

Organs from Hepatitis C Virus–Positive Donors

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Organs that are suitable for donation to the more than 113,000 persons who are waiting for transplants in the United States are in short supply; in 2018, only 36,500 persons received transplants.¹ Many potential recipients die before transplantation, and in 2018, a total of 12,225 persons were removed from the waiting list because of death or progressive illness that rendered them too sick to undergo transplantation. Given these dismal outcomes, substantial efforts have been made to find new approaches to expand the pool of donor organs that were previously considered to be unacceptable. This expansion includes the use of organs obtained from donors with hepatitis C virus (HCV) infection in candidates for transplantation who do not have HCV infection — so-called HCV-mismatched transplantation.

There are several reasons why transplantation programs are more willing to consider HCV-positive donors than they were previously. The potential pool of HCV-positive donors is substantial, in large part because of the current opioid epidemic in the United States.² These donors are typically younger than donors without HCV infection, and they have fewer coexisting conditions that are associated with decreased recipient and organ survival. Moreover, a sustained viral response and cure are now achievable with the increased availability of direct-acting antiviral agents, which have expanded efficacy against diverse HCV genotypes, favorable safety profiles, limited drug interactions, and pharmacokinetic properties that allow for administration of these agents irrespective of the patient's renal function. The published results of research involving limited numbers of HCV-mismatched transplantations have been favorable and have encouraged acceptance of a broad pool of donors.³⁻⁷ Consensus guidelines of the American Society of Transplantation have provided support for further research in this area.²

As now reported in the *Journal*, Woolley and colleagues⁸ have expanded on this experience with a large series of HCV-mismatched heart and lung transplantations. The investigators ad-

ministered a short (4-week) course of a pangenotypic antiviral regimen to preemptively treat recipients of organs from HCV-infected donors. Some recipients had enteric feeding tubes for expedited drug delivery in the early period after transplantation. Early results are promising, with a 100% sustained viral response and generally excellent patient and allograft outcomes.

This trial has some unique features that must be considered. The median donor age was surprisingly young, and HCV-positive donors were younger than those without HCV infection. Both HCV-negative and HCV-positive donors in this trial were younger than the mean age in the current donor pool in the United States. As anticipated, the availability of HCV-positive organs resulted in transplantation in candidates who were less critically ill and who had a lower priority on the waiting list for transplantation. Consequently, the shorter lengths of stay in the intensive care unit and hospital and the relative preservation of renal function probably reflect recipient factors rather than donor factors. Whether longer-term results will be equally encouraging is unknown. Nevertheless, this article clearly provides support for further consideration of the use of organs from HCV-positive donors, even for candidates for heart and lung transplantation.

Are the results of this trial sufficient to encourage more widespread use of HCV-mismatched transplantation? The early results are very encouraging, but there is still a lot to learn. Data regarding long-term outcomes are limited; one of the longest follow-up periods reported is 1 year for 20 recipients.⁴ It is unknown whether an increase in the incidence of cardiovascular disease, which was previously reported in recipients of organs from HCV-positive donors, will be a late complication.⁹ In addition, what is known about the sustained viral response may need to be reconsidered in light of a recent anecdotal report of a recipient of a mismatched lung transplant who had a severe relapse after treatment for transplant-related HCV infection.¹⁰ The effect of relapse may be minimized by the use of a longer

course of effective treatment at the time of relapse. Immune activation related to de novo viral infection may lead to other unintended consequences, including organ rejection, other infections, and metabolic complications, especially if organ donation is expanded to critically ill candidates. Finally, patient consent assumes a level of understanding about HCV infection that may not currently exist.

Successful outcomes in HCV-mismatched transplantation, with cure of HCV infection, have been predicated on rapid access to effective antiviral therapy. Woolley et al. guaranteed early treatment for their patients regardless of insurance coverage, and most investigators have provided free direct-acting antiviral agents in the early period after transplantation. These drugs are expensive, and it is uncertain who will bear that cost in nonresearch settings. It is unknown whether cheaper short-course therapy, as used in the current trial, will be consistently effective in all recipients regardless of the organ transplanted and the timing of initiation of treatment. However, if the experience of Woolley et al. is borne out by other investigators, a short course of treatment would substantially reduce the cost of transplantation. To ensure prompt and equitable access to these potentially lifesaving organs, it is imperative that transplantation centers determine how antiviral agents will be provided in advance of acceptance of organs from HCV-positive donors.

Approximately 2.4 million persons in the United States have HCV infection, with the highest incidence among injection-drug users, and organs obtained from these persons account for nearly a third of donor organs in many areas of the country. The time has come to consider expanding the use of HCV-mismatched transplantation under controlled conditions. Increasing numbers of successful outcomes in single-center studies provide support for further research with

larger-scale multicenter trials. These are exciting times for the field of transplantation, since the ability to use organs from HCV-positive donors may substantially increase the donor pool and thus increase access to organs for patients who might otherwise have died while waiting.

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