Liver Transplantation

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No Relevant Financial Disclosures
What should I talk about?

- Anatomy/Surgical Technique
- Allocation
- Indications/Donor Selection
- Early post-transplant complications
- Outcomes
Topics

- Anatomy/Surgical Technique
- Allocation
- Indications/Donor Selection
- Early post-transplant complications
- Outcomes
Donor Procedure
Donor Procedure
Donor Procedure

Diaphragm

Triangular ligament (cut)

Pars flaccida
Donor Procedure
Hepatic Artery Variants – Michel’s Classification

Type I
- Gall bladder
- Left gastric artery
- Common hepatic artery
- Splenic artery
- Superior mesenteric artery

Type II
- May or may not be present
- Accessory left
- Left gastric artery

Type III
- Normal right hepatic may or may not be present
- Accessory right hepatic artery
- Left gastric artery

Type IV
- Replaced left hepatic artery
- Left gastric artery

Type V
- Left gastric artery
- All from replaced right hepatic artery

Type VI
- Separate common hepatic artery
- Left gastric artery
- Left gastric artery
Donor Procedure

Diaphragmatic crura divided
Donor Procedure
En bloc removal of liver and pancreas with back table separation
Liver Segments

Right Hemiliver (Right Liver)
- Inferior Vena Cava
- Right Hepatic Vein

Left Hemiliver (Left Liver)
- Middle Hepatic Vein
- Left Hepatic Vein

Falciform Ligament
- Portal Vein
- Common Hepatic Artery
- Common Bile Duct

Right Posterior Section
Right Anterior Section
Left Medial Section
Left Lateral Section
Liver Transplant Procedure - Bicaval

Right atrium
Infradiaphragmatic inferior vena cava
Liver
Liver Transplant Procedure

Piggyback technique native hepatectomy
Liver Transplant Procedure

Veno-venous bypass
Liver Transplant Procedure

Suprahepatic bicaval recipient anastomosis
Liver Transplant Procedure

Hepatic arterial anastomosis
Liver Transplant Procedure – Caval Anastomosis

Bicaval

Piggyback
Liver Transplant Procedure – Biliary Anastomosis

Typical choledocho-choledochostomy

Alternative Roux-en-Y choledocho-jejunostomy
Liver Transplant Procedure – Completed Transplant
Liver Transplant Procedure – Completed Transplant

- Gallbladder
- Ligated GDA
- Reperfused Portal Vein
- Ligated Splenic Art (anterior tie)
- Completed Arterial Anastomosis
Postoperative management

❖ **Postoperative pathways**
  - 70% patients extubated in OR
  - Rapid removal of SG catheter

❖ **Transfer from unit**
  - Most ICU admits < 24 hours

❖ **Initiate early discharge planning**
  - Median LOS 8.3 days
Living Donor Liver Transplantation
Living Related Liver Transplant Donor Procedure

Typical procedure for adult to pediatric living-related transplants
Living Related Liver Transplant Recipient Procedure

- Left hepatic vein
- Inferior vena cava
- Bile ducts to segments II and III
- Roux-en-Y loop
- Left portal vein
- Portal vein
- Segment II
- Segment III
- Left hepatic artery
- Hepatic artery
- Aorta
Living Related Liver Transplant Donor Procedure

Typical procedure for adult to adult living-related transplants
Living Related Liver Transplant Recipient Procedure
Topics

- Anatomy/Surgical Technique
- Allocation
- Indications/Donor Selection
- Early post-transplant complications
- Outcomes
Assessing the Severity of Liver Disease: MELD

<table>
<thead>
<tr>
<th></th>
<th>Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>MELD score</td>
<td>$0.957 \times \log(\text{creatinine}) + 0.378 \times \log(\text{total bilirubin}) + 1.120 \times \log(\text{INR}) + 0.6431$</td>
</tr>
<tr>
<td>MELD-Na</td>
<td>$\text{MELD} + 1.59 \times (135 - \text{Na} \text{[mEq/L]})$</td>
</tr>
</tbody>
</table>
PELD Scoring

PELD Score = \(0.480 \times \log_e(\text{bilirubin mg/dL}) + 1.857 \times \log_e(\text{INR}) - 0.687 \times \log_e(\text{albumin g/dL}) + 0.436 \) if patient is less than 1 year old
+ 0.667 if the patient has growth failure \((-2 \text{ Standard deviation})\)

 Scores for patients listed for liver transplantation before the patient's first birthday continue to include the value assigned for age \(< 1 \text{ year}) until the patient reaches the age of 24 months

 Multiply the score by 10 and round to the nearest whole number.

 Laboratory values less than 1.0 are set to 1.0 for the purposes of the PELD score calculation.

