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Dealing With Liver Transplantation during Coronavirus Disease 2019 Pandemic: Normothermic Machine Perfusion Enables for Donor, Organ, and Recipient Assessment: A Case Report

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ABSTRACT

The coronavirus disease 2019 (COVID-19) pandemic has changed life on a global scale. The numbers of transplantations have plummeted as a result of fear of disease transmission, recipient coronavirus disease 2019 infection, priority shift, and resource limitations. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) complicates transplantation because donor testing, (re)allocation of limited resources, and recipient testing may exceed permissible ischemia times.

Normothermic machine perfusion (NMP) helps safely prolong liver preservation up to 38 hours. Additional time is essential under the current circumstances. Here we present the case of a 29-year-old liver transplant recipient in whom prolonged liver preservation required for SARS-CoV-2 screening was accomplished through NMP. Donor and recipient test results for SARS-CoV-2 were negative, and intensive care unit capacity was eventually available. The surgical procedure and postoperative course were uneventful.

NMP can extend preservation times in liver transplantation while awaiting SARS-CoV-2 test results and available intensive care unit capacity.

In December 2019, a novel type of coronavirus causing aggressive pneumonia emerged for the first time in Wuhan City in the province of Hubei, China. Since then, the highly contagious and pathogenic virus has been spreading worldwide [1]. Clinical presentation varies from asymptomatic and mild symptoms to acute respiratory distress syndrome and death [2].

The immunosuppressive state of solid organ transplant recipients (SOTRs) increases their susceptibility to infections. Respiratory viral infections are especially associated with higher morbidity and mortality in SOTRs compared to the general population [3]. Hence, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) screening prior to transplantation is recommended [4].

Several factors are complicating solid organ transplantation in face of the COVID-19 pandemic. 1. Performing a real-time polymerase chain reaction (PCR) from nasopharyngeal swabs in both donor and recipient is obligatory. Some centers perform computer tomography scans of the lung and/or repeat PCR testing. Although this is helpful in increasing safety, getting the PCR test results from nasopharyngeal swabs can take hours. 2. Organ procurement cannot always be delayed until SARS-CoV-2 test results are available. In hemodynamically less stable patients, the organ procurement has to be performed when demanded by the clinical course. 3. Limited operating room (OR) and intensive care unit capacity, staff shortage, and travel restrictions may further prolong the waiting time until the surgical procedure can start. Safe prolongation of organ preservation is key to avoiding discarding organs and the aggravation of organ damage through prolonged cold storage [5]. In this context, we created a pathway for liver transplantation during the COVID-19 pandemic (Fig 1).

Here we present the case of a liver transplant recipient in whom prolonged liver preservation required for SARS-CoV-2 screening was accomplished through normothermic machine perfusion (NMP), which we have recently established as a routine in liver transplantation [6].

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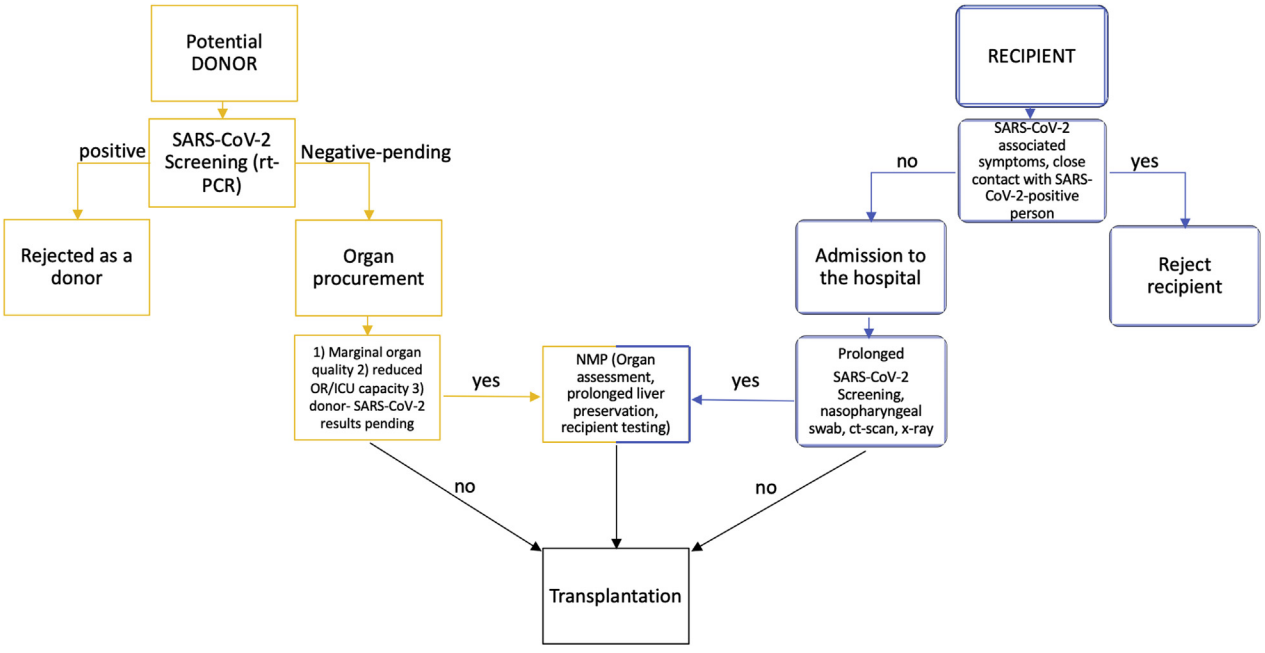

