Transplanting HCV-Infected Kidneys into Uninfected Recipients

Paulo N.A. Martins
University of Massachusetts Medical School

Let us know how access to this document benefits you.
Follow this and additional works at: https://escholarship.umassmed.edu/surgery_pp

Part of the Analytical, Diagnostic and Therapeutic Techniques and Equipment Commons, Bioethics and Medical Ethics Commons, Health Policy Commons, Health Services Administration Commons, Nephrology Commons, Surgery Commons, and the Virus Diseases Commons

Repository Citation

This material is brought to you by eScholarship@UMassChan. It has been accepted for inclusion in Surgery Publications by an authorized administrator of eScholarship@UMassChan. For more information, please contact Lisa.Palmer@umassmed.edu.
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 regimens\(^2-4\) 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.

Fabian Halleck, M.D.
Klemens Budde, M.D.
Michael Duerr, M.D.
Oliver Staeck, M.D.
Joerg Hofmann, M.D.
Charité–Universitätsmedizin Berlin
Berlin, Germany
fabian.halleck@charite.de

Ute Eisenberger, M.D.
Kerstin Herzer, M.D.
University Duisburg-Essen
Essen, Germany


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 recipients. 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 organs are available; it is unethical to let HCV-negative patients die while many usable HCV-positive organs are available. In light of the new HCV treatment options available, it is unethical to let HCV-negative patients die while many usable HCV-positive organs are available.

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

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Organ Received</th>
<th>Timing of HCV Positivity†</th>
<th>Maximum Viral Load before Start of Therapy ‡</th>
<th>Timing of Start of Therapy</th>
<th>Direct-Acting Antiviral Regimen†</th>
<th>Timing of HCV Negativity†</th>
<th>Early Virologic Response at Wk 4</th>
<th>Sustained Virologic Response at Wk 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Right kidney</td>
<td>3</td>
<td>522 IU/ml after transplantation</td>
<td>4</td>
<td>Sofosbuvir and daclatasvir</td>
<td>3</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>Left kidney</td>
<td>6</td>
<td>1.12×10⁶ IU/ml after transplantation</td>
<td>10</td>
<td>Sofosbuvir, ledipasvir, and ribavirin</td>
<td>28</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>Liver</td>
<td>5</td>
<td>5.49×10⁶ IU/ml after transplantation</td>
<td>—</td>
<td>Sofosbuvir and ledipasvir</td>
<td>25</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>4</td>
<td>Lungs</td>
<td>2</td>
<td>5×10⁶ IU/ml after transplantation</td>
<td>10</td>
<td>Sofosbuvir and ledipasvir</td>
<td>7</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>5</td>
<td>Heart</td>
<td>6</td>
<td>2.2×10⁶ IU/ml after transplantation</td>
<td>9</td>
<td>Sofosbuvir and ledipasvir</td>
<td>7</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

* 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.

TO THE EDITOR: Goldberg and colleagues demonstrated that HCV-positive kidneys can be successfully used for transplantation in HCV-negative recipients. Likewise, the use of HCV-positive livers could substantially decrease waiting time and mortality among 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 organs are available.
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. 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.

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.

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. 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.

David S. Goldberg, M.D.
Peter L. Abt, M.D.
Peter P. Reese, M.D.
University of Pennsylvania Perelman School of Medicine
Philadelphia, PA
peter.reese@uphs.upenn.edu

for the THINKER Trial Investigators

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


DOI: 10.1056/NEJMCl709315