 *May range higher or lower than the 6 - 40 range for MELD*
# Liver Cancer (HCC) Staging – Milan Criteria

<table>
<thead>
<tr>
<th>Classification</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>1 nodule &lt;=1.9 cm</td>
</tr>
<tr>
<td>T2</td>
<td>One nodule 2.0-5.0 cm; two or three nodules, all &lt;3.0 cm</td>
</tr>
<tr>
<td>T3</td>
<td>One nodule &gt;5.0 cm; two or three nodules, at least one &gt;3.0 cm</td>
</tr>
<tr>
<td>T4a</td>
<td>Four or more nodules, any size</td>
</tr>
<tr>
<td>T4b</td>
<td>T2, T3, or T4a plus gross intrahepatic portal or hepatic vein involvement as indicated by CT, MRI, or ultrasound</td>
</tr>
</tbody>
</table>

N1 Regional (portal hepatis) nodes, involved  
M1 Metastatic disease, including extrahepatic portal or hepatic vein involvement

Stage 1 T1  
Stage II T2  
Stage III T3  
Stage IVA1 T4a  
Stage IVA2 T4b  
Stage IVB Any N1, any M1

**MELD exception score has changed many times since implementation – general trend has been delayed access to points, cap on points given, and demonstration of tumor stability with locoregional therapy to maintain access to transplant**
Status 1A and 1B

1A – adult and pediatric patients in fulminant hepatic failure with expected mortality < 7 days
- Encephalopathy within 8 weeks of onset of hepatic dysfunction (no pre-existing liver dx) and In ICU with any of:
  - Vent dependent
  - Dialysis or CVVH
  - INR > 2.0
- Primary non-function of liver transplant
- Hepatic artery thrombosis within 7 days of transplant (> 7 but < 14 days receives MELD of 40)
- Acutely decompensated Wilson’s Disease

1B – pediatric patients in ICU with chronic liver disease but with vent dependence, dialysis dependence, active GI bleeding, or GCS < 10
Topics

- Anatomy/Surgical Technique
- Allocation
- Indications/Donor Selection
- Early post-transplant complications
- Outcomes
Indications for Liver Transplantation

- Cirrhosis
  - Decompensated chronic liver disease
  - Hepatocellular cancer in the setting of cirrhosis

- Acute liver failure
  - Drug toxicity
  - Acute viral infection

- Metabolic liver disease
  - Urea cycle defects, MSUD, hyperoxyllosis
Evolution of OLT over 10 years at Penn:
Recipient characteristics at transplant - disease

- Alcoholic Cirrhosis
- NASH
- Cholestatic Liver Disease
- Cryptogenic Cirrhosis
- Other
- Viral Hepatitis

Recipient characteristics at transplant:
- Metabolic syndrome
  - CAD
  - Hyperlipidemia
  - Obesity
  - Diabetes
  - Renal dysfunction
Deceased Donor Selection (DRI)

- **DRI**
  - Donor and recipient factors both considered
  - This data was derived from an earlier transplant era
    - Younger donors and recipients
    - Few DCD
    - Lower BMI

**Characteristics Associated with Liver Graft Failure: The Concept of a Donor Risk Index**

S. Feng\(^{a,*}\), N.P. Goodrich\(^{b,c}\), J.L. Bragg-Gresham\(^{b,c}\), D.M. Dykstra\(^{b,c}\), J.D. Punch\(^{d}\), M.A. DeRoy\(^{a}\), S.M. Greenstein\(^{f}\) and R.M. Merion\(^{c,d}\)

AJT 2006, 6, 783-90.
Table 3: Donor factors significantly associated with liver allograft failure (1998–2002)*

<table>
<thead>
<tr>
<th>Donor parameter</th>
<th>RR</th>
<th>95% CI</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40—49</td>
<td>1.17</td>
<td>1.08–1.26</td>
<td>0.0002</td>
</tr>
<tr>
<td>50—59</td>
<td>1.32</td>
<td>1.21–1.43</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>60–69</td>
<td>1.53</td>
<td>1.39–1.68</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>&gt;70</td>
<td>1.65</td>
<td>1.46–1.87</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>African-American race (vs White)</td>
<td>1.19</td>
<td>1.10–1.29</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Donor height (per 10 cm decrease)</td>
<td>1.07</td>
<td>1.04–1.09</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>COD = CVA</td>
<td>1.16</td>
<td>1.08–1.24</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>COD = Other†</td>
<td>1.20</td>
<td>1.03–1.40</td>
<td>0.018</td>
</tr>
<tr>
<td>DCD</td>
<td>1.51</td>
<td>1.19–1.91</td>
<td>0.0006</td>
</tr>
<tr>
<td>Partial/Split</td>
<td>1.52</td>
<td>1.27–1.83</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Characteristics Associated with Liver Graft Failure: The Concept of a Donor Risk Index

