Risk and Reward: Balancing Safety and Maximizing Lung Donors during the COVID-19 Pandemic.”American Journal of Transplantation, March 23, 2021. https://doi.org/https://doi.org/10.1111/ajt.16575.

Le ST, Kipnis P, Cohn B, Liu VX. COVID-19 Vaccination and the Timing of Surgery Following COVID-19 Infection. Ann Surg. 2022 Nov 1;276(5):e265-e272. doi: 10.1097/SLA.0000000000005597. Epub 2022 Jul 15. PMID: 35837898; PMCID: PMC9533764.

Lindner D, Fitzek A, Brauninger H, et al. “Association of Cardiac Infection with SARS-CoV-2 in Confirmed COVID-19 Autopsy Cases.” JAMA Cardiol 2020 Nov 1;5(11):1281-1285. doi: 10.1001/jamacardio.2020.3551.

Ling Y, Xu SB, Lin YX, Tian D, Zhu ZQ, et al. “Persistence and clearance of viral RNA in 2019 novel coronavirus disease rehabilitation patients.” Chin Med J. 2020; 133(9): 1039-1043.

Lu J, Peng J, Xiong Q, Liu Z, Lin H, Tan X, et al. “Clinical, immunological and virological characterization of COVID-19 patients that test re-positive for SARS-CoV-2 by RT-PCR. EBioMedicine 2020 Sep; 59:102960.

Massoth LR, Desai N, Szabolcs A, et al. “Comparison of RNA In Situ Hybridization and Immunohistochemistry Techniques for the Detection and Localization of SARS-CoV-2 in Human Tissues.” Am J Surg Pathol. 01 2021;45(1):14-24. doi:10.1097/PAS.0000000000001563.

Michaels, MG, La Hoz RM, Danziger-Isakov L, Blumberg EA, Kumar D, Green M, Pruett TL, Wolfe CR. “Coronavirus disease 2019: Implications of emerging infections for transplantation.” Am J Transplant 2020 20: 1768-1772. doi: 10.1111/ajt.15832

Miller SE. “Visualization of SARS-CoV-2 in the Lung.” N Engl J Med. 2020 Dec 31;383(27):2689. doi: 10.1056/NEJMc2030450. PMID: 33394576.

National Institutes of Health. “Covidsurg-3: Outcomes of Surgery in COVID-19 Infection - Full Text View.” CovidSurg-3: Outcomes of Surgery in COVID-19 Infection - Full Text View - ClinicalTrials.gov, December 17, 2021. https://clinicaltrials.gov/ct2/show/NCT05161299.

Nugent J, Aklilu A, Yamamoto Y, et al. “Assessment of Acute Kidney Injury and Longitudinal Kidney Function After Hospital Discharge Among Patients With and Without COVID-19.”JAMA Netw Open. 2021;4(3):e211095. doi:10.1001/jamanetworkopen.2021.1095

“Lower Respiratory SARS-CoV-2 Testing for Lung Donors Six-Month Monitoring Report.” Prepared by Sarah Booker. OPTN DTAC: December 20, 2021.

Ong SWX, Chiew CJ, Ang LW, et al. Clinical and virological features of SARS-CoV-2 variants of concern : a retrospective cohort study comparing B.1.1.7 (Alpha), B.1.315 (Beta), and B.1.617.2 (Delta). Clin Infect Dis 2021. Aug 23:ciab721. doi: 10.1093/cid/ciab721.

Organ Procurement Transplantation Network. “Lower Respiratory SARS-COV-2 Testing for Lung Donors - OPTN.” Lower Respiratory SARS-CoV-2 Testing for Lung Donors. Organ Procurement Transplantation Network, May 27, 2021. https://optn.transplant.hrsa.gov/media/5e5eqf4a/policy-notice_dtac_lrt.pdf.

Public Health Ontario. “An overview of cycle threshold values and their role in SARS-CoV-2 real-time PCR test interpretation.” Accessed August 2021. https://www.publichealthontario.ca/-/media/documents/ncov/main/2020/09/cycle-threshold-values-sars-cov2-pcr.pdf?la=en

Puelles VG, Lütgehetmann M, Lindenmeyer MT, et al. “Multiorgan and Renal Tropism of SARS-CoV-2.” N Engl J Med. 08 2020;383(6):590-592. doi:10.1056/NEJMc2011400.Rapkiewicz AV, Mai X, Carsons SE, et al. “Megakaryocytes and platelet-fibrin thrombi characterize multi-organ thrombosis at autopsy in COVID-19: A caseseries.” EClinicalMedicine. Jul 2020;24:100434. doi:10.1016/j.eclinm.2020.100434.

