



CON: Liver Transplantation in the Times of COVID-19: Patients with COVID-19 Infection Should not Undergo Liver Transplantation

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KEY POINTS

- Currently, there are insufficient data to conclude that liver transplantation (LT) is safe in patients with coronavirus disease 2019 (COVID-19) infection, because these patients may be at high risk for postoperative and COVID-19–related complications, graft loss, and death.
- Transplantation despite high transmissibility places transplant health care workers at risk for contracting the virus and may place undue stress on the health care system by requiring higher utilization of hospital resources.
- LT of COVID-19-positive patients poses an ethical dilemma, particularly regarding the principles of justice and utility.

The emergence of novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has significantly impacted the world of LT. After an initial period of unprecedented challenges and uncertainty regarding the management of SARS-CoV-2–infected candidates and recipients, the transplant community temporarily halted all nonurgent LTs. Many societies developed vigorous protocols and guidelines to safely proceed with transplantation amidst the pandemic, but no guidelines recommend transplanting patients with active COVID-19 infection. Little is known regarding the safety and outcomes of LT for COVID-19–infected patients or those who contract

Abbreviations: A1AT, alpha-1 antitrypsin; COVID-19, coronavirus disease 2019; EtOH, ethanol/alcohol; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; ICU, intensive care unit; LT, liver transplantation; MELD, Model for End-Stage Liver Disease; NASH, nonalcoholic steatohepatitis; PCR, polymerase chain reaction; POD, postoperative day; PPE, personal protective equipment; PSC, primary sclerosing cholangitis; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

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TABLE 1. OUTCOMES OF COVID-19 IN RECENT LT RECIPIENTS

	Etiology of Liver Disease/MELD Score	Date of COVID-19+	Acute Rejection	Pneumonia	Death	Other
Zhong et al. ⁸	HBV/HCV	POD 9	Yes	Yes	No	Prolonged viral shedding
Waisberg et al. ¹⁰	HCV, MELD 15	POD 9	No	Yes	Yes (POD 13)	Multisystem organ failure
	EtOH/HCC, MELD 13	POD 10	No	Yes	No	Discharged POD 17
	Cryptogenic cirrhosis, MELD 10	POD 11	Yes	Yes	No	Discharged POD 27
	PSC, MELD 10	POD 18	Yes	Yes	No	Bled post-LT biopsy requiring exploratory laparotomy; steroid-refractory acute rejection
Frager et al. ⁹	NASH/A1AT, MELD 13	POD 36	No	Yes	Yes (POD 56)	Secondary bacterial infection
	HCC	POD 68	No	Yes	No	–

SARS-CoV-2 shortly after undergoing LT. Transplanting an actively infected patient may potentially incur a high risk for postoperative and COVID-19–related complications, graft loss, and death; it also may endanger the health and safety of providers and demands utilization of significant resources in an already resource-strained health system.

EFFECT OF COVID-19 INFECTION ON LT RECIPIENTS

The tremendous physiological stress of surgery coupled with active COVID-19 could result in significant postoperative morbidity and mortality in an LT recipient. A large international surgery registry (n = 1128) evaluating the surgical outcomes of SARS-CoV-2–infected patients who require emergent or elective nontransplant surgeries demonstrated a 21% 30-day mortality, with nearly 50% of patients experiencing pulmonary complications.¹ The stress of this surgery can lead to cytokine storm and clinical decline, resulting in possible superimposed infections and graft loss.² Ongoing COVID-19 in the early postoperative period could potentially compromise graft and patient health through the development of arterial or venous thromboses, myocarditis or myocardial infarction, renal failure, or respiratory failure.^{3–5} SARS-CoV-2 infection can lead to acute hepatitis with aminotransferase elevation to one to three times the upper limit of normal, and acute liver failure with concomitant COVID-19 may be indistinguishable from COVID-induced liver injury. Thus, distinguishing acute rejection from viral-induced hepatitis would be challenging.⁵ Pediatric LT recipients with active uncontrolled respiratory viral infection inadvertently contracted at or near the time of LT had higher all-cause graft failure and increased length of stay.⁶ Although emerging therapies can potentially mitigate the severity of organ damage incurred from SARS-CoV-2 infection, there is no

efficacious antiviral therapy to control and/or eradicate the virus. Active SARS-CoV-2 infection could and should be considered a potential contraindication for LT.⁵

