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COVID-19 AND TRANSPLANTATION (RK AVERY AND DL SEGEV, SECTION EDITORS)

Solid Organ Transplantation in SARS-CoV-2 Recovered Transplant Candidates: a Comprehensive Review of Recent Literature

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Abstract

Purpose of Review As the coronavirus disease 2019 (COVID-19) pandemic continues to surge, determining the safety and timing of proceeding with solid organ transplantation (SOT) in transplant candidates who have recovered from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and who are otherwise transplant eligible is an important concern. We reviewed the current status of protocols and the outcomes of SOT in SARS-CoV-2 recovered patients.

Recent Findings We identified 44 published reports up through 7 September 2021, comprising 183 SOT [kidney = 115; lung = 27; liver = 36; heart = 3; simultaneous pancreas-kidney (SPK) = 1, small bowel = 1] transplants in SARS-CoV-2 recovered patients. The majority of these were living donor transplants. A positive SARS-CoV-2 antibody test, although not obligatory in most reports, was a useful tool to strengthen the decision to proceed with transplant. Two consecutive real-time polymerase chain test (RT-PCR) negative tests was one of the main prerequisites for transplant in many reports. However, some reports suggest that life-saving transplantation can proceed in select circumstances without waiting for a negative RT-PCR. In general, the standard immunosuppression regimen was not changed.

Summary In select cases, SOT in COVID-19 recovered patients appears successful in short-term follow-up. Emergency SOT can be performed with active SARS-CoV-2 infection in some cases. In general, continuing standard immunosuppression regimen may be reasonable, except in cases of inadvertent transplantation with active SARS-CoV-2. Available reports are predominantly in kidney transplant recipients, and more data for other organ transplants are needed.

Keywords COVID-19 recovery · Waitlist · Solid organ transplantation · Deceased donor · Living donor

Abbreviations

SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SOT	Solid organ transplantation
RT-PCR	Real-time polymerase chain test
SPK	Simultaneous pancreas-kidney transplant
IS	Immunosuppression
COVID-19	Coronavirus disease-19
LDKT	Living donor kidney transplantation
DDKT	Deceased donor kidney transplantation
CT	Cycle threshold
LDLT	Living donor liver transplantation
DDLT	Deceased donor liver transplantation
LT	Lung transplantation

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Introduction

The coronavirus disease (COVID-19) pandemic has posed major challenges to the practice of transplantation worldwide [1•, 2]. The pandemic brought transplant activities to a standstill in different regions of the world, as per the regional COVID-19 toll and available resources [3]. The resumption of transplantation activities occurred in a staged and stepwise process with interruptions by COVID-19 waves [4]. However, there were efforts by many transplant teams to explore strategies for safely resuming transplantation activities within the initial phase of the pandemic.

Globally, as of 6 September 2021, there have been 220,563,227 confirmed cases of COVID-19 reported to the World Health Organization [5]. Such mammoth numbers are a matter of focus and concern for transplant teams, as it leads to a high numbers of COVID-19 recovered patients requiring organ transplant as well as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) exposure prevalence among organ donors. We recently reviewed use of organs from SARS-CoV-2 infected donors after recovery from SARS-CoV-2 [6]. From the candidate perspective, a daunting question has arisen: how and when is it safe to proceed to transplant after COVID-19 infection? The answer to this is still not fully known and requires further review of the evidence.

An international registry study reported high rates of complications in general surgery patients with perioperative COVID-19 [7]. However, there are fewer such reports in the context of SOT. Notably, SOT recipients who contract COVID-19 in the early post-transplant period face an increased risk of adverse outcomes, suggesting that transplanting a patient with active or recently resolved COVID-19 may carry a higher rate of complications [8–10]. Hence, the decision to proceed with transplant after recent COVID-19 is a complex issue.

To advance understanding of this timely topic, we reviewed the available published evidence on SOT performed in patients who have recovered from COVID-19. We extracted information on eligibility criteria, testing protocols, and clinical outcome in this context.

