New Trends in Liver Transplantation

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Disclosure

No conflict of interest in relationship to this program / presentation

My field of interest in transplant surgery – decision analysis

Dr Tevar
Liver transplantation
Liver transplantation

Did I chose the right organ for this patient?
Will I have any “surprise” during the operation?
Will the patient make it through the operation?
Will the patient be able to recover?
Current trends in Liver Transplantation

• Advances in antiviral medications (HCV, HBV, HIV) and survival
• The role of live donation
• Geographical disparities in access to liver transplantation
• Split liver transplantation
• Combined liver transplantation and gastric sleeve resection
• The role of simultaneous liver and kidney transplantation
• New allocation systems
• Role of liver transplantation for cholangiocarcinoma, colorectal metastases

10% of liver transplant recipients die within the first 1 after surgery
Current Trends in Liver Transplantation

• **Donors**
  • Type of death (Brain dead vs. death after cardiovascular arrest)
  • Age
  • Comorbidities

• **Recipients**
  • Indications
  • Age
  • Comorbidities
  • Operative risk profile
Donors
Deceased Donors Recovered in the U.S. between 2010-2017 with Drug Intoxication Reported as Mechanism of Death

<table>
<thead>
<tr>
<th>Year of Recovery</th>
<th>Number of Donors</th>
<th>Percent of Donors</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>342</td>
<td>4.3%</td>
</tr>
<tr>
<td>2011</td>
<td>473</td>
<td>5.8%</td>
</tr>
<tr>
<td>2012</td>
<td>440</td>
<td>5.4%</td>
</tr>
<tr>
<td>2013</td>
<td>560</td>
<td>6.8%</td>
</tr>
<tr>
<td>2014</td>
<td>625</td>
<td>7.3%</td>
</tr>
<tr>
<td>2015</td>
<td>848</td>
<td>9.3%</td>
</tr>
<tr>
<td>2016</td>
<td>1,263</td>
<td>12.7%</td>
</tr>
<tr>
<td>2017</td>
<td>1,369</td>
<td>13.3%</td>
</tr>
</tbody>
</table>
Overdose death donors

- Age 20-40 years ~65%
- HCV (+) ~20%
- Polysubstance abuse ~90%
Drug overdose epidemic

Patient survival

Years post transplant

18% HCV (+)

HCV(+) recipients

HCV(-) recipients

Treatable

Direct Acting Anti-hepatitis C Virus Drugs

Durand et al. Ann Intern Med 2018
Epclusa \((\text{Sofosbuvir/Velpatasvir}) \times 12 \text{ weeks,}\)

### SVR 12

<table>
<thead>
<tr>
<th>Percent</th>
<th>All</th>
<th>GT 1a</th>
<th>GT 1b</th>
<th>GT 2</th>
<th>GT 4</th>
<th>GT 5</th>
<th>GT 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>618/624</td>
<td>206/210</td>
<td>117/118</td>
<td>104/104</td>
<td>116/116</td>
<td>34/35</td>
<td>41/41</td>
</tr>
</tbody>
</table>

**ASTRAL-1:** Feld JJ, NEJM, 2015; 373: 2599
Should we Use HCV(+) grafts for HCV(-) recipients?

<table>
<thead>
<tr>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Increase pool of currently available donors</td>
<td>- 100% risk of transmission of HCV for recipients</td>
</tr>
<tr>
<td>- Decrease wait-time mortality for very sick recipients (FHF, high MELD &gt;30)</td>
<td>- High cost of DAA</td>
</tr>
<tr>
<td>- Potentially younger donors without other comorbidities</td>
<td>- Limited access to DAA regimens</td>
</tr>
<tr>
<td>- DAA regimens have a very high rate of cure</td>
<td>- Requirement for preapproval by drug companies or insurance companies*</td>
</tr>
<tr>
<td>- Similar longterm graft and patient outcome than HCV-negative donors</td>
<td>- Possible interaction between DAA regimens and immunosuppression</td>
</tr>
<tr>
<td></td>
<td>- Ethical/society barrier</td>
</tr>
<tr>
<td></td>
<td>*only for countries where insurance companies cover the costs</td>
</tr>
</tbody>
</table>
Should I accept a liver donated after cardiac death?
DCD Liver Utilization in the U.S. 2008 – 2015

