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Authors

Mouch, Charles
Alexopoulos, Sophoclis
LaRue, Richard
et al.

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CASE REPORT

Successful liver transplantation in patients with active SARS-CoV-2 infection

Charles A. Mouch¹  | Sophoclis P. Alexopoulos¹  | Richard W. LaRue²  | Hannah P. Kim³ 

¹Division of Hepatobiliary Surgery and Liver Transplantation, Vanderbilt University Medical Center, Nashville, Tennessee, USA

²Division of Infectious Diseases, Vanderbilt University Medical Center, Nashville, Tennessee, USA

³Division of Gastroenterology, Hepatology, and Nutrition, Vanderbilt University Medical Center, Nashville, Tennessee, USA

Correspondence

Hannah P. Kim, Division of Gastroenterology, Hepatology, and Nutrition, Vanderbilt University Medical Center, Nashville, TN, USA.
Email: hannah.p.kim@umc.org

The Coronavirus Disease 2019 (COVID-19) pandemic has substantially impacted solid organ transplantation, including temporary inactivation of waitlist candidates with COVID-19 infection. We report two cases of liver transplantation (LT) in individuals with asymptomatic COVID-19 infection. The first patient is a 68-year-old female with decompensated cirrhosis complicated by worsening frailty and sarcopenia. The second patient is a 22-year-old female with acute liver failure likely secondary to drug/toxin exposure. Both patients were treated with COVID-19-directed therapies and neither patient developed symptomatic disease. These cases demonstrate that LT can be safely performed in select patients with asymptomatic COVID-19 infection at the time of transplant.

KEYWORDS

clinical research/practice, infection and infectious agents – viral: SARS-CoV-2/COVID-19, liver transplantation/hepatology, patient safety

1 | BACKGROUND

Since the Coronavirus Disease 19 (COVID-19) pandemic began, transplant centers have struggled to identify the appropriate timing of solid organ transplantation after severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection. Early studies demonstrated increased perioperative mortality and morbidity in patients with COVID-19 undergoing elective and emergent general surgery procedures.¹⁻⁴ These data led transplant centers to defer liver transplantation (LT) in patients with active COVID-19 infection. However, newer studies suggest that LT recipients with COVID-19 infection have a similar risk of mortality compared to the general population and that LT is not independently associated with death from COVID-19.^{5,6} Additionally, waitlist mortality among those with end-stage liver disease remains high, and it is unknown whether the risk of COVID-related mortality after transplant outweighs the risk of waitlist mortality. In this article, we present two patients with

asymptomatic COVID-19 infection who underwent LT at our transplant center.

2 | CASE 1

A 68-year-old female with decompensated hepatitis C cirrhosis and hepatocellular carcinoma (native MELD score 7) presented to the hospital for LT. She had hepatopulmonary syndrome and refractory hepatic hydrothorax associated with frailty and sarcopenia. She completed three doses of the Pfizer COVID-19 vaccine approximately 4 months prior to transplantation. On preoperative evaluation, she tested positive for SARS-CoV-2 by reverse transcriptase polymerase chain reaction (PCR) nasopharyngeal swab. She had no respiratory symptoms and a chest X-ray demonstrated chronic bilateral pleural effusions but no other abnormalities. Notably, she had a negative SARS-CoV-2 PCR test 1 week prior. Given her recent clinical decline,

Abbreviations: ALF, acute liver failure; AST, American Society of Transplantation; COVID-19, Coronavirus Disease 2019; LT, liver transplantation; PCR, polymerase chain reaction; POD, postoperative day; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2.

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the decision was made to proceed with LT as the potential risks of postoperative COVID-19 infection were felt to be less than the risks of progressive deterioration on the LT waitlist.

She underwent uncomplicated LT and was extubated on postoperative day (POD) 1. Transplant Infectious Disease had been consulted prior to LT and the patient was treated postoperatively with remdesivir 100mg IV daily for 3 days. She received IV solumedrol intraoperatively and was started on tacrolimus, mycophenolate mofetil 500mg BID, and prednisone. She was discharged home on POD 7 without any symptoms of COVID-19. Her posttransplant course was complicated by biliary anastomotic stricture requiring stent placement on POD 33.

