Challenges in lung allocation:
The sensitized candidate and the multi-organ candidate

Deborah Jo Levine MD
University of Texas Health Science Center
Disclosure

I have no disclosures.
Learning Objectives

• Describe how sensitized candidates are challenged by the current LAS system
• Discuss the issues of lung allocation with multi-organ candidates
• Identify pathways to possible resolutions of lung allocation challenges
Adult Lung Transplants
Number of Transplants by Year and Procedure Type

NOTE: This figure includes only the adult lung transplants that are reported to the ISHLT Transplant Registry. As such, this should not be construed as representing changes in the number of adult lung transplants performed worldwide.
Lung transplants by cPRA

Highly sensitized candidates:

- Decreased available donor pool
- Increased waiting time
- Increased death on the list

Valapour et al, SRTR 2018
Waitlist outcomes by cPRA

cPRA >50%:
- Decreased rate of transplant
- Increased wait list mortality

cPRA 50-75%:
- 25% less likely to undergo transplant
- 44% more likely to die on list

Aversa et al
Ann Transplant, 2019; 24: 383-392
Individual lung transplant candidate HLA percentages over time relative to desensitization therapy.

DSA MFI changes after perioperative desensitization

DSA MFI post transplant reduced at three time points:
- Immediately after transplant
- 3 months post transplant
- 6 months post transplant

Multiple listing (ML) associated with 2.7 fold increase in transplantation but not associated with waitlist mortality.


Annual number of ML between 2006-14.

Candidate characteristics associated with multiple listing
Lung transplants by cPRA

Valapour et al, SRTR 2018
Mrs. K. 36 yo

CF with mild portal hypertension listed for lung – liver transplantation

- 3 L FIO2
- FEV1 29%
- LAS 41
- MELD 20

Mrs. E. 40 yo

Severe NASH with Cirrhosis listed for liver transplant

- MELD 36
Mrs. K. 36 yo
CF with mild portal hypertension listed for lung – liver transplantation
- 3 L FIO2
- FEV1 29%
- LAS 41
- MELD 20

Mrs. E. 40 yo
Severe NASH with Cirrhosis listed for liver transplant
- MELD 36

Who will the liver offer go to?
How are multi-organ donors allocated?

A single donor can...

...save up to 8 lives through organ donation

...save or heal more than 100 lives through tissue donation

OR

A single donor can...

...save or heal more than 100 lives through tissue donation
Multi-organ allocation (MOT):
A challenge for every combination.
Policies differ based on organ types
• Increasing yearly over last 2 decades

• 3% of solid organ transplants are MOT

• Issue: Policies governing all MOT have not been developed consistently.

Multi-Organ Transplants Performed in the US from 2013-2017

<table>
<thead>
<tr>
<th></th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>1,459</td>
<td>1,508</td>
<td>1,625</td>
<td>1,801</td>
<td>1,853</td>
<td>8,246</td>
</tr>
<tr>
<td>Kidney-Pancreas</td>
<td>762</td>
<td>709</td>
<td>719</td>
<td>798</td>
<td>789</td>
<td>3,777</td>
</tr>
<tr>
<td>Liver-Kidney</td>
<td>494</td>
<td>558</td>
<td>627</td>
<td>730</td>
<td>739</td>
<td>3,148</td>
</tr>
<tr>
<td>Kidney-Heart</td>
<td>85</td>
<td>104</td>
<td>141</td>
<td>140</td>
<td>187</td>
<td>657</td>
</tr>
<tr>
<td>Liver-Intestines-Pancreas</td>
<td>50</td>
<td>69</td>
<td>67</td>
<td>58</td>
<td>55</td>
<td>299</td>
</tr>
<tr>
<td>Liver-Heart</td>
<td>16</td>
<td>18</td>
<td>28</td>
<td>18</td>
<td>29</td>
<td>109</td>
</tr>
<tr>
<td>Heart-Lung</td>
<td>23</td>
<td>24</td>
<td>15</td>
<td>18</td>
<td>29</td>
<td>109</td>
</tr>
<tr>
<td>Liver-Lung</td>
<td>7</td>
<td>6</td>
<td>9</td>
<td>9</td>
<td>8</td>
<td>39</td>
</tr>
<tr>
<td>Intestines-Pancreas</td>
<td>5</td>
<td>8</td>
<td>9</td>
<td>8</td>
<td>3</td>
<td>33</td>
</tr>
<tr>
<td>Kidney-Lung</td>
<td>7</td>
<td>5</td>
<td>1</td>
<td>4</td>
<td>7</td>
<td>24</td>
</tr>
<tr>
<td>Liver-Kidney-Intestines-Pancreas</td>
<td>6</td>
<td>3</td>
<td>2</td>
<td>7</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>Kidney-Intestines</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>5</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>Liver-Pancreas</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Liver-Intestines</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Kidney-Heart-Lung</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Liver-Kidney-Heart</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Liver-Heart-Lung</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Liver-Kidney-Pancreas</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Liver-Pancreas-Lung</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

https://optn.transplant.hrsa.gov/media/.../ethics_publiccomment_20190122.pdf
Potential conflicts in equity and utility in organ distribution (Both to MOT and SOT)