Source: Based on OPTN data through December 31, 2015.
DCD vs DBD liver grafts: UK experience

Suboptimal perfusion (Warm ischemia time)
- Tissue inflammation
- Increased risk of vascular thrombosis
- Increased risk of biliary injury
- Increased risk of primary graft non-function
- Increased risk of graft loss
Liver perfusion before transplantation

preconditioning

Hypothermic perfusion
Normothermic perfusion
Donors Age: SRTR Data 2002-2017

Donor Age

Recipient Survival

Donor’s Age
Category 0=0-17; 1=18-45; 2=46-65; 3=66-75; 4=76-79; 5=>76
-Age 0-17
-Age 18-45
-Age 46-65
-Age 66-65
-Age 76-79
-Age 0-17-censored
-Age 18-45-censored
-Age 46-65-censored
-Age 66-65-censored
-Age 76-79-censored
-Age 0-17-censored

ERAI = 2002-2006
ERAI = 2007-2011
ERAI = 2012-2017
Recipients
MELD Score

• In 2002 the MELD score was introduced for organ allocation
Trends in MELD at Transplantation

1 year mortality
ERA I = 2002-2006
ERA II = 2007-2011
ERA III = 2012-2017

Comorbidities

<table>
<thead>
<tr>
<th>Era</th>
<th>Diabetes</th>
<th>Dialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>18.9%</td>
<td>7.1%</td>
</tr>
<tr>
<td>II</td>
<td>22.4%</td>
<td>10.8%</td>
</tr>
<tr>
<td>III</td>
<td>26.4%</td>
<td>12.2%</td>
</tr>
</tbody>
</table>
1-year mortality by age group stratified by presence of diabetes or renal failure

- **≤65**: Era III, 13.9%; Era II, 0%; Era I, 26.3%
- **65-69**: Diabetes, 17.4%; HD, 16.6%; Era I, 17.9%
- **70-74**: Diabetes, 18.8%; HD, 26.3%
- **≥75**: Diabetes, 33.3%; HD, 33.3%
Can we improve our abilities to identify high-risk patients?

### Liver Transplant Risk Score

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group</th>
<th>Point</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&lt;65</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>65-69</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>70-74</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>≥75</td>
<td>3</td>
</tr>
<tr>
<td>MELD Score</td>
<td>&lt;25</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>25-29</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>30-34</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>≥35</td>
<td>3</td>
</tr>
<tr>
<td>BMI</td>
<td>≤18.5</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>18.5-39.9</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>≥40</td>
<td>1</td>
</tr>
<tr>
<td>Metabolic</td>
<td>Diabetes</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Dialysis</td>
<td>1</td>
</tr>
</tbody>
</table>

- **Age**
  - <65: 0 points
  - 65-69: 1 point
  - 70-74: 2 points
  - ≥75: 3 points

- **MELD Score**
  - <25: 0 points
  - 25-29: 1 point
  - 30-34: 2 points
  - ≥35: 3 points

- **BMI**
  - ≤18.5: 1 point
  - 18.5-39.9: 0 points
  - ≥40: 1 point

- **Metabolic**
  - Diabetes: 1 point
  - Dialysis: 1 point

The chart illustrates the distribution of points across different characteristics and eras, with Era I showing the highest risk across all categories.
Patient survival

- Improved pre-transplant management
  - Rehabilitation
  - Physiotherapy / Frailty
  - Nutrition
  - Interventions (TIPPS / Banding)

- Intraoperative management
  - Piggyback transplants
  - Venous-venous by pass
  - Management of coagulopathy

- Postoperative management
  - Infectious disease
  - Metabolic disorders
  - Preventive interventions (e.g. substance abuse)
  - Physiotherapy
  - Nutritional support
Conclusions

• There have been many changes in donor and recipient characteristics
• Risk index for donor and recipient
• Progressive refinement of the management of liver transplant recipients (before, during, after surgery)
• More complex recipients are transplanted (e.g. age / comorbidities)
  • Increased health-care resource utilization
• Close monitoring of selection / outcomes is needed as patient survival has not improved over the last 2 decades