The Use of HCV + Donors for HCV – Recipients in Liver Transplantation

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Figure LI 46. Total liver transplants
All liver transplant recipients, including adult and pediatric, retransplant, and multi-organ recipients.
Figure Li 1. New adult candidates added to the liver transplant waiting list

OPTN/SRTR 2017 Annual Data Report
Figure LI 6. Distribution of adults waiting for liver transplant by diagnosis

OPTN/SRTR 2017 Annual Data Report
HCV Positivity

Levitski et al. Am Jour Transplantation 2017; 17: 2790-2802
Table 1: Interpreting donor test results

<table>
<thead>
<tr>
<th>HCV antibody</th>
<th>HCV NAT</th>
<th>Clinical interpretation</th>
<th>Concern for transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>+</td>
<td>Active infection (acute or chronic)</td>
<td>Likely</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>No active infection(^1); cleared or treated prior infection, or false-positive antibody</td>
<td>No documented transmissions</td>
</tr>
<tr>
<td>-</td>
<td>+</td>
<td>Acute infection in the antibody window period or false-positive NAT</td>
<td>Likely</td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>No HCV infection(^1)</td>
<td>None</td>
</tr>
</tbody>
</table>

HCV, hepatitis C virus; NAT, nuceic acid testing.
\(^1\)No infection unless donor had ongoing risk factors for recent HCV acquisition 5–7 days before screening.
Total Liver Transplants from March 2016 to March 2017

n = 125

HCV Seropositive/Non-viremic donors to HCV seronegative recipients

n = 26 (21%)

Excluded from analysis

n=1 (4%)

(Death due to primary graft non-function)

HCV PCR testing completed at 3 months post liver transplantation

n= 25 (96%)

Did not develop HCV viremia (median follow up 11 months)

n=21 (84%)

Developed HCV viremia (median follow up 10 months)

n=4 (16%)

HCV treatment not initiated (post-LT complications)

n=1 (25%)

HCV treatment initiated

n=3 (75%)

Sustained virologic response, n=2

End of treatment response, n=1
Use of HCV + Donor Livers

• Three groups of recipients
  • HCV Viremic
  • HCV naïve
  • HCV treated and sustained viral response

• The Organ Procurement and Transplantation Network has no policy restricting the transplantation of HCV + donors
Use of HCV+ Livers for Negative Recipients: Pros

• Highly effective and well tolerated drugs available

• Could reduce time on waitlist
  • Acute liver failure
  • HCC
  • Significant symptoms with low MELD

• These donors are becoming younger with lower BMIs
Use of HCV+ Livers for Negative Recipients: Cons

• Obtaining medication coverage

• Risk of treatment failure
  • Progressive liver disease
  • Fibrosing cholestatic hepatitis

• Developing a coherent informed consent process
Percent of Deceased Donor Liver Transplants from HCV+ Donors

Gonzalez et al. Hepatology 2018; 67; 1600-1608
Opioid Epidemic

- 3 fold increase in drug overdose deaths the past 15 years
- Heroin overdose deaths >5 fold increase past decade
- Number of new HCV infections increased 4 fold from 2005 to 2016
- Demographics of overdose victims has resulted in younger HCV donors
Median Deceased Donor Age Over Time, by HCV+ Status

Donor HCV Status
- Not Reported as HCV+
- Reported as HCV+

Year of Recovery

Median Donor Age

Levitski et al. Am Jour Transplantation 2017; 17: 2790-2802
Figure LI 35. Rates of livers recovered for transplant and not transplanted by donor HCV status

OPTN/SRTR 2017 Annual Data Report

Figure LI 35. Rates of livers recovered for transplant and not transplanted by donor HCV status
Percentages of livers not transplanted out of all livers recovered for transplant. HCV, hepatitis C virus.
Figure LI 36. Rates of livers recovered for transplant and not transplanted, by donor risk of disease transmission

"Increased risk" is defined by criteria from the US Public Health Service Guidelines for increased risk for HIV, hepatitis B and hepatitis C transmission.
Outcomes of viremic donor recipients

• Reviewed data from SRTR of adults s/p a primary, nonfulminant, deceased donor OLT from 2008 thru January 2018

• Analyzed outcomes of Recipient + vs – HCV status (either Ab or NAT)

• Analyzed data pre- and post-DAA eras
  • Post-DAA defined as after November 2013
Outcomes of viremic donor recipients

• In post-DAA era donor + livers (DAb+) accounted for 7.1% of all OLTs vs 3.7% pre-DAA

• Post-DAA era 3 year graft survival improved in all patients, but most dramatically in the D+Ab/R- group (79% -> 88%)