S. Feng*, N.P. Goodrich*, J.L. Bragg-Gresham†, D.M. Dykstra†,
J.D. Punch†, M.A. DeBooy†, S.M. Greenstein†
and R.M. Merion‡

AJT 2006, 6, 783-90.
Deceased Donor Selection (DRI)

- **Allocation Factors**
  - Cold ischemia time – every hour adds 1% risk of graft failure
  - Regional share – increased failure risk by 11%
  - National share – increased failure risk by 28%
LDLT predictors of post-txp survival

Risk factors for recipient mortality
A2ALL and all other US programs

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Hazard Ratio</th>
<th>P value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDLT &lt; 15</td>
<td>1.61</td>
<td>&lt;.0001</td>
<td>1.28 - 2.02</td>
</tr>
<tr>
<td>Donor age/10 yrs</td>
<td>1.13</td>
<td>0.0002</td>
<td>1.06 - 1.20</td>
</tr>
<tr>
<td>Recipient age/per 10 yrs</td>
<td>1.20</td>
<td>0.0003</td>
<td>1.09 - 1.33</td>
</tr>
<tr>
<td>Serum Cr</td>
<td>1.52</td>
<td>&lt;.0001</td>
<td>1.26 - 1.83</td>
</tr>
<tr>
<td>Dx of HCC</td>
<td>2.12</td>
<td>&lt;.0001</td>
<td>1.68 - 2.69</td>
</tr>
<tr>
<td>ICU vs home</td>
<td>2.52</td>
<td>&lt;.0001</td>
<td>1.87 - 3.41</td>
</tr>
<tr>
<td>Hospitalized</td>
<td>1.62</td>
<td>&lt;.0001</td>
<td>1.32 - 1.98</td>
</tr>
</tbody>
</table>
High DRI – Economic Impact

Table 8: Estimated impact of highest DRI organs on overall hospital costs

<table>
<thead>
<tr>
<th>MELD category</th>
<th>Low DRI (0.0–1.0)</th>
<th>Highest DRI (2.5+)</th>
<th>Estimated increased cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–10</td>
<td>11.7 (7.2)</td>
<td>22.3 (38.1)</td>
<td>$47988</td>
</tr>
<tr>
<td>11–20</td>
<td>12.2 (11.2)</td>
<td>26.0 (28.5)</td>
<td>$62473</td>
</tr>
<tr>
<td>21–30</td>
<td>13.5 (14.0)</td>
<td>29.0 (35.0)</td>
<td>$70169</td>
</tr>
<tr>
<td>31–35</td>
<td>19.5 (17.3)</td>
<td>33.3 (22.2)</td>
<td>$62473</td>
</tr>
<tr>
<td>36+</td>
<td>23.2 (24.8)</td>
<td>41.8 (53.4)</td>
<td>$84202</td>
</tr>
</tbody>
</table>

High MELD leads to increased length of stay and High DRI leads to increased length of stay. These factors are additive.
Outcome by DRI of livers used at Penn

- 545 OLT recipients
- At 3 years, DRI did not reliably predict graft survival
  P = 0.282
Deceased Donor Age in US for Liver:

SRTR data

N = 5993

Increasing donor age: Upenn data

- Transplants performed at Penn Transplant Institute in 2010

![Age Distribution of DD OLT Donors (2010)](image)
Outcomes with elderly deceased donors

- While acceptable - general agreement that advanced age has lower graft and patient survival
- Use of older donors must be weighed against other risks

