Donor and Recipient Age Matching in Liver Transplantation: Can We Operationalize It?

David P. Foley, MD
Professor of Surgery
University of Wisconsin School of Medicine and Public Health
Disclosures

None
Learning Objectives

1. To discuss the challenges in the current liver allocation system with regard to matching donor and recipient ages.
2. To discuss liver transplant outcomes with age mismatching.
3. To discuss the potential benefits of age matching.
4. To discuss the barriers and strategies to potentially operationalize an age-matching liver allocation system.
Age Matching
Age Mismatching

34 years

25 years
US Liver Allocation and Distribution Policy
Implemented February 4, 2020

- candidates with highest medical urgency (Status 1A and 1B) listed at transplant hospitals within a radius of 500 nautical miles of the donor hospital
- candidates with a MELD or PELD score of 37 or higher listed at transplant hospitals within a radius of 150 nautical miles from the donor hospital
- candidates with a MELD or PELD score of 37 or higher listed at transplant hospitals within a radius of 250 nautical miles from the donor hospital
- candidates with a MELD or PELD score of 37 or higher listed at transplant hospitals within a radius of 500 nautical miles from the donor hospital
- a similar, continuing sequence of progressive offers (candidates at transplant hospitals within 150, 250 and 500 nautical miles of the donor hospital) for candidates with ranges of MELD or PELD scores from 33 to 36, from 29 to 32, and from 15 to 28

No Age Matching in Policy for Adults
Effects of No Age Matching

• Younger livers into older recipients
  – Good immediate function and outcomes
  – Decreased life years with transplant; DWFG?
  – Does it feel right?

• Older livers into younger recipients
  – Life saving for high MELD
  – Decreased long term survival

• Similar donor and recipient ages due to chance
Livers are allocated to patients and not to transplant centers.

A liver that is turned down for a patient goes to another patient at another center.
Utility vs. Justice

• Utility
  – System must achieve maximal possible good
  – Short term patient and graft survival
  – Life years gained or transplant benefit
  – Quality of life years added

• Justice
  – Equity in allocation
  – Patients with equal levels of need have equal opportunity/access
  – MELD system: Preserves equity over utility

Transplant Benefit

- Transplants between 2001-2007
- Post transplant survival modeled by Cox regression
- Donor and recipient factors
- Survival benefit based on “typical liver donor” (reference level for donor factors)

Schaubel et al. AJT, 2009
Distribution of Recipients by Age Categories in US and Europe

Imbalance of Donor and Recipient Age

A
Distribution of donors and recipients in liver transplantation by age categories in the United States 2016

B
Distribution of donors and recipients in liver transplantation (first transplantation) by age categories in France in 2016