LACK OF DATA TO SUPPORT TRANSPLANTING ACTIVELY INFECTED PATIENTS

There is a dearth of literature that supports transplanting actively infected patients. Outcomes of COVID-19 in LT recipients are poorly defined in patients transplanted within 1 year.⁷ It is difficult to extrapolate this information to patients who acquired COVID-19 in the perioperative period or shortly after LT when immunosuppression is typically most intense. Scarce case reports describe the postoperative courses of patients who developed COVID-19 after transplant (Table 1).^{8–10} In cases of transplantation soon after COVID-19 recovery, the viral polymerase chain reaction (PCR) was negative on more than one test for all patients prior to transplant.^{11–14} Only one case exists of transplantation with a positive PCR. However, in this lung transplant recipient’s preoperative swabs, the cycle threshold—the number of amplification cycles needed to detect genetic material of the virus—was persistently high, and virus was not cultured.¹⁵ Lower cycle threshold, indicative of a higher viral load and high levels of viable virus, correlates with risk for progression to severe disease with increased mortality, as well as increased infectivity.¹⁶

SAFETY THREAT TO HEALTH CARE WORKERS

Transmissibility of the virus is an important consideration, because an actively infected patient poses a threat to the health and safety of those involved in patient care.

Immunosuppressed patients can develop prolonged viral shedding, with a report of a kidney transplant recipient with 6 weeks of nasopharyngeal shedding and even infection recurrence with prolonged shedding after an LT.^{13,17} Establishing an efficient and reliable screening system for donor and recipient is of utmost importance to ensure that neither patient has active, viable virus. In challenging cases with positive PCR or equivocal results, infectious disease experts should be involved in the decision-making process.

RESOURCE STRAIN ON THE HEALTH CARE SYSTEM

Minimization of SARS-CoV-2 hospital transmission rates can be achieved with adequate personal protective equipment (PPE), adequate handwashing, and a health care system that can supply the necessary resources for complex post-LT care. Transplant patients have a greater expected need for high-volume transfusions and longer length of intensive care unit (ICU) stay.¹⁸ Actively infected LT recipients face the challenge of recovery from both LT and COVID-19, potentially increasing the need for additional health care resources. An overwhelmed hospital system at the peak of a pandemic may restrict services, such as imaging and endoscopy, and may not have sufficient ICU space, PPE, blood products, and intravenous medications to adequately care for such a patient.¹⁹

ETHICAL CONSIDERATIONS

The dilemma of whether to transplant an actively infected patient requires significant ethical considerations for fair allocation of perhaps the scarcest resource of all—the grafted liver. The principle of utility dictates that to achieve maximum transplant benefit, allocation must result in the greatest collective good for both the patient and society. The allocation must be beneficent by optimizing survival and health of patient and graft, and it must also be nonmaleficent by ensuring the transplant does not lead to increased mortality or significant surgical complications, as can occur with severe COVID-19. With the uncertainty regarding outcomes of LT in SARS-CoV-2-infected recipients and the potential for significant illness, graft and patient survival cannot be guaranteed. The principle of justice dictates that scarce health care resources could potentially be used in the care of other

patients, and the liver could be transplanted in a more suitable candidate with a higher probability of maximizing the benefit.²⁰

Although knowledge regarding the virus and impact on LT recipients is rapidly evolving, there is scant evidence to support the safe and successful transplantation of patients with active COVID-19. Despite increasing availability of PPE and medical supplies, the pandemic continues to significantly strain hospital systems throughout the country. The health and safety of hospital personnel must not be jeopardized through constant exposure to a highly infective LT recipient. The ethical principles of justice and utility should guide decision making regarding the just use of resources and the appropriate allocation of organs to those who would derive the maximum benefit. Thus, at this time we cannot recommend LT for patients infected with COVID-19.

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