<table>
<thead>
<tr>
<th>Author</th>
<th>Rauchfuss et al\textsuperscript{14}</th>
<th>Singhal et al\textsuperscript{13}</th>
<th>Zapletal et al\textsuperscript{15}</th>
<th>Petridis et al\textsuperscript{22}</th>
<th>Emre et al\textsuperscript{17}</th>
<th>Washburn et al\textsuperscript{23}</th>
<th>Romero et al\textsuperscript{27}</th>
<th>Grazi et al\textsuperscript{18}</th>
<th>Grande et al\textsuperscript{19}</th>
<th>Ravaiolli et al\textsuperscript{28}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of transplants</td>
<td>54</td>
<td>4200</td>
<td>5</td>
<td>10</td>
<td>36</td>
<td>29</td>
<td>4</td>
<td>36</td>
<td>40</td>
<td>89</td>
</tr>
<tr>
<td>Age of donors (y)</td>
<td>≥65</td>
<td>60–79</td>
<td>≥80</td>
<td>≥80</td>
<td>≥70</td>
<td>≥60</td>
<td>≥80</td>
<td>≥70</td>
<td>&gt;60</td>
<td>&gt;60</td>
</tr>
<tr>
<td>Patient survival (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 y</td>
<td>77.8</td>
<td>83.8</td>
<td>81</td>
<td>100</td>
<td>80</td>
<td>91</td>
<td>58.6</td>
<td>100</td>
<td>77.4</td>
<td>82</td>
</tr>
<tr>
<td>3 y</td>
<td>–</td>
<td>71.8</td>
<td>69.1</td>
<td>–</td>
<td>40</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Allograft survival (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 y</td>
<td>75.9</td>
<td>77.4</td>
<td>75.5</td>
<td>100</td>
<td>70</td>
<td>85</td>
<td>44.8</td>
<td>66</td>
<td>73.3</td>
<td>77</td>
</tr>
<tr>
<td>3 y</td>
<td>–</td>
<td>64.2</td>
<td>61.2</td>
<td>–</td>
<td>20</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

Topics

- Anatomy/Surgical Technique
- Allocation
- Indications/Donor Selection
- Early post-transplant complications
- Outcomes
Primary Non-function (PNF)

- Non-life sustaining function of the liver transplant leading to re-transplant or death within 7 days of transplant
- Distinct from IPF (Initial Poor Function) or more recent designation EAD (Early Allograft Dysfunction)
- Has become more rare event with improved preservation solution and better understanding of graft quality/ischemia time tolerance
**Primary Non-function (PNF)**

### Table 1. Donor and Recipient Risk Factors for Primary Dysfunction After Liver Transplantation

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>IF N = 250</th>
<th>IPF N = 53</th>
<th>PNF N = 20</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trauma</td>
<td>88%</td>
<td>9%</td>
<td>5%</td>
<td>.07</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>79%</td>
<td>15%</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td><strong>IC hemorrhage</strong></td>
<td>67%</td>
<td>23%</td>
<td>10%</td>
<td>.05</td>
</tr>
<tr>
<td><strong>Hospital stay (days)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;3</td>
<td>80%</td>
<td>16%</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>3–4</td>
<td>74%</td>
<td>17%</td>
<td>9%</td>
<td>.03</td>
</tr>
<tr>
<td>&gt;4</td>
<td>73%</td>
<td>16%</td>
<td>11%</td>
<td></td>
</tr>
<tr>
<td><strong>Donor age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;16 y</td>
<td>83%</td>
<td>13%</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>16–48 y</td>
<td>77%</td>
<td>17%</td>
<td>6%</td>
<td>.03</td>
</tr>
<tr>
<td>&gt;49 y</td>
<td>45%</td>
<td>36%</td>
<td>19%</td>
<td></td>
</tr>
<tr>
<td><strong>Preservation time (hours)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–6</td>
<td>83%</td>
<td>14%</td>
<td>3%</td>
<td>.004</td>
</tr>
<tr>
<td>6–12</td>
<td>83%</td>
<td>13%</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>12–17</td>
<td>74%</td>
<td>18%</td>
<td>8%</td>
<td></td>
</tr>
<tr>
<td>&gt;17</td>
<td>62%</td>
<td>27%</td>
<td>11%</td>
<td></td>
</tr>
<tr>
<td><strong>Fatty changes biopsy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>81%</td>
<td>14%</td>
<td>5%</td>
<td>.0001</td>
</tr>
<tr>
<td>Mild (&lt;30%)</td>
<td>79%</td>
<td>16%</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>Moderate (30%–60%)</td>
<td>70%</td>
<td>30%</td>
<td>0%</td>
<td>.0001</td>
</tr>
<tr>
<td>Severe (&gt;60%)</td>
<td>0%</td>
<td>20%</td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td><strong>Reduced liver</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>81%</td>
<td>14%</td>
<td>5%</td>
<td>.0001</td>
</tr>
<tr>
<td>Yes</td>
<td>50%</td>
<td>34%</td>
<td>19%</td>
<td></td>
</tr>
<tr>
<td><strong>Recipient age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;16 years</td>
<td>71%</td>
<td>23%</td>
<td>6%</td>
<td>.03</td>
</tr>
<tr>
<td>16–44 years</td>
<td>75%</td>
<td>16%</td>
<td>9%</td>
<td></td>
</tr>
<tr>
<td>&gt;44 years</td>
<td>84%</td>
<td>13%</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td><strong>Renal insufficiency</strong></td>
<td></td>
<td></td>
<td></td>
<td>.02</td>
</tr>
<tr>
<td>No</td>
<td>79%</td>
<td>15%</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>52%</td>
<td>37%</td>
<td>11%</td>
<td></td>
</tr>
</tbody>
</table>

IF: immediate function; IPF: initial poor function; PNF: primary nonfunction; IC, intracranial hemorrhage. Univariate analyses: P value shows significance for increased IPF and PNF per risk factor: chi-square and Mantel Haenszel chi-square.

