International Journal of Infectious Diseases 147 (2024) 107214

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Short Communication

Solid organ transplant in recipients with ongoing SARS-CoV-2 infection: A systematic review of case reports and series

Andrea Lombardi[1,2,*], Marta Colaneri[3,4], Cecilia Azzarà[1], Paola Saltini[1], Giulia Viero[1], Emanuele Palomba[3], Simona Biscarini[1], Andrea Gori[3,4], Alessandra Bandera[1,2]

[1] Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Infectious Diseases Unit, Milan, Italy
[2] Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy
[3] Department of Infectious Diseases, Luigi Sacco Hospital, ASST Fatebenefratelli Sacco, Milan, Italy
[4] Department of Biomedical and Clinical Sciences "L. Sacco", University of Milan, Milan, Italy

ARTICLE INFO

Article history:
Received 21 June 2024
Revised 7 August 2024
Accepted 13 August 2024

Keywords:
Solid organ transplant
Covid-19
Sars-cov-2
Recipient

ABSTRACT

Background: Whether solid organ transplant (SOT) can be safely performed in recipients with ongoing SARS-CoV-2 infection is still a debated question.
Methods: A systematic review of the literature on recipients with ongoing SARS-CoV-2 infection at the time of surgery and the associated outcomes.
Results: From 29 studies, we identified 54 recipients; their median age was 47.5 years, and over half (23/54, 54.85%) were affected by fewer than two comorbidities. Kidney was the most common transplanted organ (24/54, 44.4%). SOT was performed without knowing the ongoing infection in 11.1% (6/54) of patients. On average, 16.1 (SD 23.2) days elapsed between SARS-CoV-2 infection and SOT, with a mean Ct value at diagnosis and transplantation of 29 and 31.9, respectively. Most patients (25/39,64.1%) had received previous COVID-19 vaccinations. Twenty-four patients (45.3%) received an anti-SARS-CoV-2 therapy. Ten patients (18.5%) required oxygen support, while seven (13.7%) were admitted to the intensive care unit. There were two reported cases (3.7%) of all-cause death, while there were no cases of COVID-19-related death.
Conclusions: Deliberate SOT of recipients with ongoing SARS-CoV-2 is performed worldwide in candidates of nonlung transplant who are fit, immunized against the virus, and displaying a nonsevere disease course. No COVID-19-related deaths were recorded.

Introduction

The coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has severely impacted solid organ transplant (SOT) [1]. One issue to be addressed is whether SOT can be safely performed in recipients with ongoing SARS-CoV-2 infection. In a recent survey conducted among members of the ESGICH, we found that several transplant centers worldwide are already performing this procedure [2]. To understand the actual relevance of SOT among recipients with ongoing SARS-CoV-2 infection at the time of surgery, we performed a systematic review of the literature.

Methods

The electronic search was performed on PubMed, Scopus, and Embase databases.

The study protocol was registered on PROSPERO (CRD42024499700) and reported following the PRISMA guidelines. Supplementary files 1 and 2 contain the study's search strategy and PRISMA flowchart.

We included studies that reported at least one case of a patient who underwent SOT when infected with SARS-CoV-2, published in the period 01/03/2020-01/03/2024.

The primary outcome was to characterize (demographic data, comorbidities, immunization against COVID-19, oxygen

Abbreviations: SOT, solid organ transplant; COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; PCR, polymerase chain reaction; Ct, cycle threshold.

* Corresponding author.
E-mail address: andrea.lombardi@unimi.it (A. Lombardi).

https://doi.org/10.1016/j.ijid.2024.107214

requirement, intensive care unit (ICU) admission, death, and organ rejection) the SOT occurring in patients with a confirmed diagnosis of SARS-CoV-2 infection.

SOT occurring in an infected patient was defined if the authors reported a first positive SARS-CoV-2 nasopharyngeal swab in the patient 48 h before/after the transplant procedure. Both molecular, antigen and unspecified tests were deemed acceptable for the purpose of the review. Deliberate SOT was defined as the transplantation performed on a patient infected by SARS-CoV-2 with clinicians aware of the ongoing infection.

Study characteristics were described using counts and percentages, or medians and interquartile ranges (IQRs), as appropriate. A multivariate logistic regression was performed to assess the variables associated with an increased risk of being admitted to the ICU for COVID-19-related reasons.

