OPTN/UNOS- Thoracic Organ Transplantation Committee: Proposed Modifications to Adult Heart Allocation

1) Develop additional urgency stratifications based on relative waiting list mortality rates for all adult heart candidates
2) Modify the geographic sharing scheme to provide the most medically urgent candidates access to donors from a broader geographic area
What problems is the proposal attempting to solve?

1) Too many status 1A candidates
2) Too many exception requests required
3) Increased use of MCSDs not accommodated by current system
4) Geographic sharing scheme is inequitable
Each zone = 500 mile radius
<table>
<thead>
<tr>
<th>Status</th>
<th>Proposed Criteria</th>
</tr>
</thead>
</table>
| 1      | i. ECMO  
   ii. Mechanical ventilation  
   iii. Non-dischargeable BiVAD or RVAD  
   iv. Mechanical circulatory support with life-threatening ventricular arrhythmia |
| 2      | i. Intra-aortic balloon pump  
   ii. Acute circulatory support device  
   iii. Mechanical circulatory support with device malfunction/mechanical failure  
   iv. Total artificial heart  
   v. Dischargeable BiVAD or RVAD |
| 3      | i. LVAD for up to 30 days  
   ii. Status 1A exception  
   iii. Multiple inotropes or single high-dose inotropes with continuous hemodynamic monitoring  
   iv. Mechanical circulatory support with device-related complications other than infection, thromboembolism, device malfunction/mechanical failure or life-threatening ventricular arrhythmia  
   v. Mechanical circulatory support with device infection  
   vi. Mechanical circulatory support with thromboembolism |
| 4      | i. Diagnosis of congenital heart disease (CHD) with:  
   a. Unrepaired/incompletely repaired complex CHD, usually with cyanosis  
   b. Repaired CHD with two ventricles (e.g., TOF, TOGV)  
   c. Single ventricle repaired with Fontan or modifications  
   ii. Diagnosis of ischemic heart disease with intractable angina  
   iii. Diagnosis of hypertrophic cardiomyopathy  
   iv. Diagnosis of restrictive cardiomyopathy  
   v. Stable LVAD candidates after 30 days  
   vi. Inotropes without hemodynamic monitoring  
   vii. Diagnosis of amyloidosis  
   viii. Refractant  
   ix. Status 1B exception |
| 5      | Combined organ transplants: heart-lung; heart-liver; heart-kidney |
| 6      | All remaining active candidates |
| 7      | Inactive/not transplantable |
Heart and Lung Allocation in Europe

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Heart and Lung Transplant Program University of Bologna
Conflict of Interest Disclosure

- I received Advisory board fees from Diaxonhit and Biotest
- My institution received research support from Novartis and Qiagen
- No off label drug or device use is mentioned in this presentation
Heart Transplant in Europe in 2014 n=2146

[Bar chart showing heart transplant rates per million population (p.m.p.) for various European countries, with the U.S.A. at 8.3 p.m.p. highlighted.]
Lung Transplant in Europe in 2014 n=1822
8-year trend of heart and lung transplant in Europe

Data from the Council of Europe – 27 countries
Rate of thoracic transplants over the total

Data from the Council of Europe – 27 countries
Variability in HT numbers

<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Czech</td>
<td>-26%</td>
</tr>
<tr>
<td>Croatia</td>
<td>340%</td>
</tr>
<tr>
<td>Hungary</td>
<td>164%</td>
</tr>
<tr>
<td>Slovenia</td>
<td>230%</td>
</tr>
<tr>
<td>Poland</td>
<td>19%</td>
</tr>
<tr>
<td>France</td>
<td>13%</td>
</tr>
<tr>
<td>Spain</td>
<td>10%</td>
</tr>
<tr>
<td>UK</td>
<td>35%</td>
</tr>
<tr>
<td>Germany</td>
<td>-26%</td>
</tr>
<tr>
<td>Italy</td>
<td>-27%</td>
</tr>
</tbody>
</table>
Numbers of heart transplants in France
Rules of priority allocation in France