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**Risk Factors for Primary Dysfunction After Liver Transplantation in the University of Wisconsin Solution Era**

W. Broekelman, A.L. Stel, and R.J. Ploeg  
*Transplantation Proceedings, 31, 2067–2090 (1999)*
Primary Non-function (PNF)

- UW and Eurotransplant studies from 1999 in early UW solution era – 7% PNF
- Somewhat biased by very long cold ischemia times after UW introduced
- Relevant factors
  - Steatosis
  - Ischemia time
  - Donor age (much lower than current era)
  - Splits
  - Recipient renal failure
  - Stroke as cause of donor death
Primary Non-function (PNF)

- 2,061 of 58,576 (3.5% overall) met PNF criteria
- Risk factors
  - Donor – age, gender, race, DCD
  - Ischemia – warm and cold ischemia times
- What happens after PNF/Retransplant
  - 1121 re-transplanted (54%), 940 died (46%)

Patient Survival After PNF – IF RETRANSPANTED

<table>
<thead>
<tr>
<th></th>
<th>1 yr survival</th>
<th>3 yr survival</th>
<th>5 yr survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Function</td>
<td>87%</td>
<td>79%</td>
<td>73%</td>
</tr>
<tr>
<td>PNF/Retxp</td>
<td>67%</td>
<td>61%</td>
<td>54%</td>
</tr>
</tbody>
</table>

Long-term Analysis of Primary Nonfunction in Liver Transplant Recipients

N. Kemmer, M. Secic, V. Zacnarias, I. Kaiser, and U.W. Netter
EAD

- **EAD – Early Allograft Dysfunction**
- **300 pts from Penn, Northwestern, Columbia**
- **Factors**
  - Bilirubin $\geq 10$ on POD7
  - INR $\geq 1.6$ on POD7
  - ALT or AST $> 2000$ within first 7 days

<table>
<thead>
<tr>
<th>INR $&gt; 1.6$ at Day 7</th>
<th>Bilirubin $\geq 10$ at Day 7</th>
<th>ALT or AST $&gt; 2000$ in Week 1</th>
<th>Number of Patients (N)</th>
<th>6-Month Mortality N (% [95% CI])</th>
<th>6-Month Graft Failure N (% [95% CI])</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>+</td>
<td>+</td>
<td>5</td>
<td>2 (40.0% [5.3, 85.3])</td>
<td>2 (40.0% [5.3, 85.3])</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>-</td>
<td>28</td>
<td>3 (10.7% [2.2, 28.2])</td>
<td>4 (14.3% [4.0, 32.7])</td>
</tr>
<tr>
<td>-</td>
<td>+</td>
<td>-</td>
<td>26</td>
<td>5 (19.2% [6.6, 39.4])</td>
<td>7 (26.9% [11.6, 47.8])</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>-</td>
<td>4</td>
<td>1 (25.0% [0.1, 80.6])</td>
<td>2 (50.0% [6.8, 93.2])</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>-</td>
<td>2</td>
<td>0 (0.0% [0, 84])</td>
<td>0 (0.0% [0, 84])</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>+</td>
<td>4</td>
<td>2 (50.0% [6.8, 93.2])</td>
<td>3 (75.0% [19.4, 99.4])</td>
</tr>
</tbody>
</table>

*Validation of a Current Definition of Early Allograft Dysfunction in Liver Transplant Recipients and Analysis of Risk Factors*

*Kim M. Olthoff, Laura Kulik, Benjamin Samstein, Mary Kaminski, Michael Abecassis, Jean Emond, Abraham Shaked, and Jason D. Christie*
### TABLE 2. Univariate Association of Risk Factors with EAD