Kidney Transplantation After Recovery From COVID-19

A total of 115 kidney transplants in patients who have recovered from COVID have been reported. The first case of living donor kidney transplantation (LDKT) where both donor and recipient recovered from COVID-19 illness was reported in Turkey in February 2021 [11]. Over follow-up of 45 days, the authors reported no complications in the donor-recipient pair. Similar case reports followed from different areas of the world [12]. But the most comprehensive insight into this topic was documented in an Indian study that reported 75 LDKT in recipients who had recovered from COVID-19 [13•]. The clinical protocol in this series mandated at least two consecutive negative RT-PCR reports, an asymptomatic period of 28 days, and a normal chest x-ray before transplant. The median waiting time from COVID-19 diagnosis until transplant was approximately 60 days in this report. A notable aspect of this cohort was that none of the patients had required mechanical ventilation during COVID-19 [14••]. However, the reported post-transplant follow-up was short, limiting assessment of long-term data. The same authors had previously reported 9 COVID-19 recovered donor-recipient pairs, with similar outcomes and follow-up [13•]. More detailed data for deceased donor kidney transplantation (DDKT) in COVID-19 recovered candidates came from a US report of 13 cases [15••], in which four patients had moderate to severe COVID-19, of which one required mechanical ventilation. Median waiting time post-COVID-19 was 71 days, and postoperative course for these patients at 3 months follow-up was reported to be uneventful (Table 1).

At some centers, transplant physicians have gradually shortened the waiting time from COVID-19 recovery to transplantation, and there are reports of transplants performed in candidates who were still COVID-19 positive. In an Italian report, DDKT was performed in a candidate with recovered COVID-19 at 29 days after the first negative PCR, a significantly shorter waiting time than the previously described median 60–71 days [16]. Some transplants have been performed in patients with active COVID-19: there are five reports of kidney transplants in candidates with positive RT-PCRs, including those with high cycle threshold (CT) values [17, 18] as well as those with neutralizing antibodies [19]. Additionally, successful simultaneous pancreas-kidney transplant (SPK) after COVID-19 recovery has been reported [20]. The majority of the published data about LDKT in COVID-19 recovered patients is from developing nations, while DDKT reports predominate in developed countries, likely attributable to the fact that deceased donation is still in its infancy in the developing world; however, safety profiles appear similar for both.

A European study recently studied antibody response in hemodialysis patients and found the immune response varied with the severity of infection. They also reported a low level of seroresponse and waning of antibody response in follow-up [21]. These data demonstrate that transplant candidates with previous COVID-19 are at theoretically more risk for re-infection or reactivation even after transplantation.

Table 1 Kidney transplantation in candidates with recovered or positive SARS-CoV-2 infection. COVID-19 severity was defined as asymptomatic in cases who had incidental detection, mild in those with only upper respiratory symptoms, moderate when requiring low flow oxygen, and severe in cases with higher oxygen requirement. *=Cases which were RT-PCR positive at the time of transplant surgery. Abbreviations: *COVID-19*, coronavirus disease; *CKD*, chronic kidney disease; *CT*, cycle threshold; *DM*, diabetes mellitus; *DD*, deceased donation; *ESKD*, end-stage kidney disease; *F*, female; *HD*, hemodialysis; *IS*: immunosuppression; *LD*, living donation; *M*, male; m, months; *MMF*, mycophenolate; *nRT-PCR*, real-time polymerase chain test through nasopharyngeal specimen; *MN*, membranous nephropathy; *TIN*, tubulointerstitial nephritis; *TCR*, T cell rejection