Use of Older Donor Livers

- UNOS database analysis
- 14,796 LTx with Donor Age ≥ 60 years
- 1990 - 2014

Gao, Q et al. Ann Surg, 2018
# Use of Older Donor Livers

Gao, Q et al. Ann Surg, 2018

## TABLE 2. Characteristics of Recipients of Older Grafts (≥60), From 1990 to 2014

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of transplants (% of total)</td>
<td>730 (5.5%)</td>
<td>2137 (11.5%)</td>
<td>3382 (14.7%)</td>
<td>4431 (15.7%)</td>
<td>4116 (14.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median age, years (IQR)</td>
<td>51 (42–60)</td>
<td>52 (44–60)</td>
<td>54 (48–60)</td>
<td>56 (50–62)</td>
<td>59 (53–64)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median time on waiting list, days (IQR)</td>
<td>53 (12–151)</td>
<td>125 (26–299)</td>
<td>103 (23–348)</td>
<td>76 (18–242)</td>
<td>121 (32–321)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>White</td>
<td>589 (80.7%)</td>
<td>1644 (76.9%)</td>
<td>2511 (74.2%)</td>
<td>3244 (73.2%)</td>
<td>2995 (72.8%)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>43 (5.9%)</td>
<td>152 (7.1%)</td>
<td>254 (7.5%)</td>
<td>346 (7.8%)</td>
<td>316 (7.7%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>71 (9.7%)</td>
<td>246 (11.5%)</td>
<td>440 (13.0%)</td>
<td>569 (12.8%)</td>
<td>531 (12.9%)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>22 (3.0%)</td>
<td>67 (3.1%)</td>
<td>134 (4.0%)</td>
<td>233 (5.3%)</td>
<td>227 (5.5%)</td>
<td></td>
</tr>
<tr>
<td>Others/unknown</td>
<td>5 (0.6%)</td>
<td>28 (1.4%)</td>
<td>43 (1.2%)</td>
<td>39 (0.9%)</td>
<td>47 (1.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Patient acuity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICU</td>
<td>198 (27.2%)</td>
<td>509 (23.9%)</td>
<td>553 (16.4%)</td>
<td>468 (10.6%)</td>
<td>415 (10.1%)</td>
<td></td>
</tr>
<tr>
<td>Hospitalized, not in ICU</td>
<td>176 (24.1%)</td>
<td>512 (24.0%)</td>
<td>487 (14.4%)</td>
<td>635 (14.3%)</td>
<td>648 (15.7%)</td>
<td></td>
</tr>
<tr>
<td>Not hospitalized</td>
<td>355 (48.7%)</td>
<td>1113 (52.2%)</td>
<td>2342 (69.2%)</td>
<td>3328 (75.1%)</td>
<td>3053 (74.2%)</td>
<td></td>
</tr>
<tr>
<td>Laboratory tests, median (IQR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Albumin</td>
<td>2.9 (2.5–3.5)</td>
<td>2.8 (2.4–3.2)</td>
<td>2.8 (2.4–3.3)</td>
<td>2.9 (2.5–3.5)</td>
<td>3.1 (2.6–3.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>INR</td>
<td>N/A</td>
<td>1.5 (1.2–1.9)</td>
<td>1.5 (1.3–1.9)</td>
<td>1.6 (1.3–2.0)</td>
<td>1.6 (1.3–2.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.1 (0.8–1.7)</td>
<td>1.0 (0.8–1.4)</td>
<td>1.0 (0.8–1.5)</td>
<td>1.1 (0.8–1.5)</td>
<td>1.0 (0.8–1.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>N/A</td>
<td>N/A</td>
<td>3.2 (1.7–6.7)</td>
<td>3.4 (1.7–7.4)</td>
<td>3.3 (1.6–8.0)</td>
<td>0.181</td>
</tr>
<tr>
<td>Lab MELD</td>
<td>N/A</td>
<td>N/A</td>
<td>18 (13–24)</td>
<td>18 (13–25)</td>
<td>19 (13–27)</td>
<td>0.035</td>
</tr>
</tbody>
</table>
Liver Transplant Allocation Scenario

**Donor:**
- 22 yo male, BMI 24
- Self inflicted GSW to head
- Brain death confirmed
- No PMHx
- Minimal alcohol use
- LFTs normal
- Serologies negative

**Recipient**
- 62 yo male with cirrhosis from NASH, T2 DM, HTN
- Ascites, SBP
- BMI 38
- Hepatorenal Syndrome
- MELD 37
- CAD: 3 vessel disease, 20-30% stenosis
- Previous open ccy
Liver Transplant Allocation Scenario

**Donor:**
- 62 yo male
- Hemorrhagic CVA
- Brain death confirmed
- DM and HTN
- LFTs normal
- 5% macrosteatosis, 5% microsteatosis
- Serologies negative

**Recipient:**
- 35 yo male with cirrhosis from ALD
- Ascites, mild HE
- Recurrent variceal bleeds
- MELD 38
- No previous surgery
Recipient-Donor Age Matching in Liver Transplantation: A Single-Center Experience


