Survival Benefit of Repeat Liver Transplantation in the US: A Serial MELD analysis by HCV status and DRI

Scott W. Biggins¹, Jennifer L. Dodge², Jane Gralla¹, Kiran M. Bambha¹, Hugo R. Rosen¹

¹ University of Colorado, Denver
² University of California, San Francisco
Background

• Need for liver transplant exceeds graft supply
• Optimal use liver grafts is dependent on appropriate candidate and donor liver selection

• For first liver transplant,
  – Survival benefit (Waitlist ≥ post LT mortality) generally occurs when MELD ≥ 15
  – Increased post LT mortality: recipient HCV, DRI

Survival Benefit of First Liver Transplant

MELD Threshold for Survival Benefit at MELD = 15

Merion Am J Transplantation 2005
AIMS

• To identify the MELD threshold for survival benefit from repeat liver transplant (ReLT)

• To assess influence of graft quality (using DRI) and HCV status on MELD threshold
Methods

- All waitlist new registrants in the US for ReLT
- All lab MELD scores (Listing to ReLT)
- HCV status (by code and text review)
  - Definite (at ReLT) or Probable (at LT1 but not ReLT)
- ReLT indication uniquely in hierarchical manner, independent of HCV status
- Interval from first LT to ReLT listing
  - Early (≤90 days) or Late (>90 days)
Analysis

- Cox proportional hazard models
  - Adjusting for recipient age, gender, race
  - MELD as a time-varying covariate

- Outcomes
  - Waitlist mortality rate (Death or “too sick”)
  - Post ReLT graft failure rate with 1 year

- Hazard Ratio for each MELD category
  - Post ReLT Event Rate/Waitlist Event Rate
## Results

### Subject Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Listed for ReLT (n=2564)</th>
<th>Received ReLT (n=1980)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at ReLT listing (IQR)</td>
<td>52 (46-57)</td>
<td>52 (46-57)</td>
</tr>
<tr>
<td>Male</td>
<td>69%</td>
<td>71%</td>
</tr>
<tr>
<td>Black Race</td>
<td>12%</td>
<td>12%</td>
</tr>
<tr>
<td>HCV definite/probable</td>
<td>54%</td>
<td>52%</td>
</tr>
<tr>
<td>Median MELD entries (IQR)</td>
<td>5 (3-10)</td>
<td>5 (3-9)</td>
</tr>
<tr>
<td>Events, n(%)</td>
<td>416 (16.2)</td>
<td>565 (28.5)</td>
</tr>
<tr>
<td>Follow up (IQR)*</td>
<td>33 (10-119)*</td>
<td>365 (172-365)**</td>
</tr>
</tbody>
</table>

*Days on waiting list for ReLT

**Days from ReLT to event (truncated at 1 year)
Indications for ReLT by Interval from First LT to Listing for ReLT

- **Early (90 days or less)**
- **Late (>90 days)**

<table>
<thead>
<tr>
<th>Category</th>
<th>Early (90 days or less)</th>
<th>Late (&gt;90 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAT</td>
<td>20%</td>
<td>10%</td>
</tr>
<tr>
<td>PNF</td>
<td>15%</td>
<td>5%</td>
</tr>
<tr>
<td>Vascular</td>
<td>5%</td>
<td>2%</td>
</tr>
<tr>
<td>Biliary</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Rejection</td>
<td>1%</td>
<td>0%</td>
</tr>
<tr>
<td>Recurrent</td>
<td>70%</td>
<td>60%</td>
</tr>
</tbody>
</table>

% in category
Results
Initial and Final Lab MELD

MELD at Listing

Final MELD, no ReOLT

Final MELD, with ReOLT
Event Rates
Waitlist and Post-ReLT by MELD

Event Rate
(per 1000 patient yrs)
Survival Benefit of Repeat Liver Transplant

Hazard Ratio

MELD Category

Survival Benefit of Repeat Liver Transplant

MELD Threshold for Survival Benefit at MELD = 21

Harm with ReLT

No Harm with ReLT
## Event Rate Modifiers in Waitlist and Post ReLT

<table>
<thead>
<tr>
<th></th>
<th>Waitlist Mortality (per 1000 patient years)</th>
<th>Post ReLT Mortality or GF (per 1000 patient years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>376</td>
<td>374</td>
</tr>
<tr>
<td>Increasing MELD</td>
<td>Increased*</td>
<td>Not increased</td>
</tr>
<tr>
<td>HCV vs Non-HCV</td>
<td>394 vs 351</td>
<td>417 vs 282 *</td>
</tr>
<tr>
<td>From first LT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 90 days vs &gt; 90 days</td>
<td>915 vs 311*</td>
<td>381 vs 371</td>
</tr>
<tr>
<td>DRI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low (&lt;1.15)</td>
<td>n/a</td>
<td>264*</td>
</tr>
<tr>
<td>Medium (1.15-1.45)</td>
<td></td>
<td>404</td>
</tr>
<tr>
<td>High (&gt;1.45)</td>
<td></td>
<td>467</td>
</tr>
</tbody>
</table>

* p<0.05

GF=Graft Failure
Survival Benefit MELD Threshold for ReLT by HCV status and Interval to ReLT Listing

<table>
<thead>
<tr>
<th>MELD Threshold for Benefit</th>
<th>First LT</th>
<th>ReLT</th>
<th>ReLT non-HCV</th>
<th>ReLT HCV</th>
<th>ReLT HCV Early</th>
<th>ReLT HCV Late</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>15</td>
<td>21</td>
<td>21</td>
<td>27</td>
<td>27</td>
<td>27</td>
</tr>
</tbody>
</table>
Survival Benefit MELD Threshold for ReLT by HCV status and DRI

MELD Threshold for Benefit

- First LT: Overall = 15
- ReLT: Low DRI = 21, Medium DRI = 24, High DRI = 21
- ReLT non-HCV: Overall = 2121
- ReLT HCV: Overall = 2727

Legend:
- Overall
- Low DRI
- Medium DRI
- High DRI
Conclusions

- MELD threshold for survival benefit with repeat liver transplantation is 21
- ReLT MELD threshold is higher than for first LT (MELD 15)
- For ReLT with HCV, MELD threshold is even higher (MELD 27) regardless of interval from first transplant
- Lower DRI livers can lower the MELD threshold in HCV candidates to a level similar to non-HCV candidates
Implications

• Urgency based allocation
  – High waitlist mortality rates in ReLT candidates may justify additional priority for ReLT candidates

• Utility based allocation
  – Higher MELD threshold for Survival Benefit with ReLT (21 v 15) may justify deferring or avoiding ReLT

  – If choosing to proceed with ReLT, good quality donors (low DRI) are needed, particularly in HCV infected candidates