Authors	*n*	Type	Age/sex	Cause of ESKD	COVID-19 severity	Negative nRT-PCR prior to transplant	Waiting time after a negative RT-PCR	IgG antibody test Pre-Transplant	Donor's COVID-19 status	IS regimen	Outcome	Follow-up
Singh N et al., Sept 2020 [20]	1	DD	66/F	DM	Mild (home)	2 negatives (24 h apart)	3 mos	Done (positive)	Negative	No change	Uneventful	7 wks
Varotti et al., Oct 2020 [16]	1	DD	28/F	MN- CKD	Mild	2 negative (48 h apart)	2 wks	Done (positive)	Negative	No change	*E. coli* infection	60 d
Waghmare I et al., Dec 2020 [12]	1	LD	46/M	Not reported	Severe	≥2	3 mos	Not reported	Negative	No change	Uneventful	1 mos
Kanchi et al., Jan 2021 [66]	2	• DD • LD	• 44/M • 35/F	• DM • CKD unknown	• Severe • Mild	• 2 negatives • 3 negatives	• 4 wks • 6 wks. of COVID-19 diagnosis	Done (positive) in both	• Negative • Positive	• No change • No induction	• Uneventful • Uneventful	• 15 wks • 14 wks
Viana L A et al., Jan 2021* [61]	4	DD	• 34/M • 27/M • 41/M • 65/F	Not reported	• Mild • Mid • Asymptomatic • Asymptomatic	All 4 cases were RT-PCR positive retrospectively after surgery	-	Not done	Negative in all	In 3 cases, MMF was halved	Two patients got TCR	1 mo
Kucuk et al., Feb 2021 [11]	1	LD	31/M	CKD unknown	Mild	4 negatives	30 d after recovery	Done (both negative)	Positive with mild illness	No change	None	45 d
Murad et al., Feb 2021* [18]	1	DD	64/F	Alport syndrome	Mild	Positive (high CT value)	6 wks. after COVID-19	Not reported	Negative	No change	Uneventful	4 mo
Yoshinaga et al., March 2021 [67]	1	DD	49/M	Not reported	Moderate	3	3 mos	Not done	Negative	No change	Uneventful	95 d
Reyad Al et al., March 2021 [68]	1	DD	65/F	CKD unknown	Severe	3	46 d	Positive	Negative	No change	Uneventful	2 mos
Kute et al., April 2021 [13•]	9 of 31	LD	Median: 39 yr Sex: M:7 F:2	HTN and DM	• Asymptomatic ($n=5$) • Mild ($n=4$)	≥2	73 (34–92) d	Not mandatory	All donors were COVID-19 recovered	No change	Uneventful	44 d

Table 1 (continued)

Authors	*n*	Type	Age/sex	Cause of ESKD	COVID-19 severity	Negative nRT-PCR prior to transplant	Waiting time after a negative RT-PCR	IgG antibody test Pre-Transplant	Donor's COVID-19 status	IS regimen	Outcome	Follow-up
Villanego F et al., May 2021 [69]	1	DD	70/M	Chronic TIN	Asymptomatic	3 consecutive negatives	3 mos. after first + ve	Done (positive)	Negative	No change	Uneventful	2 mos
Santeusanio AD et al., June 2021 [15••]	13	• DD:10 • LD: 3	Median: 2.8 yr Sex: 84% M	• HTN (38%) • DM (30%)	• Mild ($n=9$) • Moderate–severe ($n=3$) • Mechanical ventilation ($n=1$)	1 Negative	Median of 71 (56.6–135) d	10 out of 13; and all reports positive for antibodies	Negative	No change	Uneventful: no difference vs controls	3.6 mos
Puodziukaite et al., June 2021 [19]	2	DD	• 38/F • 36/M	• DM • IgA nephropathy	• Mild • Asymptomatic	1 Negative	• 2.5 mos. after COVID-19 • 2 mos. after COVID-19	Done (positive)	• RT-PCR + ve • Mild	No change	Uneventful	3 mos
Hogan et al., July 2021* [17]	1	DD	8/M	Congenital nephrotic syndrome	Asymptomatic	Positive with high CT value	Active; RT-PCR + ve with high CT value	Done (positive)	Negative	No change	Uneventful	44 d
Tuschen et al., July 2021 [70]	1	DD	65/F	IgA nephritis	Moderate	3	65 d	Positive	Negative	No change	Uneventful	9 mos
Kute et al., July 2021 [14••]	75	LD	Median: 47 (29–72) Sex: M:23 F:52	• Not reported • Indication of early transplant: Difficult vascular access ($n=8$) and severe left ventricular dysfunction ($n=12$); Others: Financial constraint for continuing HD	• Asymptomatic ($n=17$, 22.7%) • Mild ($n=3$, 6.48%) • Moderate ($n=1$, 5.20%) • Severe ($n=7$, 9.3%)	≥2	Median: 60 d; Increased significantly from asymptomatic, mild, moderate, and severe disease (49, 57, 83, 94 d; $P=0.019$), respectively	Not mandatory	COVID-19 recovered donors ($n=16$)	No change	Uneventful	Median: 81 d (56–117)