OPTN Ethics Committee analyzed current policy and literature building a foundation in order to modify policies in a consistent manner.
OPTN Policies for Specific Multi-Organ Combinations

• 6.6.F: Allocation of **Heart-Lungs**
• 9.9: Allocation of **Liver-Kidney**
• 11: Allocation of Pancreas, **Kidney-Pancreas and Islets**. Specifically these subsections:
  11.2.B Kidney-Pancreas Registration
  11.3.A Kidney-Pancreas Waiting Time Criteria for Candidates at least 18 years old
  11.4.A kidney-pancreas allocation

OPTN, 2019
Policy for all other combinations: 5.10C

5.10.C Other Multi-Organ Combinations

When multi-organ candidates are registered on the heart, lung, or liver waiting list, the second required organ will be allocated to the multi-organ candidate from the same donor according to Table 5-4.

<table>
<thead>
<tr>
<th>Organ</th>
<th>Candidate is registered at a transplant hospital that is at or within the following this distance of the donor hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>250NM</td>
</tr>
<tr>
<td>Liver</td>
<td>150NM</td>
</tr>
<tr>
<td>Lung</td>
<td>250NM</td>
</tr>
</tbody>
</table>

If the multi-organ candidate is on a waiting list outside the geographical areas listed above, it is permissible to allocate the second organ to the multi-organ candidate receiving the first organ.
5.10.C: It can get confusing

- Priority may impact areas of the country differently depending on whether a high volume MOT is near the donor hospital.

- It doesn’t specify prioritization *within* multi-organ combinations, that’s left up to *OPO discretion*. 
### 250 NM, MELD or PELD 33 to 36, O and B candidates

<table>
<thead>
<tr>
<th>Seq#</th>
<th>Center</th>
<th>Name</th>
<th>Age</th>
<th>ABO</th>
<th>Donor Weight (lbs)</th>
<th>Score</th>
<th>Height</th>
<th>Weight</th>
<th>BMI</th>
<th># Prev LTx</th>
<th>LI seg</th>
<th>Other Organs</th>
<th>SLK</th>
<th>Email/Fax Status</th>
<th>Offer Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>OHCOM-TX1</td>
<td></td>
<td>22</td>
<td>O</td>
<td>44-265</td>
<td>33.00</td>
<td>155cm / 61in</td>
<td>43kg / 96lbs</td>
<td>18</td>
<td>1</td>
<td>Y</td>
<td>KI</td>
<td>RQ</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 500 NM, MELD or PELD 33 to 36, O and B candidates

<table>
<thead>
<tr>
<th>Seq#</th>
<th>Center</th>
<th>Name</th>
<th>Age</th>
<th>ABO</th>
<th>Donor Weight (lbs)</th>
<th>Score</th>
<th>Height</th>
<th>Weight</th>
<th>BMI</th>
<th># Prev LTx</th>
<th>LI seg</th>
<th>Other Organs</th>
<th>SLK</th>
<th>Email/Fax Status</th>
<th>Offer Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>GAEM-TX1</td>
<td></td>
<td>68</td>
<td>O</td>
<td>50-350</td>
<td>36.00</td>
<td>160cm / 63in</td>
<td>73kg / 160lbs</td>
<td>28</td>
<td>0</td>
<td>Y</td>
<td>KI</td>
<td>P</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 150 NM, MELD or PELD 30 to 32, O and B candidates

<table>
<thead>
<tr>
<th>Seq#</th>
<th>Center</th>
<th>Name</th>
<th>Age</th>
<th>ABO</th>
<th>Donor Weight (lbs)</th>
<th>Score</th>
<th>Height</th>
<th>Weight</th>
<th>BMI</th>
<th># Prev LTx</th>
<th>LI seg</th>
<th>Other Organs</th>
<th>SLK</th>
<th>Email/Fax Status</th>
<th>Offer Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>WISE-TX1</td>
<td></td>
<td>55</td>
<td>O</td>
<td>40-400</td>
<td>31.00</td>
<td>165cm / 65in</td>
<td>95kg / 209lbs</td>
<td>35</td>
<td>0</td>
<td>Y</td>
<td>KI</td>
<td>RQ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>WISE-TX1</td>
<td></td>
<td>30</td>
<td>B</td>
<td>40-400</td>
<td>31.00</td>
<td>165cm / 65in</td>
<td>66kg / 145lbs</td>
<td>24</td>
<td>0</td>
<td>Y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>WISE-TX1</td>
<td></td>
<td>55</td>
<td>O</td>
<td>40-400</td>
<td>30.00</td>
<td>170cm / 67in</td>
<td>78kg / 171lbs</td>
<td>27</td>
<td>0</td>
<td>Y</td>
<td>KI</td>
<td>RQ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>ILUC-TX1</td>
<td></td>
<td>60</td>
<td>O</td>
<td>120-440</td>
<td>30.00</td>
<td>180cm / 71in</td>
<td>110kg / 243lbs</td>
<td>34</td>
<td>0</td>
<td>Y</td>
<td>KI HR</td>
<td>RQ</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Policy should reflect a balance between equity and utility