Results

Overall, 54 patients from 29 studies were included. Specifically, 22 case reports of single patients [3-23], 4 case reports of 2 patients [24-27], 3 case series describing 4 patients [28-30], and 1 comprising 12 cases were included [31]. The provenience of each included study is reported in Supplementary Figure 1.

Table 1
Demographic and clinical characteristics of SOT recipients transplanted with ongoing SARS-CoV-2 infection.

Demographic data		
Age	Median (IQR)	47.5 (35.5-60.0)
Biological sex	Male	34 (63.0)
BMI	Mean (SD)	23.5 (7.2)
	missing	48
SOT data		
Transplanted organ	Heart	4 (7.4)
	Kidney	24 (44.4)
	Liver	19 (35.2)
	Lung	6 (11.1)
	Kidney and liver	1 (1.9)
Accidental transplant		6 (11.1)
Urgent transplant		11 (23.4)
	missing	7
Comorbidities		
Cardiovascular disease		5 (11.9)
	missing	12
Diabetes		5 (11.9)
	missing	12
Chronic lung disease		6 (14.3)
	missing	12
Rheumatological disease		6 (14.3)
	missing	12
Chronic liver disease		12 (28.6)
	missing	12
Chronic kidney disease		13 (31.0)
	missing	12
RRT		11 (26.2)
	missing	12
Cancer		3 (7.1)
	missing	12
Count of comorbidities	< 2	23 (54.8)
	≥ 2	19 (45.2)
	missing	12
CCI	Mean (SD)	2.5 (2)
	missing	15
Anti-SARS-CoV-2 status		
COVID-19 vaccination		25 (64.1)
	missing	15
COVID-19 vaccine shots	≤ 2	20 (54.1)
	> 2	17 (45.9)
	missing	17
Previous SARS-CoV-2 infection		3 (18.8)
	missing	38
Tixagevimab-cilgavimab combination		2 (4.1)
	missing	5

BMI: body mass index; SOT: solid organ transplantation; RRT: renal replacement therapy; CCI: Charlson comorbidity index.

Table 2
Outcomes data of SOT recipients transplanted with ongoing SARS-CoV-2 infection.

Need for oxygen support		10 (18.5)
ICU admission		7 (13.7)
	missing	3
All-causes death		2 (3.7)
90-days death		2 (4.3)
	missing	8
Days between Tx and discharge	Mean (SD)	28.2 (23.6)
	missing	33
LOS	Median (IQR)	36.5 (18.2, 61.0)
	missing	44
Acute rejection		7 (13.0)

ICU: intensive care unit; Tx: transplantation; LOS: length of stay.

The main characteristics of the SOT recipients transplanted with ongoing SARS-CoV-2 infection are reported in Table 1. In the 11.1% of SOT recipients, the decision to transplant the organ was made unknowingly because of the SARS-CoV-2 infection (accidental infection), which was detected after transplantation.

Data regarding SARS-CoV-2 infection diagnosis, symptoms, and complications are described in Supplementary Table 1. Regarding the cycle threshold (Ct) results, the mean Ct value at diagnosis was 29, while the mean Ct value at SOT was slightly higher at 31.9.

Data on specific SARS-CoV-2 treatment and immunosuppressive drugs administered are reported in Supplementary Table 2. Of 54 cases, 24 patients (45.3%) received anti-SARS-CoV-2 specific therapy. Remdesivir was the most administered treatment, with 17 patients (32.1%) receiving it.

The primary clinical outcomes of these SOT recipients are shown in Table 2. There were two reported cases (3.7%) of all-cause death, while there were no cases of death which might be explicitly attributed to COVID-19.

Finally, the presence of COVID-19-related symptoms (OR 2.044, 95% CI 0.18-17.66, $P = 0.52$), receiving lung transplantation compared to other types of solid organ transplants (OR 6.32, 95% CI 0.59-60.91, $P = 0.10$), and accidental transplantation (OR 1.3, 95% CI 0.04-16, $P = 0.83$) were not significantly associated with worsening clinical conditions requiring ICU admission.

Discussion

We have identified a non-negligible number of SOT recipients who performed transplantation while infected with SARS-CoV-2, with a median age below 50 years and a few comorbidities, who primarily received kidney and liver transplants. In most cases, clinicians were fully aware of the ongoing infection, thus performing the procedure deliberately despite only a few procedures being classified as urgent. The infections were generally mild, with limited symptoms, likely due to substantial immunization from previous infections and vaccinations. Interestingly, less than half of patients received specific anti-SARS-CoV-2 treatments, mainly remdesivir. Nonetheless, the need for ICU readmission after SOT was limited; COVID-19-related deaths were not reported, and only two all-cause deaths were recorded in the 90-day post-transplant period.