Lung and Heart Transplantation After Recovery From COVID-19

There are reports of successful extracorporeal membrane oxygenation (ECMO) use as salvage therapy in severe COVID-19 [22, 23]. But there are also considerable numbers of COVID-19 cases who fail ECMO and are potential candidates for lung transplantation (LT). The first case series of LT in a SARS-CoV-2 recovered patient was reported in a US study, where 3 patients suffering from irreversible lung injury benefited from LT [24]. There are also a few reports of successful LT in other nations [25–28]. In general, conducting a LT in a recipient after recovered SARS-CoV-2 infection is relatively difficult compared to other SOT. The logistics involved in a successful LT can be inferred from a report where a candidate with COVID-19 was transferred from Mexico to Korea for LT [29]. Some insight into the status of LT after recovery from SARS-CoV-2 comes from a recently published multi-institutional series of 12 cases [30••]. The authors proposed criteria for LT in COVID-19 patients with end-organ lung damage, suggesting that this procedure should be reserved for those aged < 65 years, and with approximately 4–6 weeks of irreversible lung injury. They also suggested two negative lower respiratory tract fluid RT-PCRs, and early weaning of sedation in the post-transplant period to promote early recovery. They also favored double lung transplantation, as the majority of their cohort had superimposed pulmonary hypertension. In follow-up, the outcomes of LT in patients recovered from COVID have been encouraging [31].

Another complex procedure is a heart transplant in a COVID-19 recovered patient. The first such case was performed in the USA [32]. In another report, a heart re-transplantation was performed in a patient in the recovery phase of COVID-19 with an RT-PCR positive report. The outcome was good but the patient remained SARS-CoV-2 positive until day 44 of follow-up [33]. There is also a report of emergency heart transplantation in a patient who developed fulminant myocarditis related to COVID-19 [34].

Liver Transplantation After Recovery From COVID-19

The first and largest cohort of living donor liver transplantation (LDLT) COVID-19 recovered patients was described in an Indian study [35••]. A US study described the first and largest series of deceased donor liver transplantation (DDLT) in COVID-19 recovered patients [36••]. There are also case reports from different parts of the world [37–39]. There has not been consensus on a specific waiting time before transplant, but 4 weeks seems justified. However, many reports describe proceeding to transplantation with no waiting time as transplant was judged to be a life-saving procedure. Liver transplantation has also been offered to COVID-19 recovered recipients with other complicating factors, such as HIV [40] and very young age (Table 2) [41].

