Commentary: Fish or cut bait: The importance of defining the safety and efficacy of thoracic transplantation using donors with hepatitis C

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The demand for thoracic organ transplantation has continued to increase and despite better use and distribution of organs, mortality while waiting for an organ is high. In 2017, 7% to 8% of heart and lung transplant candidates died on the waitlist.1,2 Although thoracic transplant centers have gained more experience in donor management and are actively expanding the standard donor criteria established in 2003,3 we continue to search for options to increase organ availability. Recently, access to direct-acting antiviral (DAA) therapies coupled with an increasing number of potential donors infected with hepatitis C virus (HCV) has led the transplant community to consider the use of organs from HCV-positive donors for recipients without HCV infection.

Since 2002, there has been a significant increase in acute HCV infection, closely tied to the opioid epidemic in the United States and primarily affecting persons younger than the age of 30 years.4 The global prevalence of hepatitis C has been estimated as antibody sero-positivity in 110 million people and HCV viremia in 80 million people.5 Deaths related to intravenous drug use or opioid overdose now account for 20% to 30% of potential donors and for 65% of donors in the United States who test positive for HCV by nucleic acid amplification testing.6 It is reasonable to consider that donors with HCV may become a significant source of organs suitable for transplant if hepatitis C can be effectively treated.

In this issue of the Journal, Van Raemdonck and colleagues7 present an invited expert opinion detailing some of the most recent experiences using organs from HCV-infected donors in patients awaiting thoracic transplantation and share some of the potential challenges of this strategy. As presented by the authors, the results seen in heart and lung transplantation demonstrate no difference in the early survival of patients who received organs from HCV-positive donors as compared with patients who received organs from HCV-negative donors, with a rate of seroconversion between 67% and 95%. The potential challenges of using HCV-positive donors include possible interactions of DAAs with other drugs administered early after transplant, an unknown impact of preemptive versus delayed treatment, and the efficiency of short-duration versus full-course DAA therapy. As Van Raemdonck and colleagues note, there are potentially negative effects of immune activation from de novo viral infection that may lead to unintended consequences such as organ rejection, other infections, and metabolic complications. These were previously encountered in lung and heart transplant recipients who received organs from human immunodeficiency virus–positive donors.

Although preliminary results are encouraging, several issues merit further exploration and research. We have a limited understanding of the virologic factors that may play a role in the successful thoracic transplantation of organs from HCV-positive donors to HCV-negative recipients. Preliminary data suggest that late relapses of HCV may occur after lung transplantation.8 Although these reactivations may be easily controlled, it will be important to evaluate the impact on allograft and patient outcomes.
The incidence of primary graft dysfunction, acute and chronic rejection, and transplant vasculopathy must be determined. The immunology of donor-derived HCV may be an important predictor of short- and long-term outcomes. In addition, other manifestations of immune activation, specifically the risk of coinfections with other infectious pathogens, may lead to comorbidities. As the use of HCV-infected donors expands, consideration may be given to including donors with coinfection of other hepatitis viruses, such as hepatitis B virus, and safety must be examined. Patient education and counseling is recommended to promote medication adherence, recognition of adverse events, and prevention of HCV transmission.

Another important issue, which is not addressed in this article, is the financial implications of using HCV-positive donors. The enthusiasm for DAA therapies has often been tampered by challenges to drug access, largely due to cost barriers to payer approval, which delay therapy initiation. Despite these challenges, recent evidence suggests that the use of HCV-positive organs can reduce waitlist time, improve waitlist survival, and potentially could lead to a significant reduction in health care costs. Finally, it is important to emphasize to urgency of deriving a universal consensus on the management, education, and follow-up of patients awaiting thoracic organ transplant who may receive an organ from an HCV-positive donor.

References