This is the first systematic attempt to describe SOT among recipients with ongoing SARS-CoV-2 infection at the time of surgery. Interestingly, in a previous survey of our group, we identified several similar elements associated with the decision to perform SOT in recipients with ongoing SARS-CoV-2 infection. [2] Namely, COVID-19 symptoms absence, a previous immunization against the virus, and the administration of remdesivir.

Scientific societies generally recommend a cautious approach regarding transplantation in patients with active infections. American and European guidelines for adult SOT advise delaying transplantation until the infection is resolved or controlled [32], typically recommending a minimum of two weeks postrecovery before proceeding with the transplant. [33]

Our study has several inherent limitations. First, it relies on data recovered from published studies, making it likely that publication bias is present. Despite this bias, the cases recorded showed a generally good outcome, suggesting that in a larger population, the impact of SARS-CoV-2 could be even less relevant. Second, the data were gathered from various sources and not collected systematically, resulting in several missing values. For example, the post-transplant follow-up was not standardized and therefore, events such as acute rejection can be underestimated. Third, an average of 16 days has elapsed between the diagnosis of SARS-CoV-2 infection and the surgical procedures. This could have allowed the clinicians to assess the impact of the infection on the transplant candidate, excluding those with severe COVID-19. Moreover, such a long period is usually associated with a clearance of the viral infection, even though, for those patients with this data available, the SARS-CoV-2 PCR Ct on nasal swabs was 31.9, a value representing a low viral burden but still detectable.

Overall, the data collected in our study suggest that deliberate SOT of recipients with ongoing SARS-CoV-2 is ongoing worldwide in candidates of nonlung transplant who are fit, immunized against the virus, and displaying a nonsevere course of disease. Interestingly, no COVID-19-related deaths were recorded.

It is difficult to understand the reasons behind the apparent suitability of the transplant procedure among this peculiar population of infected recipients. Nonetheless, we could highlight that (1) the viral strain has changed during the pandemic, with the appearance of strains characterized by a lower virulence, (2) the population, including SOT candidates, has been immunized, both by vaccination and previous infections, thus acquiring elements able to reduce disease's severity, (3) the SOT recipients included in our analysis were transplanted after a considerable time since the infection, allowing to select patients without severe manifestations and to control the disease by the immune system of the host, and (4) only a handful of lung transplants have been reported; thus we do not have reliable data regarding the transplantation of the organ most profoundly affected by the infection.

It is challenging to propose radical changes to the standard of care based on the results of merged, small, and not systematically collected experiences. Nonetheless, it seems reasonable to consider the transplantation of extrapulmonary organs among infected young (age $<$ 50 years) recipients with limited comorbidities, displaying reduced COVID-19 symptoms, previously immunized against the virus, and providing antiviral treatments in the early post-transplant.

Although the pandemic's impact on our daily lives has significantly diminished, many SOT candidates continue to find their needs unmet. This underscores the critical importance of ensuring that no opportunity for transplantation is fruitless.

Declarations of competing interest

All the authors have nothing to declare.

Funding

This study was partially supported by IRCCS Ricerca Corrente Funds 2024.

Ethical approval statement

Not required.

Acknowledgments

None.

Author contributions

AL, AG, and AB conceived the study. AL built and performed the research strategy. EP, SB, GV, and CA reviewed the literature and extracted relevant variables. MC performed the statistical analyses. AL wrote the first draft of the manuscript. All the authors reviewed the final version of the manuscript.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2024.107214.

References

[1] Danziger-Isakov L, Blumberg EA, Manuel O, Sester M. Impact of COVID-19 in solid organ transplant recipients. *Am J Transplant* 2021;**21**:925–37. doi:10.1111/ajt.16449.

[2] Lombardi A, Grossi P. Solid organ transplantation in SARS-CoV-2 positive recipients: a web-survey among ESGICH members. *Clin Microbiol Infect* 2024;**30**:684–7. doi:10.1016/j.cmi.2024.01.012.

[3] Okubo K, Iqbal S, Lizaola-Mayo B, Aqel B, Graf EH, Banacloche JCG, et al. Liver transplant in a polymerase chain reaction–positive COVID-19 recipient: a case report. *Transplant Proc* 2021;**53**:2490–4. doi:10.1016/j.transproceed.2021.07.045.

