The Changing Landscape for Liver Transplantation

Part I - Organ Allocation
Part II - Hepatocellular Carcinoma (HCC), Fatty Liver and Hepatitis B & C

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Disclosures

None
Objectives

Discuss the burden and changes in organ transplantation for

- ALD
- HCV
- HCC
- NAFLD/NASH

Briefly discuss proposed UNOS/OPTN new organ allocation policy
Indications for transplant in the US

UNOS liver transplant report 2017
The burden of Alcohol

3rd CAUSE OF PREVENTABLE DEATHS

90,000 DEATHS/YEAR

18,000 ALD/YEAR

National trends in LT for AALD

A Liver transplants for alcohol-associated liver disease

B Liver transplants for alcoholic hepatitis

Lee BP, et Al. JAMA Intern Med. 2019
Real world experience in AH

American Consortium of Early Liver Transplantation for Alcoholic Hepatitis: ACCELERATE-AH
12 centers in 8 UNOS regions

Post-Transplant Outcomes
1 Year 3 Year
Survival
94% 84%

Early Transplant = no specific sobriety period (n=147)

Mortality without transplant up to 70% at 6 months

Lee BP, et al. Gastroenterology. 2018
Pre-transplant selection

- Decompensated cirrhosis from ALD/AH
  - Referral to LT center
  - Extensive psycho-social evaluation and random drug screen for risk of relapse

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, female</td>
<td>1.32 (0.60-2.92)</td>
<td>.49</td>
</tr>
<tr>
<td>Race, non-Caucasian</td>
<td>1.66 (0.66-4.19)</td>
<td>.28</td>
</tr>
<tr>
<td>Age (per year)</td>
<td>0.95 (0.92-0.99)</td>
<td>.01</td>
</tr>
<tr>
<td>Non-private insurance</td>
<td>1.29 (0.60-2.78)</td>
<td>.51</td>
</tr>
<tr>
<td>Single/divorced/widowed</td>
<td>1.54 (0.73-3.25)</td>
<td>.25</td>
</tr>
<tr>
<td>History of comorbid psychiatric disease</td>
<td>1.22 (0.56-2.64)</td>
<td>.62</td>
</tr>
<tr>
<td>History of illicit substance abuse</td>
<td>1.31 (0.45-3.76)</td>
<td>.62</td>
</tr>
<tr>
<td>History of failed rehabilitation attempt</td>
<td>1.56 (0.72-3.39)</td>
<td>.26</td>
</tr>
<tr>
<td>Family history of alcohol use disorder</td>
<td>1.33 (0.63-2.82)</td>
<td>.46</td>
</tr>
<tr>
<td>Unemployed immediately before hospitalization</td>
<td>1.22 (0.58-2.55)</td>
<td>.60</td>
</tr>
<tr>
<td>History of alcohol-related legal issues</td>
<td>2.03 (0.93-4.41)</td>
<td>.08</td>
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<tr>
<td>More than 10 drinks/d at presentation</td>
<td>1.28 (0.60-2.72)</td>
<td>.53</td>
</tr>
<tr>
<td>Years of heavy drinking</td>
<td>0.98 (0.94-1.01)</td>
<td>.21</td>
</tr>
<tr>
<td>Days of pretransplantation abstinence</td>
<td>1.00 (0.99-1.01)</td>
<td>.74</td>
</tr>
</tbody>
</table>
Transplant in HCV

Alcohol as the United
Georg Division

Percentage of liver transplant recipients

<table>
<thead>
<tr>
<th>Year</th>
<th>HCV</th>
<th>Alcohol</th>
<th>NASH</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>30%</td>
<td>15%</td>
<td>11%</td>
</tr>
<tr>
<td>2013</td>
<td>20%</td>
<td>16%</td>
<td>13%</td>
</tr>
<tr>
<td>2014</td>
<td>28%</td>
<td>18%</td>
<td>14%</td>
</tr>
<tr>
<td>2015</td>
<td>27%</td>
<td>22%</td>
<td>16%</td>
</tr>
<tr>
<td>2016</td>
<td>19%</td>
<td>18%</td>
<td>16%</td>
</tr>
</tbody>
</table>

Cholankeril, et Al. Clin Gastroenterol Hepatol. 2018
Impact of DAAs

Universal Relapse
Cirrhosis @5y

DAAs

Complete
cure

Transplants for HCV
New listings

De-list (ing)
Available organs

Available organs
Use of HCV infected organs

Annual number of transplants based on HCV viremia D/R

Graft Survival at 3yrs based on HCV D/R status in the pre- and post- DDA eras

Cotter, TG et Al. Hepatology 2019
Hepatocellular carcinoma | HCC
HCC is now #1

Yang JD, et Al. Clin Gastroenterol Hepatol. 2017
The Evolution of LT for HCC

- 1996: Not metastatic
- 2002: In Milan = Child’s C
- 2003: T1 = 24, T2 = 29
- 2004: T1 = 0, T2 = 24
- 2005: T1 = 0, T2 = 22
- 2015: 6 m delay, T2 = 28
- 2017: 6 m delay, T2 = MMAT-3

Increase q3m CAP @34
HCC downstaging AFP restriction NLRB approved
Milan Criteria

- Lesions must be $\geq 2$ cm (T2) to receive EP
- Lesions < 2cm (T1) do not get EP

Mazzaferro, et Al. NEJM 1996
UCSF Down-Staging

Changes in U.S. Liver Transplant Criteria

- AFP > 1,000 ng/ml is an exclusion
- UCSF criteria → Down staged to Milan eligible for exception MELD points

Yao, et Al. Hepatology 2016
NAFLD | Non-Alcoholic Fatty liver disease
Decompensated cirrhosis, HCC, and liver-related deaths in NAFLD population in the US, 2015-2030.

Estes, C. et Al, Hepatology
Impact of NAFLD on mortality

Do not forget CV disease and Diabetes
Road to transplant

- Increased barriers to transplant:
  - Older
  - Increased CV comorbidities
  - Higher BMIs
  - PVT
Incidence of NAFLD and NASH after OLT
Factors that influence post LT outcomes
How it works
U.S. organ transplant rules get an overhaul

By Susannah Luthi | December 7, 2018

A powerful but obscure panel, which governs which chronically ill people get critical organ transplants and when, overhauled its rules for these decisions last week, transforming the long-time geography-based system.
Take Home points

- LT is lifesaving for medically refractory AH, and the 3-year survival rate and frequency of alcohol use after transplant are comparable to other etiologies.

- Careful patient selection remains the key to successful transplantation in ALD. We are still in search for the characteristics that may positively or negatively affect outcomes.

- HCV is no longer the #1 reason for transplantation. DAAs have not only saved lives of patients with HCC, but also increased the organ pool/availability for all other etiologies.
**Take home points**

- LT for HCC has continued to increase over the past 12 years, making HCC the leading indication for registration.

- NAFLD is projected to become the leading cause of transplant by 2030. Patients with NAFLD will be increasingly challenging due to age and CV risk factors.

- The new transplant allocation system proposed by UNOS/OPTS was designed to eliminate geographic inequalities of MELD score at time of transplantation. It is now on hold in Federal court.
Thank you