Similar to kidney transplantation, the need for an interval from COVID-19 clearance has been challenged. In Italy, a DDLT was performed in as early as 9 days after being diagnosed with asymptomatic COVID-19 and just 2 days after a negative RT-PCR; the outcome was uneventful [42]. In another Italian report, a decision to perform an emergency DDLT was made, using a COVID-19 positive donor. The recipient was RT-PCR positive but had neutralizing antibodies [42]. In the USA, an emergency DDLT was performed in an RT-PCR positive critical COVID-19 patient. The decision to proceed was taken in view of his deteriorating liver illness and high CT values despite having no antibody response [43]. In the USA, an urgent DDLT was performed successfully in a patient who had COVID-19 illness for 2 months and was persistently RT-PCR positive at the time of transplant [44]. In general, there have been no obvious COVID-19 related complications in the follow-up of these cases. However, there are reports of portal venous thrombosis and hepatic artery thrombosis in two DDLT transplanted to COVID-19 recovered patients [45, 46]. Although the association of this complication with COVID-19 is not clearly delineated, it raises a word of caution. There are very few reports of reactivation or re-infection with COVID-19 following SOT in recovered patients. One such report demonstrated repeated positive viral loads till 1 month of successful DDLT. However, the patient remained asymptomatic throughout [47]. Post-COVID-19 cholangiopathy emerged as a new cause of chronic liver disease requiring transplantation in this pandemic [48, 49], but has not yet been reported as a complication of liver transplantation to COVID-19 positive recipients.

Deciding to Proceed to Transplantation: Weighing Risks vs Benefits

It is difficult to delineate any uniform guidelines for assessing eligibility for transplant in COVID-19 recovered patients. Various international bodies have come up with a consensus for surgeries in recovered patients. The American Society of Anesthesiologists and Anesthesia Patient Safety Foundation Joint Statement on elective surgery, published on 8 December 2020, recommended 4 weeks waiting time for asymptomatic or mild cases; 6 weeks for hospitalized

patients; 8–10 weeks for patients hospitalized with comorbid conditions; and 12 weeks for severe cases [50]. The International Society of Heart and Lung Transplantation guidelines revised on 1 February 2021 recommended at least 1 negative RT-PCR with normal chest imaging along with no symptoms and waiting time of at least 14 days for asymptomatic, and 21 days for symptomatic COVID-19 cases [51]. If RT-PCR remains positive beyond 21 days of illness in a recovered candidate, the patient can still proceed for transplant. Recently, the Indian Society of Organ Transplant guidelines for SOT from recovered donors and recipients recommended at least 2 negative RT-PCR, with an asymptomatic period of 28 days and normal chest radiology before [52].

There are a few studies that have proceeded with one RT-PCR negative report, while some have more than 3 negative reports. From the available evidence, it is justified to document at least two negative RT-PCR reports, to eliminate the possibility of a false negative. The other salient criterion is that the patient must be asymptomatic after recovery. The optimal symptom-free duration before transplant is not known, but recovery for more than 1 month seems safe before an elective transplant. Nevertheless, there are reports of life-saving transplantation in extremely ill patients as well. As clinical practice and understanding have evolved with time in this pandemic, the threshold for proceeding to a transplant has become less strict. In the current era, there are no data to indicate that a particular waiting time is ideal for proceeding with SOT; this decision should be based solely on the urgency of transplant [53]. There is emerging evidence to support transplant from RT-PCR positive patients in some circumstances. The rationale behind proceeding for transplant here is the high lag time for a negative RT-PCR report in chronic conditions like chronic kidney disease. The studies which successfully transplanted such case were buttressed by a report of protective antibody level in many cases. There are multiple studies which show that a low cycle threshold of RT-PCR is associated with high viral loads; hence, candidates with persistently positive RT-PCRs but with high CT values, if asymptomatic, could be considered for proceeding to transplant based on the urgency of the procedure [54, 55]. Low CT values in RT-PCR are associated with the growth of COVID-19 in cultures with high viral loads, so it would be safest to avoid transplanting patients with low CT values [56]. If the candidate is in the second week of illness, then the chances of lesser viral loads are higher [57]. A recent meta-analysis in the general population showed the incidence of RT-PCR positivity as 14.7% between day 41 and day 60 post-discharge [58]. Another meta-analysis showed a 12% incidence of recurrent RT-PCR positivity in post-discharge recovered patients in the general population [59]. The above two studies imply that the fluctuations in RT-PCR between negative and positive after recovery can affect the timing of transplant, so again RT-PCR should not be the sole consideration in a decision about the timing of a transplant (Table 3).