[4] Gao F, Zheng KI, Gu JY, George J, Zheng MH. COVID-19 and liver transplantation: lessons learned from three reported cases. *Transpl Infect Dis* 2020;**22**:e13335. doi:10.1111/tid.13335.

[5] Manzia TM, Gazia C, Lenci I, Angelico R, Toti L, Monaco A, et al. Liver transplantation performed in a SARS-CoV-2 positive hospitalized recipient using a SARS-CoV-2 infected donor. *Am J Transplant* 2021;**21**:2600–4. doi:10.1111/ajt.16548.

[6] Lang C, Jaksch P, Hoda MA, Lang G, Staudinger T, Tschernko E, et al. Lung transplantation for COVID-19-associated acute respiratory distress syndrome in a PCR-positive patient. *Lancet Respir Med* 2020;**8**:1057–60. doi:10.1016/s2213-2600(20)30361-1.

[7] Yokoyama Y, Terada Y, Nava RG, Puri V, Kreisel D, Patterson GA, et al. Coronavirus disease 2019 positivity immediately after lung transplantation: a case report. *Transplant Proc* 2022;**54**:1572–4. doi:10.1016/j.transproceed.2022.03.032.

[8] Yohanathan L, Campioli CC, Mousa OY, Watt K, Friedman DZP, Shah V, et al. Liver transplantation for acute liver failure in a SARS-CoV-2 PCR-positive patient. *Am J Transplant* 2021;**21**:2890–4. doi:10.1111/ajt.16582.

[9] Yetmar ZA, Ranganath N, Huebert RC, Rosen CB, Razonable RR, Beam E. Successful liver transplantation from a SARS-CoV-2 positive donor to a positive recipient: potential role of monoclonal antibodies. *Transplantation* 2022;**106**:E181–2. doi:10.1097/TP.0000000000004032.

[10] Vadlamudi GD, Keerthy M, Goyert G. Postpartum bilateral lung transplantation in COVID-19 associated respiratory failure. *BMJ Case Rep* 2022;**15**:e249159. doi:10.1136/bcr-2022-249159.

[11] Soquet J, Rousse N, Moussa M, Goeminne C, Deblauwe D, Vuotto F, et al. Heart retransplantation following COVID-19 illness in a heart transplant recipient. *J Heart Lung Transplant* 2020;**39**:983–5. doi:10.1016/j.healun.2020.06.026.

[12] Shimizu S, Sakamoto S, Yamada M, Funaki T, Fukuda A, Uchida H, et al. Successful pediatric liver transplantation case with a positive SARS-CoV-2 test at the time of transplant. *Hepatol Res* 2023;**53**:569–73. doi:10.1111/hepr.13881.

[13] Seet C, Dabare D, Forbes S, Khurram M, Mohamed IH. Kidney transplant surgery in a recipient with COVID-19 at the time of transplantation. *Transplantation* 2021;**105**:e54–5. doi:10.1097/tp.0000000000003652.

[14] Sellarès-Nadal J, Esperalba J, Márquez-Algaba E, Los-Arcos I, Antón A, Nuvials X, et al. Positive polymerase chain reaction for SARS-CoV-2 in a candidate does not always preclude liver transplantation: case report and literature review. *Exp Clin Transplant* 2022;**20**:321–4. doi:10.6002/ect.2021.0387.

[15] Radisic MV, Walther JC, Werber G, Pujato N, Beltramino S, Bravo PM, et al. Kidney transplantation in a recipient with positive RT-PCR for SARS-CoV-2. *Int J Organ Transplant Med* 2021;**12**:42–7.

[16] Kidson KM, Park J, Charles MK, Wright AJ, Hussaini T, Omar M, et al. Successful liver transplantation in a patient with acute liver failure and acute COVID-19 infection. *Transplantation* 2021;**105**:160. doi:10.1097/01.tp.0000789500.50801.c7.

[17] Jacob R, Liu K, Marinelli T. Successful liver transplantation for hepatitis B-related acute liver failure in a patient with active COVID-19. *Transplant Infect Dis* 2022;**24**:e13889. doi:10.1111/tid.13889.

