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

In this issue of the *Journal*, Li and colleagues⁴ from Massachusetts General Hospital queried the United Network for Organ Sharing registry to examine trends in the use of HCV⁺ cardiac donors. The authors report that a single cardiac transplant using an HCV⁺ donor was performed in 2015 rising to 137 in 2018. The trend appears to continue in 2019 with 127 HCV⁺ donors as of September. This increase was in the setting of stable numbers of HCV⁻ donors. In fact, the growth in cardiac transplants in 2018 and 2019 is almost entirely attributed to the use of HCV⁺ donors.

Thirty day mortality was remarkably low in both groups (2.5% for HCV⁺ vs 3.7% for HCV⁻ after propensity matching; $P = .3$). Post-transplantation serologic data were available for 236 of 336 transplant recipients who received a heart from an HCV⁺ donor. At a median follow-up of just over 6 months, 41 patients (13%) had positive HCV serology, of whom 38 had been negative before transplantation.

These data are encouraging and support the increased use of HCV⁺ donor hearts. However, the effect of HCV⁺ donors on long-term survival, HCV-free survival, and potentially cardiac allograft vasculopathy-free survival remains to be determined.

Despite these encouraging results, several concerns were identified in this study. First, the regional adoption of HCV⁺ donors was highly variable. More than 75% of HCV⁺ hearts were transplanted in the Northeast or East Coast (regions 1, 2, 9, 10, and 11). In fact, 27% of these transplants were performed in region 11, more than double the activity of the next highest region. In contrast, region 7 accounted for only 3 of these 336 transplants, with the first HCV⁺ donor used in April 2019. This maldistribution did not mirror overall transplantation activity in these regions and thus does not reflect differential demand, but rather demonstrates different thresholds for the use of HCV⁺ hearts. At an institutional level, only 39 of the 129 centers (30%)

represented in this study used HCV⁺ donors. A single institution performed >20% of HCV⁺ transplants. This institutional and regional discrepancy led to differences in transport distances and ischemic times (mean distance, 299 miles vs 173 miles [$P < .001$]; mean ischemic time, 3.5 hours vs 3.1 hours [$P < .001$]).

Of interest, and counterintuitively, HCV⁺ hearts were less likely to be used in high-status recipients. In 2019, only 35% of HCV⁺ hearts were used in status 1-2 recipients. Of all 1009 high-status transplantations in 2019, only 44 (4%) used an HCV⁺ heart. In 2015-16, 0.3% of the 2934 high-status transplantations used HCV⁺ donors, suggesting minimal adoption of this potential source of organs for urgent transplants.

In summary, the report by Li and colleagues should provide added assurance that the use of HCV⁺ donors can lead to acceptable short-term outcomes. There is now little justification for declining an otherwise suitable HCV⁺ heart, particularly for a high-status recipient. Further evaluation of the 1- and 5-year post-transplantation outcomes will likely lead to additional supporting data justifying this important expansion of the potential donor pool.

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