<table>
<thead>
<tr>
<th>Donor Variables</th>
<th>No EAD N = 228</th>
<th>EAD N = 69</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor age, years as continuous variable</td>
<td>43.8 ± 17.9</td>
<td>49.6 ± 15.8</td>
<td>0.019</td>
</tr>
<tr>
<td>Donation after cardiac death</td>
<td>10%</td>
<td>9%</td>
<td>0.81</td>
</tr>
<tr>
<td>Donor age &gt;45 years</td>
<td>53%</td>
<td>72%</td>
<td>0.004</td>
</tr>
<tr>
<td>Female sex</td>
<td>43.3%</td>
<td>39%</td>
<td>0.54</td>
</tr>
<tr>
<td>Race/ethnicity:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>70%</td>
<td>70%</td>
<td>0.80</td>
</tr>
<tr>
<td>African American</td>
<td>21%</td>
<td>23%</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>7%</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>Not reported</td>
<td>2%</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>170.9 ± 11.7</td>
<td>171.5 ± 11.5</td>
<td>0.74</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>76.3 ± 17.7</td>
<td>80.1 ± 16.6</td>
<td>0.13</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>26.0 ± 5.4</td>
<td>27.3 ± 5.6</td>
<td>0.11</td>
</tr>
<tr>
<td>Cause of death</td>
<td></td>
<td></td>
<td>0.089</td>
</tr>
<tr>
<td>Anoxia</td>
<td>12%</td>
<td>11%</td>
<td></td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>40%</td>
<td>48%</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>11%</td>
<td>21%</td>
<td></td>
</tr>
<tr>
<td>Trauma</td>
<td>30%</td>
<td>14%</td>
<td></td>
</tr>
<tr>
<td>N/A</td>
<td>7%</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>Traumatic death vs. all other causes</td>
<td>30%</td>
<td>14%</td>
<td>0.014</td>
</tr>
<tr>
<td>Recipient and Surgical Variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>53.5 ± 9.8</td>
<td>51.3 ± 10.4</td>
<td>0.10</td>
</tr>
<tr>
<td>Female sex</td>
<td>26%</td>
<td>30%</td>
<td>0.46</td>
</tr>
<tr>
<td>MELD</td>
<td>20.3 ± 8.9</td>
<td>22.0 ± 9.6</td>
<td>0.17</td>
</tr>
<tr>
<td>On ventilator</td>
<td>3%</td>
<td>6%</td>
<td>0.21</td>
</tr>
<tr>
<td>Status 1</td>
<td>4%</td>
<td>6%</td>
<td>0.61</td>
</tr>
<tr>
<td>On dialysis</td>
<td>5%</td>
<td>8%</td>
<td>0.46</td>
</tr>
<tr>
<td>Diagnosis of hepatitis C virus</td>
<td>60%</td>
<td>54%</td>
<td>0.34</td>
</tr>
<tr>
<td>Diagnosis of alcoholism</td>
<td>17%</td>
<td>16%</td>
<td>0.82</td>
</tr>
<tr>
<td>Total ischemic time, minutes</td>
<td>375.7 ± 131.9</td>
<td>397.4 ± 139.8</td>
<td>0.26</td>
</tr>
</tbody>
</table>

**NOTE:** Continuous variables are presented as means with standard deviations, and categorical variables as column percentages.
TABLE 3. Multivariable Analysis of Risk Factors for EAD

<table>
<thead>
<tr>
<th>Risk Factor Variable</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor age &gt;45</td>
<td>3.12</td>
<td>1.44, 6.69</td>
<td>0.004</td>
</tr>
<tr>
<td>MELD (per 10 units)</td>
<td>1.44</td>
<td>1.01, 2.05</td>
<td>0.043</td>
</tr>
<tr>
<td>Recipient age (per 10 year increase)</td>
<td>0.72</td>
<td>0.52, 1.01</td>
<td>0.060</td>
</tr>
<tr>
<td>Donor body mass index (per 5 kg/m²)</td>
<td>1.30</td>
<td>0.96, 1.75</td>
<td>0.087</td>
</tr>
<tr>
<td>Traumatic cause of death</td>
<td>0.63</td>
<td>0.26, 1.52</td>
<td>0.300</td>
</tr>
</tbody>
</table>

NOTE: The final model is also adjusted for total ischemic time and center.
- EAD associated with graft loss and patient death within 6 months
- Incidence of EAD – 23%

<table>
<thead>
<tr>
<th></th>
<th>Graft Loss (%)</th>
<th>Patient Death (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No EAD</td>
<td>3.5</td>
<td>1.8</td>
</tr>
<tr>
<td>EAD</td>
<td>26.1</td>
<td>18.8</td>
</tr>
</tbody>
</table>
EAD and DCD

- 205 DCD liver only recipients Mayo, Florida
- Incidence of EAD – 39.5% (1998-2011)

<table>
<thead>
<tr>
<th></th>
<th>1 year (%)</th>
<th>3 year (%)</th>
<th>5 year (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graft survival +EAD</td>
<td>79</td>
<td>61</td>
<td>54</td>
</tr>
<tr>
<td>-EAD</td>
<td>97</td>
<td>89</td>
<td>79</td>
</tr>
<tr>
<td>Patient Survival</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ EAD</td>
<td>64</td>
<td>53</td>
<td>43</td>
</tr>
<tr>
<td>-EAD</td>
<td>90</td>
<td>75</td>
<td>72</td>
</tr>
</tbody>
</table>
HAT