3 | CASE 2

A previously healthy 22-year-old female presented to an outside hospital with a 1-day history of abdominal pain and a 1-week history of severe sore throat. SARS-CoV-2 PCR was negative at that time. She received one dose of the Pfizer COVID-19 vaccine approximately 5 months prior to presentation. She was found to have elevated liver enzymes and INR on laboratory analysis. Acetaminophen levels, viral hepatitis serologies, autoimmune markers, ceruloplasmin, and abdominal doppler ultrasound were negative or normal. She progressed rapidly to acute liver failure (ALF) with INR 8.5, grade 3 encephalopathy, and acute kidney injury. An expedited LT evaluation was performed. Repeat SARS-CoV-2 PCR nasopharyngeal swab returned positive. She was not requiring supplemental oxygen and her chest X-ray appeared normal. Her imminent risk of death from ALF was felt to outweigh the risk of postoperative COVID-19-related mortality so she was listed as status 1A on the LT waitlist.

She underwent uncomplicated LT. Explant pathology suggested drug/toxin mediated liver injury. Transplant infectious disease had been consulted prior to LT and she received sotrovimab on POD 1. She was extubated on POD 2 after her mental status improved. Postoperative immunosuppression included tacrolimus, mycophenolate mofetil 500mg BID, and prednisone. Her course was complicated by acute renal failure requiring dialysis and mild acute cellular rejection that was treated with IV steroids. She never had any COVID-19 symptoms and repeat SARS-CoV-2 PCR test on day of discharge (POD 20) returned negative.

4 | DISCUSSION

There is no consensus regarding the optimal timing of LT in patients with COVID-19 infection. The American Society of Transplantation (AST) recommends that recipients be asymptomatic and test negative for COVID-19 prior to transplantation.⁷ However, the AST also emphasizes that the decision to proceed with transplantation in a COVID-19-positive recipient must weigh the likelihood of postoperative COVID-19 illness compared to the risk of waitlist mortality. Therefore, providers must weigh the risks of perioperative morbidity with the need for life-saving transplantation in patients with COVID-19 infection.

We report two cases of LT in patients with newly diagnosed asymptomatic COVID-19 who were transplanted during the Omicron era. In the first case, LT was pursued due to the patient's rapidly worsening functional status and uncertain future LT candidacy. In the second case, the patient presented with ALF and emergent LT was the only life-saving option. In both cases, the benefits of proceeding with LT were felt to outweigh the risks of progression to severe COVID-19 infection, and efforts were made to mitigate such risk by administration of COVID-19-directed therapies (remdesivir and sotrovimab, respectively). Both recipients received COVID-19 vaccinations prior to transplant. Immunosuppression was also modified with both patients receiving half of the usual mycophenolate mofetil dose typically used at our center.

Our case reports are the first to report LT in patients with active COVID-19 infection. The only other published case of LT in a SARS-CoV-2 PCR-positive recipient was a patient who had been exposed to COVID-19 and developed mild cough approximately 6–10 weeks prior to transplant.⁸ Their positive preoperative test was believed to represent residual virus rather than active disease. In other published cases, patients with recent COVID-19 infections were only reactivated on the LT waitlist after a documented negative SARS-CoV-2 PCR test.^{9–12} In these cases, outcomes were good with no evidence of adverse consequences from COVID-19.

Many transplant centers delay LT in patients with a recent COVID-19 diagnosis due to perceived risk of severe COVID-19 infection and death in the setting of posttransplant immunosuppression. However, a recent literature review concluded that age and comorbidities are more significant risk factors for COVID-19 severity than immunosuppression status.¹³ Another matched cohort study found that solid organ transplant recipients with COVID-19 had similar mortality rates as non-transplant patients,¹⁴ while a prospective Italian study found that LT was not associated with increased risk of hospitalization or death due to COVID-19.¹⁵ Data on the importance of immunization status are not available but we believe that recipients should be vaccinated prior to undergoing transplantation. The decision to proceed with LT in a COVID-19-positive recipient should, therefore, be made cautiously while weighing age, severity of COVID-19 illness, and additional comorbidities rather than immunosuppression status.

In conclusion, we present two patients with newly diagnosed COVID-19 who underwent LT without developing postoperative COVID-19 symptoms. These cases illustrate the importance of considering individual patient factors and risk of waitlist mortality when deciding whether to pursue LT in this high-risk population.

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DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Charles A. Mouch  <https://orcid.org/0000-0002-8705-4946>

Sophoclis P. Alexopoulos  <https://orcid.org/0000-0001-8785-7469>

Richard W. LaRue  <https://orcid.org/0000-0002-8554-7384>

Hannah P. Kim  <https://orcid.org/0000-0001-5518-452X>

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