1. Medical benefit: (survival, urgency)
2. Quality of benefit
3. Avoiding futile transplants

1. Equality of opportunity
2. How it affects "worse off"
3. Fair innings concept
4. Those near death
5. First-come, first-served

https://optn.transplant.hrsa.gov/media/.../ethics_publiccomment_20190122. pdf
Impact on Equity versus Utility:
Ethical Implications of Multi-Organ Transplants

OPTN/UNOS Ethics Committee

• Degree of need
• Waitlists and the “pulling of organs”
• Organ quality
• Treatment options other than transplantation
• Prioritization of MOT over SOT
• Regionalization

• Protected subgroups
• Monitoring MOT in transplant programs
• Fairness to patients awaiting SOT
• Standardized criteria for MOT
• Relative futility
• Impact of adult MOT on pediatric SOT

https://optn.transplant.hrsa.gov/media/.../ethics_publiccomment_20190122. pdf
Need for transplant

• Candidates have varying levels of “need”
• What do we all consider “need”?
• Need can mean:
  – Lifesaving measure
  – Improve quality of life and longer term survival
  – Improves the short term post transplant period
Organ quality
Distribution of KDPI for kidney recipients

MOT recipients commonly receive lower KDPI kidneys than SOT recipients.

OPTN, 2019
MOT and Alternative Supportive Treatments

• MOT should be prioritized for candidates who have no alternative supportive treatments options.

  – Ie: Dialysis, LVAD, ECMO can support a candidate until an organ is available.
  – Many MOT are not eligible for these supportive therapies.
Standardized criteria for MOT

• Would bring clarity to MOT policy
  – No standard listing criteria for most MOT combinations.
  – Leads to inconsistency in the meaning of medical urgency.
  – ie: Candidate for kidney-lung who would not be eligible for SOT, (ie: eGFR > 20) but would be eligible for MOT.
  – No real criteria for MOT
Medical eligibility for liver-kidney

Candidate's Transplant Nephrologist Confirms a Diagnosis of | Transplant Program Must Document at least 1 of the following
---|---
CKD with a measured or calculated GFR $\leq$ 60 mL/min for $> 3$ months | - Candidate is on regular hemodialysis
- Candidate's most recent GFR is $\leq 30$ mL/min at the time of registration for kidney transplant
- Candidate is on dialysis at least 6 weeks
- Candidate's GFR is $\leq 25$ mL/min for at least 6 weeks (as documented in weekly measurements)
- Candidate has any combination of above 2 criteria for 6 weeks
Sustained AKI | - Hyperoxaluria
- aHUS from mutations in factor H or I
- Familial nonneuropathic systemic amyloidosis
- Methylmalonic aciduria
Metabolic disease |

Legend: CKD = chronic kidney disease, AKI = acute kidney injury. GFR = glomerular filtration rate, aHUS = atypical hemolytic uremic syndrome.

OPTN, 2019
“Safety-net” kidney transplant criteria for liver recipients with non-renal recovery

<table>
<thead>
<tr>
<th>Sequence A (KDPI ≤ 20%)</th>
<th>Sequence B (KDPI &gt; 20% &lt; 35%)</th>
<th>Sequence C (KDPI &gt; 35% &lt; 85%)</th>
<th>Sequence D (KDPI &gt; 85%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highly sensitised</td>
<td>Highly sensitised</td>
<td>Highly sensitised</td>
<td>Highly sensitised</td>
</tr>
<tr>
<td>O-ABO mismatch</td>
<td>O-ABO mismatch</td>
<td>O-ABO mismatch</td>
<td>O-ABO mismatch</td>
</tr>
<tr>
<td>Prior living donor KT</td>
<td>Prior living donor KT</td>
<td>Prior living donor KT</td>
<td>Local CLKT safety net</td>
</tr>
<tr>
<td>Local pediatrics</td>
<td>Local pediatrics</td>
<td>Local candidates</td>
<td>Local + regional</td>
</tr>
<tr>
<td>Local top 20% EPTS</td>
<td>Local CLKT safety net</td>
<td>Regional candidates</td>
<td>National candidates</td>
</tr>
<tr>
<td>O-ABO mismatch (all)</td>
<td>Local adults</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local (all)</td>
<td>Regional pediatrics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regional pediatrics</td>
<td>Regional adults</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regional (in 20%)</td>
<td>National pediatrics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regional (all)</td>
<td>National adults</td>
<td></td>
<td></td>
</tr>
<tr>
<td>National pediatrics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>National (top 20%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>National (all)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A place to start...

Data collecting of each MOT combination

Risk analysis for each model

Base MOT allocation on this risk assessment

Public reporting of all data and analysis

Standard of excellence as in SOT
Thank you!