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Transplanting HCV-Infected Kidneys into Uninfected Recipients

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facilitate rapid implementation of the intervention in large numbers of patients by the clinical staff at different institutions, all in the chaos of emergency departments; and to avoid potential responder bias in the outcome assessments of patients (or surrogates) who may have thought they had received “nonstandard” care. Our decision to view the matter of head position as involving “low risk” was based on several considerations: the insufficient amount of level 1 evidence specifying the benefits and harms of head positioning for patients with acute stroke; the fact that people change their head position within the ranges being tested during routine hospital care and in daily life, as they shift from activity during the day to rest and sleep at night; and the view that patient care would not be compromised by either of the interventions.

Finally, Taito and Yamauchi raise an important point regarding an unresolved issue that should be addressed in another trial — that of the appropriate timing (and intensity) of early mobilization after acute stroke that follows from the

unexpected results of the AVERT trial.² Unfortunately, we did not collect data on the specific time that patients began to move outside the confines of the bed.

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Since publication of their article, the authors report no further potential conflict of interest.

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Transplanting HCV-Infected Kidneys into Uninfected Recipients

TO THE EDITOR: Goldberg et al. (June 15 issue)¹ report cure of hepatitis C virus (HCV) infection, after transplantation of kidneys infected with HCV (genotype 1) into HCV-negative recipients, with the use of a 12-week course of elbasvir-grazoprevir. However, data on other types of solid-organ transplantation are lacking. Here, we report cure of HCV infection after accidental transmission of HCV from one organ donor to five different recipients (Table 1). The 55-year-old female donor did not belong to a group considered to be at high risk for HCV infection, and routine testing for anti-HCV IgG was negative. However, retrospective analysis revealed low-level HCV RNA (genotype 1a) viremia. All the transplant recipients were HCV-negative before transplantation and had development of HCV viremia in the early post-transplantation period. A 12-week course of different sofosbuvir-based anti-HCV regimens²⁻⁴ was used to treat four of the patients. The liver-transplant recipient died from septic shock early after transplantation, before treatment could have been initiated. All four

recipients who received treatment currently have stable graft function and cure of HCV infection (sustained virologic response at week 12 after treatment).

In summary, we contribute further evidence that the early initiation of a sofosbuvir-based regimen is an efficient and safe treatment option in the context of different types of solid-organ transplantation from an HCV-positive donor to an HCV-negative recipient.

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Table 1. Course of Infection in Patients Who Received Hepatitis C Virus (HCV)-Infected Organs.

Patient No.	Organ Received	Timing of HCV Positivity* <i>day after transplantation</i>	Maximum Viral Load before Start of Therapy* <i>IU/ml</i>	Timing of Start of Therapy <i>day after transplantation</i>	Direct-Acting Antiviral Regimen†	Timing of HCV Negativity* <i>day after start of therapy</i>	Early Virologic Response at Wk 4	Sustained Virologic Response at Wk 12
1	Right kidney	3	522	4	Sofosbuvir and daclatasvir	3	Yes	Yes
2	Left kidney	6	1.12×10 ⁶	10	Sofosbuvir, ledipasvir, and ribavirin	28	Yes	Yes
3	Liver	5	5.49×10 ⁵ ‡	—	—	—	—	—
4	Lungs	2	5×10 ⁶	10	Sofosbuvir and ledipasvir	25	Yes	Yes
5	Heart	6	2.2×10 ⁶	9	Sofosbuvir and ledipasvir	7	Yes	Yes

* Virus was detected and viral loads measured with the use of quantitative nucleic acid testing.

† Patients received treatment for 12 weeks.

‡ The patient died from septic shock before therapy could have been initiated; the viral load provided is the maximum viral load measured before the patient died.

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No potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: Goldberg and colleagues demonstrated that HCV-positive kidneys can be successfully used for transplantation in HCV-negative recipients. Likewise, the livers of many HCV-positive donors are of good quality and can be transplanted, with outcomes similar to those obtained with HCV-negative livers. In 2015, however, 11% of procured HCV-positive livers were discarded.¹ The new direct-acting antiviral agents have dramatically changed the landscape of HCV treatment, with sustained virologic response rates of up to 95%, independent of HCV genotype, stage of fibrosis, or previous response to antiviral therapy.^{2,3} The use of HCV-positive livers could substantially decrease waiting time and mortality among HCV-negative patients on the transplant waiting list. Clinical trial data on intentional transplantation of HCV-positive livers into HCV-negative recipients are lacking. HCV-negative patients who have, without the knowledge of the physician, received HCV-positive livers have had good responses to treatment.⁴ In our center, we have successfully performed two intentional transplantations of HCV-positive livers into HCV-negative recipients. In light of the new HCV treatment options available, it is unethical to let HCV-negative patients die while many usable HCV-positive

liver grafts are discarded. It is now time to challenge dogmatic beliefs and the current transplant-allocation algorithm.

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THE AUTHORS REPLY: Halleck et al. describe five patients who were infected with HCV after transplantation with organs from a deceased donor in whom HCV infection had not been suspected. Four recipients survived the early post-transplantation period and were cured of HCV infection. Their experience adds to the small but growing body of evidence indicating that transplantation-related immunosuppression does not substantially diminish the effectiveness of direct-acting antiviral agents for HCV treatment.¹ The donor's profile also offers a cautionary tale: risk stratification for bloodborne viral infections has limited value, because this stratification is based on whatever information happens to be available about the donor's social and medical history. We advocate that all organ donors undergo nucleic acid screening for HCV and HIV infection, which is more sensitive than antibody testing and has enhanced relevance during this era of widespread and sometimes unsuspected opiate abuse in many places, including the United States.²

Martins et al. report two instances in which HCV-infected livers were intentionally used for transplantation into HCV-negative recipients. We support continued study of this practice, which we believe should not yet be the standard of care. Research oversight is appropriate. Most candidates for transplantation know little about HCV. The risks of complications and noncure after new

HCV transmission during transplantation are uncertain. Therefore, robust processes of informed consent that acknowledge the unknown magnitude of risks are needed. Centers should collaborate, develop best practices, and publish on their experience with transplanting HCV-infected organs into HCV-negative patients.³

The biggest impediment to expanding the use of HCV-infected organs in some nations is guaranteeing access to expensive antiviral therapy. Leaders of transplantation programs and professional societies must work with payers to prospectively authorize treatment, so that patients who consent to donor-derived HCV infection are assured of timely therapy. In addition, the selection of antiviral therapy requires consideration of the viral genotype and interactions with commonly used drugs after transplantation. Renal insufficiency is also common with transplantation, and this may complicate the safe use of antivirals, including sofosbuvir; acute kidney injury occurs among more than a third of liver-transplant recipients specifically.⁴ Although we are optimistic that HCV-infected organs will expand the donor pool substantially, more data are needed to define the safest and most effective use of these organs for recipients who do not have HCV infection.

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Since publication of their letter, the authors report no further potential conflict of interest.

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