- Single center, retrospective study
- 221 Adult liver transplants (2006-2009)
- Donor age < 60 and > 60
- Recipient age < 60 and > 60
- Age Matched
  - Donor < 60, Recipient < 60
  - Donor > 60, Recipient > 60
- Age Unmatched
  - Donor < 60, Recipient > 60
  - Donor > 60, Recipient < 60
Recipient-Donor Age Matching in Liver Transplantation: A Single-Center Experience


- Single center, retrospective study
- 221 Adult liver transplants (2006-2009)
- Donor age < 60 and > 60
- Recipient age < 60 and > 60
- Age Matched
- Donor < 60, Recipient < 60
  - Donor > 60, Recipient > 60
- Age Unmatched
  - Donor < 60, Recipient > 60
  - Donor > 60, Recipient < 60
• Retrospective, single center study
• 642 adult liver transplants in Barcelona (2000-2013)
• Donor age < 60 and ≥ 60 years
• Recipient age < 60 and ≥ 60 years
Does Matching Donor-Recipient Age Affect Long-Term Survival in Liver Transplantation?

Retrospective, single center study

642 adult liver transplants in Barcelona (2000-2013)

Donor age < 60 and > 60 years

Recipient age < 60 and > 60 years
Donor Age-Based Analysis of Liver Transplantation Outcomes: Short- and Long-Term Outcomes Are Similar Regardless of Donor Age

William C Chapman, MD, FACS, Neeta Vachharajani, BS, Kelly M Collins, MD, Jackie Garonzik-Wang, MD, Yikyung Park, ScD, Jason R Wellen, MD, FACS, Yiing Lin, MD, PhD, Surendra Shenoy, MD, PhD, Jeffrey A Lowell, MD, FACS, MB Majella Doyle, MD, FACS


- Retrospective, single center study
- 1036 Adult liver transplants (2001-2013)
- Donor age < 60 and > 60
- Recipient age < 60 and > 60
- Old to old (n = 60)
- Old to young (n=120)
- Young to young (n=489)
- Young to old (n =188)
Impact of Donor and Recipient Age

A

Survival probability

0.50 0.60 0.70 0.80 0.90 1.00

Analysis time (years)

0 1 2 3 4 5

Absolute 5-year survival difference 10.7%
p<0.001

Recipients < 40 years

Donor age <40 years
Donor age 40-59
Donor age ≥60 years

B

Survival probability

0.50 0.60 0.70 0.80 0.90 1.00

Analysis time (years)

0 1 2 3 4 5

Absolute 5-year survival difference 5.7%
p<0.001

Recipients > 60 years

Bitterman and Goldberg, Transplantation, 2018
## Impact of Donor and Recipient Age

### TABLE 1.
Results of multivariable model evaluating the interaction of donor and recipient age on the risk of graft failure and posttransplant mortality

<table>
<thead>
<tr>
<th>Donor age category, y</th>
<th>Recipient age category</th>
<th>Hazard ratio for the risk of graft failure (95% CI)</th>
<th>Hazard ratio for the risk of posttransplant mortality (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;40 y</td>
<td>1.43 (1.25-1.65)</td>
<td>1.37 (1.15-1.62)</td>
</tr>
<tr>
<td></td>
<td>40-59 y</td>
<td>0.90 (0.81-0.99)</td>
<td>1.10 (0.97-1.25)</td>
</tr>
<tr>
<td></td>
<td>≥60 y</td>
<td>1.07 (0.96-1.19)</td>
<td>1.49 (1.30-1.69)</td>
</tr>
</tbody>
</table>

Bitterman and Goldberg, Transplantation, 2018
Thinking about Age Matching

• Is it a transplantable donor liver?
• Is it a good match for my liver recipient?
• Is the “window closing?”
• Can I get the patient through the operation?
• Can I achieve good early post operative outcomes?
• Is this the best use of a scarce resource?
Can I get this patient through the operation with optimal outcome?