Fig 1. Flow chart describing the decisional pathway for donor and recipient screening of SARS-CoV-2 and the algorithm of using NMP. NMP, normothermic machine perfusion; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

CASE REPORT

Donor

The donor was a 66-year-old brain-dead woman with bacterial meningitis caused by *Streptococcus pyogenes* as the underlying cause of death. Donor demographics are shown in Table 1. The donor risk index was 2.04, and the donor met expanded criteria donor requirements [7]. As per recommendations and local policy, the donor was screened for SARS-CoV-2, and test results were awaited prior to organ procurement.

Recipient

The liver was allocated to a 29-year-old woman with end-stage liver disease due to primary biliary cholangitis and overlapping autoimmune hepatitis with a Model for End-stage Liver Disease score of 20.

Table 1. Demographics of the Donor, Recipient, and Preservation Time

Variable	Donor	Recipient
Sex (f/m)	f	f
Age (years)	66	29
Height (cm)	168	159
Weight (kg)	68	48
BMI	24	19
DRI	2.04	
Donor type	DBD	
Overall preservation time	16 h 11m	
CIT	5 h 35 m	
WIT	42 m	
NMP time	10 h 36 m	

Abbreviations: BMI, body mass index; CIT, cold ischemia time; DBD, donation after brain death; DRI, donor risk index; f, female; m, male; NMP, normothermic machine perfusion; WIT, warm ischemia time.

Following the hospital safety measures, a telephone questionnaire was performed to exclude exposure or symptoms of infection and SARS-CoV-2 screening prior to admission at the transplant unit was performed. A nasopharyngeal swap was analyzed for SARS-CoV-2 by real-time polymerase chain reaction, and a thoracic x-ray and lab work were performed. The recipient remained under preemptive isolation while awaiting the results.

NMP

After procurement of the organ, the liver was stored and transported according to cold storage routines. Total cold preservation time was 5 hours and 36 minutes upon arrival at the recipient center. On the basis of prolonged waiting time for SARS-CoV-2 test results of the recipient, the expanded criteria donor status of the donor liver requiring extensive liver quality and functional

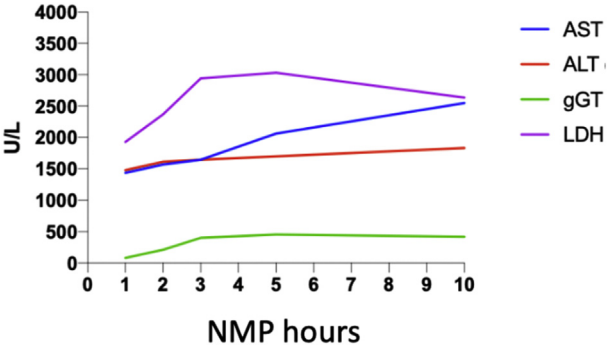

Fig 2. AST, ALT, gGT, and LDH levels in the perfusate during NMP. ALT, alanine transaminase; AST, aspartate aminotransferase; gGT, gamma-glutamyl transferase; LDH, lactate dehydrogenase; NMP, normothermic machine perfusion.