- **Hepatic Artery Thrombosis**
  - 2.5-6% in adults
  - 15-20% in pediatrics

Although, in many cases of HAT, no anatomical or technical causes can be identified, the following conditions are among the prominent predisposing factors: graft oedema due to poor initial graft function, multiple recipient arteries, coeliac trunk stenosis, lienalis steal syndrome, injury of the intima of the donor hepatic artery, previous transarterial chemoembolisation, split and living related liver transplantation, aneurysm of the donor hepatic artery, aberrant arteries with fragile intima and long backtable arterial reconstruction before implantation. Additional risk factors include increased blood product transfusion during transplant procedure, aortohepatic grafting, the need for infrarenal aorta vascular extension with respect to the use of supracoeliac aorta, and the presence of portal vein thrombosis before transplant.
Hepatic Artery Thrombosis

- ASA may reduce rate – 3.6% v 0.6%
- Early HAT
  - Graft ischemia/necrosis
  - Fever/sepsis
  - Increased transaminases
- Late HAT
  - Biliary complications (stricture/cholangitis)
  - May have preserved graft function otherwise

Within week 1 – relist 1A
Within week 2 – relist MELD 40
After week 2 - petition
Small for Size Syndrome

- Too small a functional mass of liver for the recipient
- Cholestasis
- Prolonged coagulopathy
- Portal hypertension
- Ascites
- Encephalopathy
- +/- GI Bleeding
Small for Size Syndrome

- Japanese experience with LDLT 2012
- Kiuchi – SFSG <0.8% graft to recipient weight (GW/RW)
- Sugawara – SFSG has graft volume: standard liver volume ratio < 40%
- As experience expanded, grafts down to 0.6% GW/RW have been successful with portal venous pressure modulation
- Acknowledge risk to donor larger with larger grafts
Small for Size Syndrome - Pathophysiology

- Can resect a normal liver to 25-27% residual volume
- Transplant impairs/restricts splanchnic circulation modulation (denervation)
- Portal hypertension increases flow/pressure
- Hepatocyte ballooning/cholestasis may be due to this microcirculation disturbance and shear stress
Small for Size Syndrome – Additive Factors

- Steatosis
- Age
- Ischemic injury (surgical complexity)
- Venous outflow impairment
- MELD (high MELD likely needs larger graft)
Topics

- Anatomy/Surgical Technique
- Allocation
- Indications/Donor Selection
- Early post-transplant complications
- Outcomes
Outcome after OLT: can you turn back time?

- **Survival Outcomes Following Liver Transplant (SOFT) score**
  - UNOS database, 2002-2006, > 21,000 recipients
  - Identified independent donor and recipient risk factors for post-txp mortality
  - 18 risk factors identified by multivariate analysis (13 recipient, 4 donor, 2 operative) and assigned points (0-14)
    - Most significant – previous transplant (14) and life support (9), followed by ICU (6), and then AGE
  - Add **4 points** for Age > 60 for P-SOFT score
  - Can **remove 5 points** if Donor <20 and **CIT <6 hours** for SOFT score

Rana et al, AJT 2008
Overall US post-OLT survival by MELD

Post-transplant patient survival of transplant recipients since 2010

Number at risk
- lab_meld_olt = <15
  - Months post-transplant:
    - 0: 9753
    - 15-29: 5421
    - 2436
    - 693
  - Proportion alive:
    - 1.00
- lab_meld_olt = 15-19
  - Months post-transplant:
    - 0: 5694
    - 15-29: 3290
    - 1558
    - 481
  - Proportion alive:
    - 1.00
- lab_meld_olt = 20-29
  - Months post-transplant:
    - 0: 8802
    - 15-29: 5075
    - 2429
    - 754
  - Proportion alive:
    - 1.00
- lab_meld_olt = 30-34
  - Months post-transplant:
    - 0: 8288
    - 15-29: 1822
    - 837
    - 226
  - Proportion alive:
    - 1.00
- lab_meld_olt = ≥35
  - Months post-transplant:
    - 0: 5623
    - 15-29: 2687
    - 1151
    - 323
  - Proportion alive:
    - 1.00

Legend:
- MELD<15
- MELD 15-19
- MELD 20-29
- MELD 30-34
- MELD ≥35
Overall US post-OLT survival by MELD

LDLT vs. DDLT - OPTN/UNOS database 2002-2012

Post-Transplant Patient Survival from 2002-2012

LDLT MELD < 15

DDLT MELD ≥ 30

LDLT MELD ≥ 30 (N=25)
- 5 died
- All were in the hospital pre-txp
- “Older” than those that survived (55-68)
- 3 on HD