• Recipient risks of surgery:
  – Re transplant
  – Portal vein thrombosis
  – Significant portal hypertension
  – Previous upper abdominal surgery (open gastric bypass, previous major liver resection, open ccy)
  – Cardiac disease
Mortality Risk with Declining Liver Offer

Mortality Risk with Declining Liver Offer

Table 2: Unadjusted and adjusted waitlist outcomes among all non-Status 1 patients ranked first on at least one match run based on center acceptance patterns for first-ranked organ offers from 5/1/07-6/17/13, n = 11,533.*

<table>
<thead>
<tr>
<th>Adjusted percentage of first-ranked offers accepted at center</th>
<th>Centers</th>
<th>Patients</th>
<th>Waitlist mortality, No. (%)</th>
<th>Transplanted, No. (%)</th>
<th>Estimated adjusted waitlist mortality rates (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥50%</td>
<td>9</td>
<td>1002</td>
<td>61 (6.1)</td>
<td>926 (92.4)</td>
<td>5.4% (3.5-7.3%)</td>
</tr>
<tr>
<td>40-49.9%</td>
<td>31</td>
<td>4392</td>
<td>338 (7.7)</td>
<td>3937 (89.6)</td>
<td>8.4% (7.2-9.6%)</td>
</tr>
<tr>
<td>30-39.9%</td>
<td>37</td>
<td>3889</td>
<td>451 (11.6)</td>
<td>3316 (85.3)</td>
<td>12.0% (10.5-13.4%)</td>
</tr>
<tr>
<td>&lt;30%</td>
<td>27</td>
<td>2250</td>
<td>471 (20.9)</td>
<td>1689 (75.1)</td>
<td>17.9% (15.6-20.2%)</td>
</tr>
</tbody>
</table>

Age Matching

• Does the benefit of age matching outweigh the risks of waiting for another liver.
  – It depends on liver quality and MELD

• Should I skip a patient on the list to get a better age match?
  – It depends on liver quality and MELD
Impact of Donor and Recipient Age

A

Recipients < 40 years

Absolute 5-year survival difference 10.7%

Survival probability vs. Analysis time (years)

B

Recipients > 60 years

Absolute 5-year survival difference 5.7%

Survival probability vs. Analysis time (years)

Bitterman and Goldberg, Transplantation, 2018
Association between Kidney Transplant Center Performance and the Survival Benefit of Transplantation Versus Dialysis

Jesse D. Schold,*†‡ Laura D. Buccini,*§ David A. Goldfarb,†| Stuart M. Flechner,†| Emilio D. Poggio,†| and Ashwini R. Sehgal‡

Impact of Donor and Recipient Age

Recipients < 40 years

Absolute 5-year survival difference 10.7%

p < 0.001

Recipients > 60 years

Absolute 5-year survival difference 5.7%

p < 0.001

Bitterman and Goldberg, Transplantation, 2018
Liver Allocation Based on MELD

Figure 2. Estimated 3-month survival as a function of the MELD score.

Wiesner R et al. Gastroenterology, 2003
Age Matching in Current System

- Age matching in liver transplantation in current “equity” model of “sickest first” is challenging
- Age matching up front without considering MELD will lead to increased wait list deaths
- Fewer lives saved
Age Matching in Current System

• Without dialysis and VADs, liver transplantation more difficult
• Avoid futile transplants
• Continue “sickest first” at expense of utility
• Try for age matching at center level without significant risk of death on wait list
Liver Allocation for Pediatric Livers

• Priority for pediatric recipients before adult recipients at same level medical urgency
• Offered initially to compatible pediatric recipients within 500 nm of donor hospital

Age Matching in the Pediatric Liver Policy
Operationalize Age Matching to Increase Utility

- Is benefit of increased utility (age matching) greater than risk of increased wait list deaths?
- Donor livers: Age 18-30
- Prioritize for adult recipients: Age 18-30 at same level of medical urgency (within MELD)
- Will likely increase wait list deaths
- Challenging to change paradigm..