[18] Giovannico L, Ramirez AD, Parigino D, Fischetti G, Losito C, Lenoci S, et al. Heart transplant in a Sars-CoV-2 positive recipient: management protocol of the world's first case. *Clin Transplant* 2023;**37**:e15045. doi:10.1111/ctr.15045.

[19] Garcia LR, Garzesi AM, Sinatora JB, Grotto RMT, Passaroni AC, Campos N, et al. Orthotopic heart transplantation in a Covid-19 recipient. *Arq Bras Cardiol* 2023;**120**:e20220234. doi:10.36660/abc.20220234.

[20] Francisco D, Ávila G, Jorge C, Mansinho K, Toscano C, Weigert A. Decision making—should we perform kidney transplantation on a patient with a positive RT-PCR test for SARS-CoV-2? *Nefrologia* 2022. doi:10.1016/j.nefroe.2022.04.007.

[21] Hogan JI, Kotton CN. A call for caution in the immunocompromised: coronavirus disease 2019 associated with mortality in a vaccinated lung transplant recipient. *Open Forum Infect Dis* 2021;**8**:ofab557. doi:10.1093/ofid/ofab557.

[22] Donald JS, Yeoh D, McCarthy HJ, Larkins NG. Successful kidney transplantation for children within 3 weeks of COVID-19 infection. *Transplantation* 2022;**106**:E515–16. doi:10.1097/TP.0000000000004346.

[23] Barros N, Ermel A, Mihaylov P, Lacerda M, Fridell J, Kubal C. Deceased donor liver transplantation from a SARS-CoV-2–positive donor to a SARS-CoV-2–positive recipient. *Liver Transplant* 2021;**27**:1849–51. doi:10.1002/lt.26253.

[24] Natori Y, Anjan S, Simkins J, Abbo L, Manickavel S, Salgado J, et al. Successful lung transplantation in COVID-19 PCR positive patients: a single-center experience. *J Heart Lung Transplant* 2023;**42**:1478–9. doi:10.1016/j.healun.2023.05.019.

[25] Mouch CA, Alexopoulos SP, LaRue RW, Kim HP. Successful liver transplantation in patients with active SARS-CoV-2 infection. *Am J Transplant* 2022;**22**:2694–6. doi:10.1111/ajt.17134.

[26] Vissichelli NC, Morales MK, Bryson A, Bruno D. Successful deceased donor liver transplantation in candidates with high MELD and ongoing positive SARS-CoV-2 PCR. *Transplant Infect Dis* 2022;**24**:e13816. doi:10.1111/tid.13816.

[27] Bhandari TR, Shrestha KK, Shrestha PC. COVID-19 infection in renal transplant recipients in early post-renal transplantation period: report of three cases. *Transpl Infect Dis* 2022;**24**:e13837. doi:10.1111/tid.13837.

[28] Natori Y, Anjan S, Martin EF, Selvagi G, Villavicencio A, Coro A, et al. When is it safe to perform abdominal transplantation in patients with prior SARS-CoV-2 infection: a case series. *Clin Transplant* 2021;**35**:e14370. doi:10.1111/ctr.14370.

[29] Viana LA, Cristelli MP, Ficher KN, Rezende JT, Villanueva LAA, Santos D, et al. Kidney transplantation in patients with SARS-CoV-2 infection: a case series report. *Transplantation* 2021;**105**:e1–3. doi:10.1097/tp.0000000000003521.

[30] Hawkins RB, Mehaffey JH, Charles EJ, Mannem HC, Roeser M. Lung transplantation for severe post-coronavirus disease 2019 respiratory failure. *Transplantation* 2021;**105**:1381–7. doi:10.1097/tp.0000000000003706.

[31] Zavala S, DeLaurentis C, Aaron JG, Miko BA, Fox AN, Bergelson M, et al. When you need to dive in the deep end—transplanting SARS-CoV-2 PCR+ recipients. *Transplant Infect Dis* 2023;**25**:e14110. doi:10.1111/tid.14110.

[32] Malinis M, Boucher HW. Screening of donor and candidate prior to solid organ transplantation—guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. *Clin Transplant* 2019;**33**:e13548. doi:10.1111/ctr.13548.

[33] Len O, Garzoni C, Lumbreras C, Molina I, Meije Y, Pahissa A, et al. Recommendations for screening of donor and recipient prior to solid organ transplantation and to minimize transmission of donor-derived infections. *Clin Microbiol Infect* 2014;**20**:10–18. doi:10.1111/1469-0691.12557.