While most reports required normal chest imaging before transplant, owing to high likelihood of residual radiographic changes for months following infection, we suggest the transplant should proceed even in cases of underlying residual damage. There is a report of an ABO kidney transplant where the team waited for inflammatory markers to resolve despite being RT-PCR negative and asymptomatic [60]. However, normalization of inflammatory markers before transplant should not be a mandatory prerequisite. There is an interesting report of four kidney transplantation where the candidates had no symptoms and their RT-PCRs came back positive retrospectively [61]. Interestingly, all recipients did well and remained asymptomatic, except for acute cellular rejection in two cases, which may be attributable to reduction of IS post-operatively out of concern for a possible flare of COVID-19.

Limitations

The limitation of this review is that there are only two cases of heart transplants and one case of SPK in a recovered patient. Hence, our review cannot provide much information about these organs. Future reports with these organs and prospective studies from international registries will throw more light on this topic.

The sensitivity of RT-PCR approximates 70%, so there will be high chances of false-negative reports [62]. A validated better test in the future will be more helpful. At this point, it is prudent to be on the safe side, with repeated RT-PCR assessments in non-emergency transplants.

The follow-up in most reports was short, and longer follow-up data in these transplant recipients will provide important information regarding safety and outcomes.

In an additional note, there is a report of a 9-year-old female with short bowel syndrome 3 months of post-COVID-19, which required a small bowel transplant [63]. This indicates that COVID may be part of the transplant world in ways we have not yet anticipated.

Conclusion

In summary, transplantation from SARS-CoV-2 recovered patients has been reported to be safe with good short-term outcomes in multiple case reports and case series, although kidney transplantation is predominant in these reports. The optimal criteria to proceed with transplant should include evidence of a lack of viral replication. Emerging data suggest that a negative RT-PCR report should not be mandatory

Table 2 Liver transplantation in candidates with recovered or positive SARS-CoV-2 infection. COVID-19 severity was defined as mild in those with only upper respiratory symptoms, moderate when requiring low flow oxygen, and severe in cases with higher oxygen requirement. *=Cases which were RT-PCR positive at the time of transplant surgery. Abbreviations: *ALF*, acute liver failure; *ACLF*, acute on chronic liver failure; *COVID-19*, coronavirus disease; *CT*, cycle threshold; *DD*, deceased donation; *F*, female; *HAT*, hepatic artery thrombosis; *LD*, living donation; *HCC*, hepatocellular carcinoma; *HCV*, hepatitis C virus; *HBV*, hepatitis B virus; *HIV*, human immunodeficiency virus; *IS*: immunosuppression; *M*, male; m, months; *MMF*, mycophenolate; *NASH*, non-alcoholic steatohepatitis; *nRT-PCR*, real-time polymerase chain test through nasopharyngeal specimen; *PVT*, portal venous thrombosis

Authors	*n*	Type	Age/sex	Cause of liver disease	COVID-19 severity	Negative nRT-PCR prior to transplant	Waiting time after negative RT-PCR	IgG antibody test Pre-Transplant	Donor's COVID-19 status	IS regimen	Outcome	Follow-up
Martini et al., July 2020 [71]	1	DD	39/F	Autoimmune cirrhosis	Mild	1	2 d after first negative and 9 d after diagnosis of COVID-19	Not done	Negative	No change	Uneventful	9 d
Tabrizian P et al., Nov 2020 [40]	1	DD	57/F	HCV, HIV, HCC	Mild	2	2 mos	Positive	Negative	No change	Uneventful	5 mos
Goss MB et al., Nov 2020 [41]	1	DD	4 yr/M	Hepatoblastoma		4	4 wks. after resolution of symptoms	Positive	Negative	No change	Early neutropenia which recovered	6 wks
Raut V et al., Feb 2021 [38]	1	DD	36/M	Alcoholic cirrhosis	Moderate	4	6 wks. of recovery	Not reported	Negative	No change	None	10 d
Rouphael et al., March 2021* [44]	1	DD	27/F	Acetaminophen overdose	Mild	Positive	COVID-19 illness started 2 mos. earlier	Not reported	Negative	No change	Uneventful	27 d
Durazo FA, March 2021 [48]	1	DD	47/M	Post-COVID-19 cholangiopathy	Severe	Negative		Not known	Negative	No change	Uneventful	7 mos
Gambato et al., April 2021 [45]	1	DD	63/F	Ethanol CLD	Mild	1	45 d from COVID-19; 16 d from –ve report	Negative	Negative	No change	PVT	6 mos
Raj A et al., April 2021 [46]	1	LD	51/M	Ethanol CLD	Mild	2 negative	23 d from recovery	Not reported	Negative	Lowered dose of maintenance drugs	HAT; 14 and 18 post-op d	Graft loss; Re-transplant at 70 d Death at 80 d
Dhand et al., April 2021 [37]	1	DD	42/M	Alcoholic	Mild	1	71 d from COVID-19; 24 d from negative	Done (negative)	Negative	No induction/ no MMF	Acute rejection responded	25 d