Romagnoli R., Gruttadauria S., et al. “Liver transplantation from active COVID-19 donors: A lifesaving opportunity worth grasping?” Am J Transplant. 2021 Dec;21(12):3919-3925. doi: 10.1111/ajt.16823. Epub 2021 Sep 13.

Safa K, Elias N, Gilligan HM, Kawai T, Kotton CN. “Successful Living Kidney Donation After COVID-19

Infection." Transplantation. Jan 2021;105(1):e4-e5. doi:10.1097/TP.0000000000003510.

Salvalaggio PR, Ferreira GF, Caliskan Y, et al. "An International survey on living kidney donation and transplant practices during the COVID-19 pandemic." Transpl Infect Dis. Nov 2020:e13526. doi:10.1111/tid.13526.

Sanchez-Vivaldi JA, Patel MS, Shah JA, et al. "Short-term kidney transplant outcomes from severe acute respiratory syndrome coronavirus 2 lower respiratory tract positive donors". Transpl Infect Dis. 2022 Jun 25;e13890.doi: 10.1111/tid.13890.

Schold JD, Koval CE, Wee A, et al. "Utilization and outcomes of deceased donor SARS-CoV-2- positive organs for solid organ transplantation in the United States". Am J Transplant. 2022 Jun 22;10.1111/ajt.17126.doi: 10.1111/ajt.17126

Shah MB, Lynch RJ, El-Haddad H, Doby B, Brockmeier D, Goldberg DS. "Utilization of deceased donors during a pandemic: argument against using SARS-CoV-2-positive donors." Am J Transplant. Jul 2020;20(7):1795-1799. doi:10.1111/ajt.15969.

UK Health Security Agency. "SARS-CoV-2 variants of convern and variants under investigation in England. Technical briefing: Update on hospitalization and vaccine effectiveness for Omicron VOC-21NOV-01 (B.1.1.529)." 31 December 2021. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1044481/Technical-Briefing-31-Dec-2021-Omicron_severity_update.pdf

Ushiro-Lumb, Ines, Chris Callaghan, Jasvir Parmar, Jonathon Olsburgh, Marius Berman, Ian Currie, John Forsythe, and Dale Gardiner. "Screening for SARS-CoV-2 in Potential Deceased Organ Donors." American Journal of Transplantation, March 23, 2021. https://doi.org/https://doi.org/10.1111/ajt.16577.

United Network for Organ Sharing. "Covid-19 Resources for Organ Transplants and Donations." UNOS, January 3, 2023. https://unos.org/covid/.

van Kampen J, van de Vijver D, Fraaij P, et al. "Shedding of infectious virus in hospitalized patients with coronavirus disease-2019 (COVID-19): duration and key determinants." (Preprint) Medrxiv 2020. doi: 10.1101/2020.06.08.20125310.

Veyer D, Kernéis S, Poulet G, et al. "Highly sensitive quantification of plasma SARS-CoV-2 RNA shelds light on its potential clinical value." Clin Infect Dis. Aug 2020; doi:10.1093/cid/ciaa1196.
Wang W, Xu Y, Gao R, et al. "Detection of SARS-CoV-2 in Different Types of Clinical Specimens." JAMA. 05 2020;323(18):1843-1844. doi:10.1001/jama.2020.3786.

Wang Y, Liu S, Liu H, Li W, Lin F, Jiang L et al. "SARS-CoV-2 infection of the liver directly contributes to hepatic impairment in patients with COVID-19." J Hepatol. 2020 Oct; 73(4): 807-816.

Wolfel R, Corman VM, Guggemos W, et al. "Virological assessment of hospitalized patients with COVID-2019." Nature 2020; 581(7809):465-469.

Wu Z, McGoogan JM. "Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention." JAMA. Feb 2020; doi:10.1001/jama.2020.2648.

Young BE, Ong SWX, Kalimuddin S, et al. “Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore.” JAMA. Mar 2020;doi:10.1001/jama.2020.3204.