Hepatitis C-infected hearts and lungs safely transplanted

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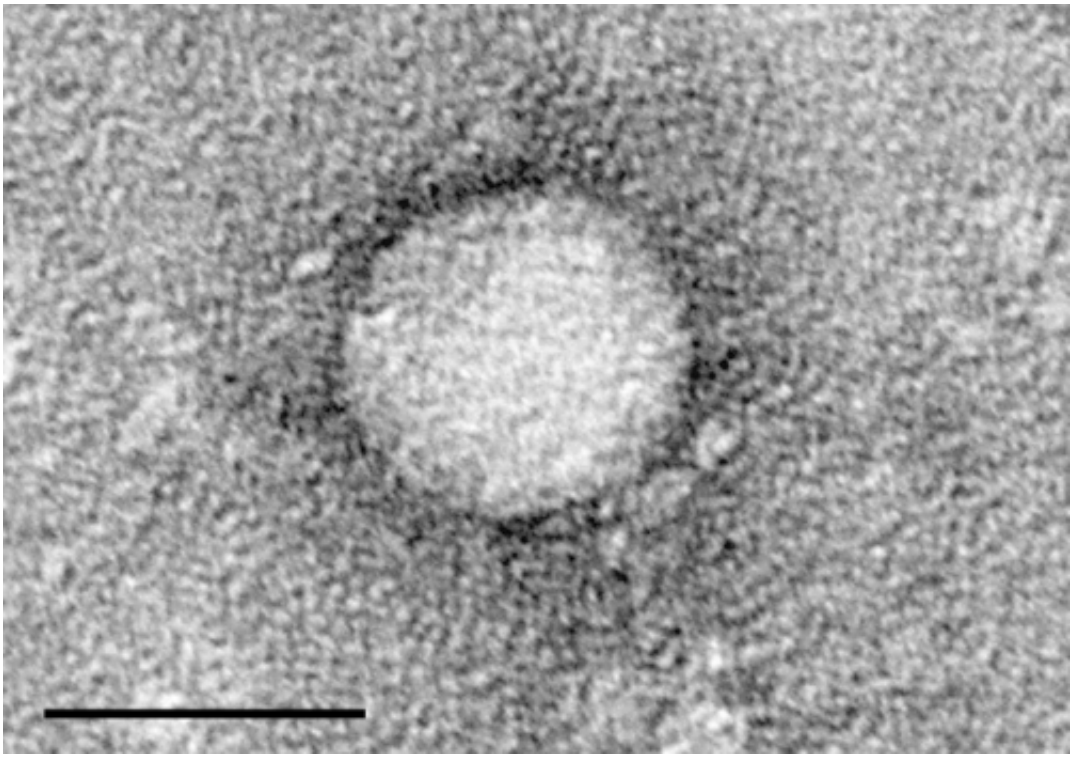

Electron micrographs of hepatitis C virus purified from cell culture. Scale bar is 50 nanometers. Credit: Center for the Study of Hepatitis C, The Rockefeller University.

Infectious diseases experts and transplant physicians and surgeons at Brigham and Women's Hospital have blocked the transmission of hepatitis C from infected organ donors to recipients in need of hearts or lungs. The DONATE HCV Trial Team reports that hepatitis C-infected

thoracic organs can be safely transplanted, detecting no signs of the disease and good outcomes for the transplanted organs in all patients treated with a preemptive, short course of antivirals. In a paper published in the *New England Journal of Medicine*, the team describes a four-week antiviral treatment regimen started within hours of organ transplantation surgery, preventing establishment of hepatitis C virus (HCV) infection in all patients, and, in so doing, expanding the pool of eligible heart and lung donor organs.

"There was a 100 percent success rate in terms of HCV treatment and six-month graft survival," said corresponding author Ann Woolley, MD, MPH, of the Division of Infectious Diseases at the Brigham. "Direct acting antivirals have revolutionized the field of hepatitis C treatment and have also created an opportunity to transplant organs from hepatitis C positive donors. While transplants from hepatitis C positive donors have previously been done, the best approach to doing this—when to initiate treatment and how long to treat patients after transplant—as well as the outcomes for heart and lung transplant recipients have not previously been systematically studied. This is the largest clinical trial to date for HCV thoracic organ transplantation and provides clear evidence that this shortened regimen, initiated within hours of transplant, can prevent the establishment of hepatitis C in the recipients and lead to excellent outcomes for patients."

In their paper, the researchers present data on the 35 patients who had enrolled in the study by February 2018. Each of those 35 patients met the trial's primary endpoints—all had undetectable hepatitis C viral loads and functioning transplanted organs six months or more after transplant surgery. Given the study's successful outcomes, enrollment continues and the team has now enrolled a total of 69 participants to date.

The team found that nearly all of the patients who received organs from HCV viral load positive donors had evidence of HCV virus immediately

post-transplantation. However, very early preemptive treatment prevented HCV from establishing infection, despite the fact that patients were taking high-dose, induction immunosuppressive medications as part of the transplant process. All recipients cleared the virus by about two weeks and hepatitis C viral loads remained undetectable thereafter.

"It was critically important to us to determine that this treatment not only prevented transmission of hepatitis C but also didn't worsen outcomes for our transplant patients," said co-author Steve Singh, MD, former surgical director of the Heart Transplantation and Mechanical Circulatory Support in the Department of Cardiac Surgery. "Our short-term findings to date suggest that graft survival is just as excellent in patients who were transplanted with thoracic organs from hepatitis C positive donors as it was in those who received thoracic organs from non-hepatitis C positive donors during the same period."

Although the number of organ transplants in the U.S. has increased over the last five years, it is estimated that about 1,000 patients die every year waiting for a lung or heart transplant. Drug intoxication deaths have led to a rise in available organs for transplantation, but donor hepatitis C viral infection has been a leading reason that otherwise medically suitable organs are deemed ineligible for transplantation.

Direct-acting antivirals, such as sofosbuvir/velpatasvir, are used to treat patients infected with hepatitis C. Standard treatment for people who are chronically infected with hepatitis C is typically 8-to-12 weeks, depending on the treatment regimen used. Other studies have found that it is feasible to treat kidney and liver transplant patients with these drugs early after transplantation, and such treatments are beginning to be used to treat heart and lung transplant recipients. Woolley and colleagues set out to treat a much larger cohort of patients with a shortened course of therapy and collected data on outcomes over a longer period of time.

The authors noted the importance of a shorter duration of antiviral treatment leading to successful outcomes for patients.

"HCV infection has been a long-standing reason to decline donation of suitable organs," said co-author Lindsey Baden, MD, director of Clinical Research in the Division of Infectious Diseases at the Brigham. "What the data show is that transmission does occur, but a short, four-week course of antiviral therapy led to rapid HCV clearance. These data demonstrate how preemptive therapy can stop transmission thus decreasing medication burden, drug interactions, and cost."

The team also analyzed safety outcomes, finding that there were no hepatitis C-attributable adverse events. The researchers reported a numerical increase in acute cellular rejection among lung transplant patients, but this trend was not statistically significant.

"This study provided a unique opportunity to explore the utilization of thoracic organs from hepatitis C positive donors for transplantation, which to date have been underutilized despite being relatively common in the current donor population," said co-author Hilary Goldberg, MD, MPH, the medical director of the Lung Transplant Program and the former lead for the Solid Organ Transplant Quality Assurance and Process Improvement Program at the Brigham. "I am very encouraged by the results so far, and the potential that this study may allow us to provide transplantation successfully to the many recipients who might otherwise never have access to it."

Provided by Brigham and Women's Hospital