Table 2 (continued)

Authors	*n*	Type	Age/sex	Cause of liver disease	COVID-19 severity	Negative nRT-PCR prior to transplant	Waiting time after negative RT-PCR	IgG antibody test Pre-Transplant	Donor's COVID-19 status	IS regimen	Outcome	Follow-up
Niess et al., April 2021 [47]	1	DD	56/M	HBV cryptogenic	Mild	2 (31 d after illness)	15 d after negative; and 45 d after illness	Done (positive)	Negative	Tac level kept low, rest no change	Viral loads retested positive post-transplant	70 d
Natori et al., May 2021 [36••]	14	DD:15 LD:1	Median:52.3 yr Sex: M:11 F:3	Not reported	4 patients had RT-PCR positive at transplant but were IgG positive	Negative PCR not a criterion (4 out of 14 were RT-PCR positive at transplant)	Median: 147 (range 61–202) d	Done in all (4 had IgG positive with PCR positive)	Negative	No change	• 13 good outcomes • 1 rejection • 1 death (86 d due to fungal infection)	79 (22–190) d
Kulkarni A V et al., June 2021 [35••]	6	LD	Median:35.8 Sex: M:5 F:1	• ACLF ($n=3$) • Alcohol cirrhosis ($n=2$) • NASH ($n=1$)	• Mild ($n=5$) • Moderate ($n=1$)	2; Last test was done 24 h before transplant	• 4 patients after 2 wks • 2 patients after 4 wks	1	Negative	No change	• 5 did well • 1 had TCR at POD 42 • 1 died sepsis at POD 24	~1 mo
Manzia et al., July 2021* [42]	1	DD	35/F	HBV	Asymptomatic; X-ray showing ground glass opacities	RT-PCR + ve	Positive RT-PCR	Positive	Positive	No change	Uneventful	2 mos
Faruqui S. et al., July 2021 [49]	1	LD		Post-COVID-19 cholangiopathy	Severe				Negative	No change	Uneventful	
Gonzalez A et al., July 2021 [39]	1	DD	46/F	Alcoholic cirrhosis	Mild	2	2 wks., 30 d from symptom onset	Not done	Negative	No change	Uneventful	140 d
Yohanathan L et al., Aug 2021* [43]	1	DD	18/F	ALF Wilson's disease	Critical; intubated	Positive with low CT values	17 d from the onset of COVID-19 symptom	Negative	Negative	MMF not started initially	Uneventful	37 d

Table 3 Thoracic organ transplantation in candidates with recovered or positive SARS-CoV-2 infection. COVID-19 severity was defined as mild in those with only upper respiratory symptoms, moderate when requiring low flow oxygen, and severe in cases with higher oxygen requirement and critical COVID-19 defined as organ failure. Abbreviations: *ARDS*, acute respiratory syndrome; *COVID-19*, coronavirus disease; *ECMO*, extracorporeal membrane oxygenation; *F*, female; *M*, male; *m*, months; *nRT-PCR*, real-time polymerase chain test through nasopharyngeal specimen; *POD*, postoperative day