All centers, all experience

Penn Transplant Institute
Location associated with mortality:
UNOS data 2002-2013

Pre-transplant ICU status impacts post-txp mortality independent of MELD score

- 3-month mortality: 4.9% at home, 7.5% hospitalized, 14.7% ICU
- 6-month mortality: 7.1% at home, 10.6% hospitalized, 18.6% ICU
- 12-month mortality: 10.5% at home, 14.8% hospitalized, 23.4% ICU

P < 0.001
DDLT Graft Survival: the Impact of Age

UNOS Database 2014

UNOS database 1990-2006
5630 pts >65

Survival Rate for Patients 65 and Over

Age 65-74

Age 75+

P=0.36
Impact of Pre-transplant Kidney Function

MELD >35

MELD 30-34

MELD 20-29

MELD 15-19
Sarcopenia, frailty, post-transplant survival, QoL

- X-sec imaging of psoas mm in 163 liver transplant recipients
- Negative assoc with survival

- Frailty and QoL measured in 457 patients
- QoL negatively associated with frailty but not MELD

Englesbee et al J Am Coll Surg 2010
Derck et al Transpl 2015
Pre-Transplant Comorbidities: Cardiac disease

- **Diffuse, non-repairable coronary artery disease**
  - Consider combined HLT

- **Severe portopulmonary hypertension**
  - Consider combined LLT
  - New medications available
    - Safdar et al Liver Trans 2012

- **Presence of LVDD found to predict 2 year mortality (p = 0.017)**
  - Karagiannakis et al, Hepatol Int 2014
Pre-Transplant Comorbidities: CKD and Diabetes

- 40 pts with pre-txp CKD (Cr > 2 for at least 3 mos) received OLT alone
- 35% mortality (mean 1.6 yrs post txp)
- Post-txp RRT - significant association with pre-txp diabetes

Impact of Functional Status and MELD score on Post-Transplant Coast

Adjusted total costs in the first post-transplant year by MELD score at each functional status category
Pre-Transplant Conditions Precluding Candidacy: when to say NO

High MELD has lower survival and requires more resources but is not an absolute

Recipients in ICU infected and intubated

Very old recipients (>75? >70?)

Significant renal dysfunction without the potential for kidney transplantation

Significant sarcopenia and frailty

Some medical comorbidities, such as pulmonary hypertension, severe CAD, etc.
Questions?
There does not seem to be any good risk stratification for whether this liver will work or not.

In such circumstances we should make a very nice publication on this subject.
Diagnostic Tree for Early Graft Issues

Levine MH, Feng S.
Small for Size Syndrome

- Symptoms abate with adequate liver regeneration
- Associated with elevated risk of mortality
- Graft loss
  - Absolute need
  - Concerns about slow recovery can lead to relisting/petition for points
- Tanaka *Transplantation* 1999 – ≥0.8% body ratio leads to 90% survival in LDLT
Small for Size Syndrome

- Sicker patients may need greater liver mass to avoid SFSS
  - Especially those with severe portal hypertension
- Increased portal flow relative to graft size speculated to be in part responsible
- Shunting *may* be of benefit
## High DRI – Economic Impact

![Bar chart showing hospital LOS by MELD category and DRI scores.](chart.png)

<table>
<thead>
<tr>
<th>MELD Category</th>
<th>0-10</th>
<th>11-20</th>
<th>21-30</th>
<th>31-35</th>
<th>&gt;35</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0-1.0</td>
<td>11.5</td>
<td>12.9</td>
<td>15.5</td>
<td>30.2</td>
<td>36.8</td>
</tr>
<tr>
<td>1.0-1.5</td>
<td>14.9</td>
<td>15.8</td>
<td>18.7</td>
<td>28.7</td>
<td>39.1</td>
</tr>
<tr>
<td>1.5-2.0</td>
<td>18.8</td>
<td>18.8</td>
<td>18.3</td>
<td>26.7</td>
<td>38.9</td>
</tr>
<tr>
<td>2.0-2.5</td>
<td>18.7</td>
<td>16.7</td>
<td>21.2</td>
<td>31.8</td>
<td>43.5</td>
</tr>
<tr>
<td>2.5+</td>
<td>23.2</td>
<td>27.9</td>
<td>38</td>
<td>42.1</td>
<td>53.4</td>
</tr>
</tbody>
</table>

**The Economic Impact of the Utilization of Liver Allografts with High Donor Risk Index**
Decision Making and DRI

Decision Making in Liver Transplantation—Limited Application of the Liver Donor Risk Index