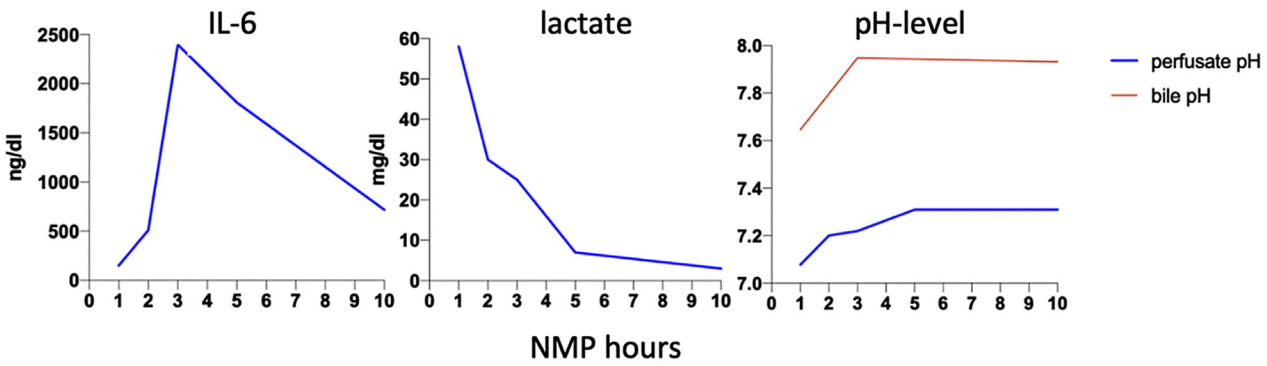

Fig 3. IL-6, lactate, pH levels, and pH of the bile in the perfusate during NMP. IL-6, interleukin 6; NMP, normothermic machine perfusion.

assessment, and the limited OR capacity, we opted to place the donor liver on a NMP device.

Total NMP time was 10 hours and 36 minutes, and total preservation time reached 16 hours and 11 minutes (Table 1).

Perfusate was collected as per protocol at 5 time points during NMP. Median aspartate aminotransferase was 1644 U/L (1434-2547), median alanine transaminase 1645 U/L (1479-1837), and median lactate dehydrogenase 2634 U/L (1929-2634) (Fig 2). Lactate was dropping rapidly, and physiological pH-levels were maintained without buffering (Fig 3). The interleukin 6 levels were decreasing after a peak at the initiation of NMP. Total bile production was 200 mL with a mean bile pH of 7.95 (7.64-7.93) (Fig 2). Overall, liver performance during NMP was good. Eventually, the SARS-CoV-2 test turned out to be negative, and OR and intensive care unit capacities were available to proceed with liver transplantation.

After transplantation, patients were shielded against infections through visitor restrictions, mandatory facial mask and glove protection by health care workers, and distancing. The patient had good initial liver function, and no infectious or immunological complications were recorded. She was discharged 16 days after liver transplantation with good function (bilirubin 0.9 mg/dL, aspartate aminotransferase 20 U/L, alanine transaminase 14 U/L, international normalized ratio 1.2).

DISCUSSION

This is a profoundly unspectacular case report. None of the elements in the treatment are essentially new, and the clinical course of the patient was very smooth. Yet the constellation of the circumstances and the effect of NMP in the context of time for donor (organ) assessment, logistics, and recipient preparation (testing) illustrates the relevance of time in liver transplantation and delivers an example of how liver transplantation might be organized and coordinated routinely in the future.

Disease course and prognosis of SARS-CoV-2 in SOTRs remain poorly defined. In the small number of case reports describing the course of transplant recipients infected with SARS-CoV-2, benign courses but also fatal outcomes have been reported [8,9]. Further, disease transmission poses a threat of unknown severity. The risk of false negatives of nasopharyngeal or oropharyngeal swab results [10], especially at an early or asymptomatic stage of coronavirus disease 2019 [2], emphasizes the importance of careful assessment of history, clinical examination, laboratory work, chest x-ray, and computed tomography scan prior to transplantation.

NMP of the donor liver is a novel preservation method in liver transplantation. It enables the shortening or elimination of cold storage, but also the perfusion and assessment of the organ ex vivo [6]. This is a fundamental advancement for the field because organ quality can be assessed more precisely prior to transplantation. Furthermore, the factor of time for logistics and recipient testing becomes ultimately apparent in the conditions and circumstances arising with the COVID-19 pandemic. Assessing the organ quality while awaiting COVID-19 test results illustrates the multifactorial benefit of this technology and its relevance and potential for any kind of situation where more testing is required before an organ can be safely transplanted.

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