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Expanding the Use of Organs from Hepatitis C-Viremic Donors: The Evidence Continues to Build

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Together, the long waiting times for solid organ transplants, high rates of discard of organs from deceased donors with hepatitis C virus (HCV), and advent of direct-acting antiviral (DAA) agents have created a dialogue about the use of organs from HCV-positive donors for HCV-negative recipients.¹ In this issue, Trotter et al. examined this topic in 3 parts: first, how many potential donors in the United Kingdom (UK) are ruled out due to HCV-positive or injection drug use status? Second, what were the trends in utilization versus discard of recovered HCV-positive deceased donor organs in the UK? And third, what is the cost-effectiveness of transplanting kidneys from HCV-positive deceased donors into HCV-negative recipients?²

To quantify the potential increase in transplants if HCV-positive donors were not ruled out due to HCV status, Trotter et al studied the UK Potential Donor Audit, a registry of all individuals under age 80 years who die in critical care units in the UK.² They found that 120 individuals in the Potential Donor Audit between 2009 and 2016 were not considered as potential donors solely due to injection drug use or HCV-positive status. A limitation in this step was the lack of laboratory testing to identify HCV antibody versus RNA status of potential donors. Trotter et al then examined 244 HCV-positive deceased donors in the UK Transplant Registry between 2000 and 2015, of whom only 31% proceeded to donation. The quality of declined organs did not differ from the quality of transplanted organs, and the reason given for declining was positive HCV status in 69% of offers. Patient and graft survival was no different for recipients of kidneys and livers from HCV-positive donors compared to HCV-negative donors. Finally, to examine cost-effectiveness of treating transmitted HCV in recipients of kidneys from HCV-positive donors, cost of sofosbuvir and ledipasvir along with costs of renal transplantation were compared to the cost of hemodialysis. Transplantation with use of DAAs was cost-neutral with continued

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DISCLOSURE

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hemodialysis after 5 years. Importantly, this cost analysis examined 1 approved DAA regimen (sofosbuvir and ledipasvir for 12 weeks) in the UK; however other approved DAA regimens and pricing in other countries may lead to a faster “break even” point.² Furthermore, Trotter et al did not consider the mortality between hemodialysis and transplantation, and thus certainly underestimated the benefit in increased years of life following transplantation.

In the United States (US), these questions must be considered in the context of recent consensus guidelines from the American Society of Transplantation (AST), which include projections of availability of HCV-positive donors.¹ These donors are anticipated to be from 2 broad groups: baby boomers with chronic HCV and younger people who inject drugs.¹ In the setting of the opioid epidemic in the US,³ current estimates of 300-500 additional HCV-positive donors per year might be expected to increase over time.⁴ While it is an accepted practice to transplant livers and kidneys from HCV-positive donors to HCV-positive recipients as a way to decrease waiting time and adverse waitlist outcomes substantially,¹ less is known about transplantation to HCV-negative recipients⁵ and transplantation of other organs from HCV-positive donors.^{6,7} To assess the safety and efficacy of DAA treatment in HCV-negative recipients of kidneys from HCV-positive donors, there is ongoing study by 2 groups in the US.^{8,9}

At the University of Pennsylvania, Goldberg et al conducted a pilot trial (Transplanting Hepatitis C Kidneys into Negative Kidney Recipients [THINKER]; ClinicalTrials.gov number, NCT02743897) to examine the safety and efficacy of transplantation of kidneys from HCV genotype 1-viremic donors to 10 HCV-negative recipients.⁸ All recipients became infected with HCV by postoperative day 3 and were treated preemptively with elbasvir-grazoprevir. All recipients were considered cured of HCV by demonstration of a sustained virologic response 12 weeks after antiviral treatment ended.

Our group at Johns Hopkins University conducted a trial (Exploring Renal Transplants Using Hepatitis C Infected Donors for HCV-negative Recipients [EXPANDER-1]; ClinicalTrials.gov number, NCT02781649) to examine the safety and efficacy of transplantation of kidneys from HCV-viremic donors to 10 HCV-negative recipients with DAA prophylaxis to prevent infection in recipients.⁹ All recipients received a single dose of elbasvir-grazoprevir pretransplant and then daily for 12 weeks posttransplant.⁹ Kidneys from donors with all HCV genotypes were included, and in cases of donors with HCV genotype 2 or 3, sofosbuvir was added. There were no adverse events related to DAA treatment and no recipients had clinical evidence of acute or chronic HCV.

After establishment of the safety and efficacy of DAAs in HCV-negative transplant recipients of organs from HCV-viremic donors, the high cost of HCV treatment must be considered in terms of feasibility of treatment. Trotter et al reported cost-neutrality of transplantation of a kidney from an HCV-positive donor to an HCV-negative recipient at 5 years posttransplant, as compared to cost of hemodialysis.² Importantly, simulation data from the US, where drug prices are generally higher than other countries, has shown that DAAs are cost-effective even for those with chronic kidney disease who do not have costs of hemodialysis.¹⁰ In other words, DAAs are cost-effective in the most expensive drug market

even without comparison to the cost of hemodialysis. Recent consensus guidelines from the AST point out that the already high cost of care for those awaiting transplantation are increasing each year, while access to DAAs and options for treatment are generally improving with time.¹

In summary, the argument for use of organs from HCV-viremic donors is growing. Initial data demonstrate the safety and efficacy of HCV treatment for HCV-negative recipients of kidneys from HCV-positive donors in the study setting, both as prophylaxis⁹ and preemptive treatment in response to HCV viremia.⁸ Larger studies are needed to confirm these initial findings, characterize drug-drug interactions and impact of HCV infection on transplanted organ function, and examine the cost-effectiveness of differing DAA treatment strategies. The initial studies in kidney recipients provide the groundwork for investigation in heart and lung recipients.⁵⁻⁷ If successful, this approach could dramatically decrease the high discard rate of organs from HCV-viremic donors and save lives by expanding donor options for those in need of transplantation.

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ABBREVIATIONS

AST	American Society of Transplantation
DAAs	Direct-acting antivirals
HCV	Hepatitis C virus
UK	United Kingdom
US	United States

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