• In post-DAA era Dab+/R- received younger and leaner donors, but longer waitlist times vs pre-DAA
  • Opioid epidemic
  • Pre-DAA area recipients had more emergent need
“Proof of Concept” Case

• 57yo ESLD from HCV s/p SVR with sofosbuvir/simeprevir
• Wait-listed 3 years MELD 12 and developed hepatopulmonary syndrome 6 months after SVR
• Obtained RRB exception points (MELD 22) for the HPS, but O2 requirements were rising
• Consented for HCV+ organ and received an 18yo HCV Ab-, +NAT donor who died from heroin overdose
• 3 days s/p OLT the HCV PCR in recipient was 5.17 million and genotype 1a

Saberi et al. Liver Transplantation 2018; 24: 140-143
“Proof of Concept” Case

• Given issues with anemia and past ribavirin intolerance, no ribavirin used, thus request for Harvoni X24wks was made
• Insurance approved and treatment started postop day 25
• HCV PCR 20 IU/mL at 4wks and undetectable at 8 wks
• 2 yrs s/p OLT HCV PCR undetectable
UT Health Case

• 45yo female ESLD from NASH decompensated by ascites and refractory hydrothorax MELD-Na 12, A blood type

• Listed for OLT January 2019

• Hydrothorax continued to be problematic thus underwent a TIPS

• Hydrothorax persisted in spite of revisions and eventual “parallel” TIPS placement with end portosystemic gradient of 8mmHg from max of 13mmHg
UT Health Case

• Pleurex catheter placed in R chest, but not tolerated

• Pt had no living donor options

• Attempt made for exception points

• Pt consented for HCV+ organ

• Underwent OLT from a PHS high risk HCV NAT+ donor on 6/11/19
28. I understand that if I am Hepatitis C positive and have not received Hepatitis C treatment, I will be listed as accepting a Hepatitis C Antibody Positive offer and Hepatitis C Nucleic Acid Testing (NAT) Positive organ offer.

29. **Hepatitis C Positive Donors**
   I have been informed of the option to be listed as accepting a Hepatitis C positive donor organ although I am Hepatitis C negative. It was explained to me that by accepting this type of organ, I will contract Hepatitis C and require treatment. I have been educated by the physician in detail of the risks and benefits of accepting an organ from a Hepatitis C positive donor, the side effects of Hepatitis C medication, and by signing this acknowledgement form, places me on the list for accepting a Hepatitis C positive organ knowing the potential risks involved and further described below:

a. **Treatment for Hepatitis C**
   I understand that the medication to treat Hepatitis C requires insurance coverage and approval. I further acknowledge that the cost of this medication is my responsibility, however in most cases, insurance will cover the full cost of Hepatitis C therapy. In the event that my insurance denies payment for the costs of therapy, University Health System may assist with seeking alternate funding for the medication. However, I understand that no guarantee has been made to me regarding this financial support.

b. I understand that the success rate to treat Hepatitis C is very effective, however there is a possibility that the initial course of therapy may not be successful. I further understand that there are additional medications that can be used in instances where initial treatment fails, and I acknowledge that this will also require insurance approval.

c. I understand that if I do not respond to treatment and continue to have Hepatitis C, it can cause damage to my liver and other organs and possibly lead to death.

d. I have been informed that during the time I have active Hepatitis C, there is a low chance of sexual transmission to a sexual partner. However, I am aware that I must inform my sexual partner(s) of this risk prior to engaging in intimate behavior.

**Hepatitis C Positive Donor:** YES □ NO □
UT Health Case

- Post op complicated by anastomotic bile leak POD#7 requiring ERCP with stent

- High drain output (nonbiliious) delayed d/c till POD# 15
UT Health Case

• HCV PCR POD# 4 20.8 million; Genotype 1a

• HCV PCV POD #24 18 million

• Last clinic 7/12/19 normal liver tests and had just received Rx for 12 wks of Glecaprevir and pibrentasvir
Will Treatment Work?...ALLY-1 Study

- Assessed efficacy of Daclatasvir, Sofobuvir and Ribavirin for 12 wks with advanced ESLD or post-OLT recurrence
  - Tx naïve or tx experienced
  - All genotypes eligible
- 52 of 53 pts in post-transplant cohort completed 12 wks tx
  - One d/c after 31d due to headaches
- 50 of 53 in post-OLT group had SVR-12 (94%)
  - 55% of these pts had advanced fibrosis
  - Only GT 1,3 and 6 in this group
- No major AEs described
In Conclusion...

• HCV viremic donors are an underutilized resource

• The development of DAA therapy has dramatically changed management and course HCV patients

• A thorough informed consent process is warranted for those nonviremic accepting viremic donors

• More studies needed looking at outcomes and risks