Authors	*n*	Age/sex	Cause of native organ disease	COVID-19 severity	Waiting time after negative nRT-PCR	IgG antibody test Pre-Transplant	Outcome	Follow-up
Lung transplantation								
Chen J Y et al., Jun 2020 [25]	3	• 66/M • 58/M • 73/M	All had critical COVID-19	All three on ECMO	• 42 d • 37 d • 44 d of COVID-19 illness		• 1 case died POD 1 • 2 uneventful	POD 22 and 12 for 2 alive patients
Han W et al., Jul 2020 [26]	2	• 66/F • 70/M	Both had critical COVID-19	Both on ECMO at the time of transplant	PCR negative; around 2 mos. after first positive report		Uneventful	Short follow-up
Lang C et al., Oct 2020 [27]	1	44/F	Critical COVID-19	On ECMO at the time of transplant	RT-PCR + ve with high CT value; On 58 d since first positive report		Uneventful	121 d
Bharat A et al., Dec 2020 [24]	3	Median: 44.3 ± 13.9; Sex: M:2 F:1	All had Critical COVID-19	All three on ECMO	All three had repeated negative RT-PCR • 6 wks. on MV and ECMO • On 100 d of ECMO • On 90 d of ECMO		Uneventful	3 to 5 mos
Croci GA et al., March 2021 [31]	1			Mild illness	2 mos. back	Positive		6 mos
Gok et al., April 2021 [72]	2	• 69/M • 63/M	• Severe, ARDS on d 0 • ARDS on d 6	• Noninvasive ventilation d 57 • d 68	• 41 d • 34 d	• Positive 55 d • Positive 41 d		30 d
Bharat A et al., May 2021 [30••]	12	Median:48 yr (IQR 41–51) Sex: M:9 F:3	All had critical COVID-19	All on ECMO	All were on life support		All patients weaned off ECMO	Short follow-up
Oh DK et al., May 2021 [29]	1	55/F	Critical COVID-19; ARDS	On ECMO	• 88 d • 49 d of ECMO		Uneventful	3 mos
King CS et al., Sept 2021 [28]	1	37/F	Critical COVID-19	On ECMO for 7 wks	• 10 wks. after COVID-19 illness • RT-PCR negative		Uneventful	D 16
Heart transplantation								
Soquet et al., Sept 2020 [33]	1	22/F	Giant cell myocarditis; re-transplant	Critical required ECMO	Within 1 mo	Done (negative throughout hospital course)	Uneventful but persistent RT-PCR + ve	44 d

Table 3 (continued)

Authors	*n*	Age/sex	Cause of native organ disease	COVID-19 severity	Waiting time after negative nRT-PCR	IgG antibody test Pre-Transplant	Outcome	Follow-up
Johnstad CM et al., March 2021 [32]	1	63/M	Ischemic heart disease	Moderate	15 d of a positive report	Not reported	Uneventful	17 d
Gaudriot B et al., May 2021 [34]	1	38/M	Post-COVID-19 infectious fulminant myocarditis	On ECMO	D 11 of illness	Not reported	Uneventful	1 mo

in all cases to proceed with transplantation. Alteration of early post-transplant immunosuppression in this context does not appear to be necessary, as per the available data. Nevertheless, in cases of life-saving or inadvertent transplantation with active SARS-CoV-2, modifications in the immmunosuppressive regimen are justified. There is also a need to gather further information for transplantation of organs such as the lung, pancreas, and intestine, where data are relatively scant. This review of data from available reports through September 2021 may serve as a foundation for decision-making in the challenging approach to transplantation for SARS-CoV-2 recovered patients. Hopefully, the vaccination era will bring a steep decline in these challenging clinical scenarios [64, 65].

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Compliance with Ethical Standards

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