See Article page 1873.

Commentary: Heart transplantation using hepatitis C–positive donors: What are we waiting for?

Michael Ibrahim, MD, PhD,^a and Arman Kilic, MD^b

Since the THINKER (Transplanting Hepatitis C Kidneys into Negative Kidney Recipients) trial established that solid-organ transplantation from hepatitis C nucleic acid amplification test (NAT)+ kidney donors into hepatitis C–negative patients was possible without infecting recipients, an entirely new pool of organ donors became available.¹ This era was ushered in by the advent of direct-acting antiviral agents that cure the vast majority of patients infected with hepatitis C. Over the last 5 decades, hepatitis C infection rates have dramatically fallen in the population but are now rising again due to the opioid epidemic. Hepatitis C infection is therefore disproportionately common in organ donors, who include a disproportionate number of overdose victims. Lack of available organs remains the most pressing limiting factor in transplantation, and expanding the donor pool is one of the most practical ways of addressing this problem.

Li and colleagues² present an analysis of hepatitis C NAT+ heart transplants in the United Network for Organ Sharing database between 2015 and 2019, with a median follow-up of 580 days. They show that there is no difference in absolute or propensity-matched survival between the hepatitis C NAT+ and non-hepatitis C cohorts. We previously showed, in a similar cohort of both matched and non-matched patients, that survival was also equivalent³; we also demonstrated that rates of rejection, stroke, and dialysis-dependence were equivalent. This present study

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CENTRAL MESSAGE

Heart transplants using hepatitis C–positive donors should be expanded to more centers and patients, although continued evaluation of acute rejection and coronary allograft vasculopathy is needed.

adds some granularity in showing the pattern of hepatitis C NAT+ donor use nationally and over time. Strikingly, more than 75% of these transplants occurred in the Northeast or Eastern regions, and more than 50% were performed in just 5 transplant centers. Only 11.7% of hepatitis C–negative recipients seroconverted following heart transplantation with a hepatitis C NAT+ donor heart. The long-term implications of this seroconversion are unknown. Although the rate of coronary allograft vasculopathy was slightly greater in the seroconverted group, the rates of hospitalization and graft function were equivalent. Unfortunately, we do not have data on the direct-acting antiviral therapy protocols used for these patients. Of note, in the original THINKER trial, all patients were cured of hepatitis using a direct acting antiviral therapy regimen lasting 12 to 16 weeks. Standardization of an optimized drug regimen would be of great benefit in extending the use of hepatitis C NAT+ donors. Furthermore, acute cellular rejection appears to occur more frequently following hepatitis C NAT+ organ transplantation, although again details are lacking as to grade, extent, and reversibility of these changes. Similar limitations apply to the finding of coronary allograft vasculopathy. These details will require data from large single-center and multicenter studies.

This important contribution highlights the safety of hepatitis C NAT+ heart transplantation and further defines some

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areas for future study. Standardization of direct-acting antiviral therapy, understanding the implications and mechanisms of more frequent coronary allograft vasculopathy, and acute cellular rejection are some of the elements that need to be addressed as hepatitis C NAT+ donation becomes standard practice. In the meantime, these data should reassure nascent centers that this practice is safe and indeed effective at expanding the donor pool, which is our urgent duty.

See Article page 1873.

Commentary: Expanding the donor pool: One virus at a time

Vivek Rao, MD, PhD

Cardiac transplantation remains the gold standard for the treatment of end-stage heart disease. According to the most recent International Society of Heart Transplant (ISHLT) Registry data, there has been no appreciable increase in heart transplantation activity over the past 24 years.¹ However, there have been significant changes in donor characteristics during this period, including an average age of 35 compared with 31 years and changes in the donors' causes of death. Although head trauma remains the most common cause of death in heart donors, there has been a staggering increase in death due to anoxic brain injury (from 4% to 26%), reflective of our current opioid crisis.

In an attempt to increase the donor organ pool, other solid organ transplantation groups have used living related donation (obviously not relevant to cardiac transplantation) and donation after circulatory determination of death.² Although these activities have substantially increased transplantation activity in liver, kidney and lung programs, there has been minimal adoption in heart transplantation. Another

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The hepatitis C virus.

CENTRAL MESSAGE

The limited number of donor organs continues to restrict the capacity of all transplantation programs. Based on the excellent results in other organ groups, donors with current or historical hepatitis C viral exposure can be considered for heart transplantation.

area of interest has been the use of organs previously discarded due to viral exposure. Before the introduction of potent direct antiviral therapies, donors with a previous exposure to hepatitis B virus (HBV) or hepatitis C virus (HCV) (as confirmed by nucleic acid testing) were excluded owing to proven viral transmission, early transaminitis, and inferior post-transplantation survival. However, more recently, other organ groups have reported acceptable survival with low seroconversion rates with appropriate post-transplantation antiviral therapy.³ In the ISHLT registry report, HBV⁺ or HCV⁺ donors were rare (approximately 1%-3%).¹