SU1: Inotropes and/or ECMO with no implantable MCS

SU2: Complicated implantable MCS

SU3: TAH or pulsatile MCS (i.e. excor) non complicated >3 months
Rate of urgent cases over the total in 2014 (n= 423)

- SU1: 44%
- SU2: 11%
- SU3: 2%
- Non-Urgent: 43%
Cumulative incidence of transplant according with priority

Mortality/deterioration while on SU1 = 5%

Overall 1 y mortality on WL: 24%

<table>
<thead>
<tr>
<th>Dernière priorité</th>
<th>N</th>
<th>à 3 mois</th>
<th>à 6 mois</th>
<th>à 12 mois</th>
<th>à 24 mois</th>
<th>à 36 mois</th>
</tr>
</thead>
</table>
Survival according to urgency status
Increasing mean age of utilized donors
Coronary angiography increases heart utilization

In the CA performed group 74% of organs have been accepted vs. 64% in the CA not performed group (P=0.02)
Heart and Lung Transplant in Italy

Data from the National Transplant Center
Allocation system in Italy

• Standard allocation
  – Based on regional donor pool

• High urgency tier
  – Country-wide organ sharing area
  – ECMO or complicated VAD or IABP plus ventilator
  – Payback for urgency
High urgency for lung transplant

Table 1: Inclusion and exclusion criteria for Italian Urgent Lung Transplantation programme

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≤50 y/o</td>
<td>BMI &lt; 18 or &gt;30</td>
</tr>
<tr>
<td>MV and/or ECLS (except for DECAP°)</td>
<td>Sepsis</td>
</tr>
<tr>
<td>Previous LTx waiting list</td>
<td>Multiorgan failure</td>
</tr>
<tr>
<td></td>
<td>Haemorrhagic shock</td>
</tr>
<tr>
<td></td>
<td>Neurological damage</td>
</tr>
<tr>
<td></td>
<td>ECLS and/or MV &gt;14 days</td>
</tr>
</tbody>
</table>

MV: mechanical ventilation, ECLS: extracorporeal lung support, BMI: body mass index; LTx: lung transplantation.

Urgency program in Italy

Death/deterioration while waiting in urgent status:
- Heart: 23%
- Lung: 30%
High urgency lung Tx outcomes

1-y survival for non-high urgency cases: 70%

1-y heart survival trend

Data from the National Transplant Center
Heart donor age in Bologna

[Bar chart showing the median donor age from 2008 to 2015.]

- 2008: 30
- 2009: 35
- 2010: 40
- 2011: 45
- 2012: 50
- 2013: 55
- 2014: 40
- 2015: 60
Post-HT survival and donor age in Bologna

HTX 2001-10 (n=346)
Median donor age = 36 (24-47)

HTX 2011-15 (n=106)
Median donor age = 45 (18-52)
Ethical pillars of decision making

- Beneficence
  - Provide a benefit with transplant

- Non maleficence
  - Do not run unacceptable risks

- Autonomy
  - give the patient the possibility to make an informed and rationale choice
    - Are we enough rationale and informed to make a choice?

- Distributive justice
  - Allocate appropriately a scarce resource
    - What are the parameters for justice?
Equality doesn’t mean Justice

Equality  Justice
Ideal allocation system

- High-priority patients do have a high risk without transplantation;
- Transplantation will be performed with appropriately short waiting times for the highest priority patients;
- A reasonable proportion of patients can undergo transplantation at a lower priority level.

No priority system can be effective or even evaluable except in the context of a waiting list length that is matched to the current donor heart supply.

Stevenson LW, J Heart Lung Transplant 2013; 32: 861
### Urgency tiers and waiting times in Europe

<table>
<thead>
<tr>
<th>Country</th>
<th>Urgency tiers</th>
<th>Transplant rate per tier (%)</th>
<th>Median waiting list (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>Urgent</td>
<td>60</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>Non Urgent</td>
<td>40</td>
<td>293</td>
</tr>
<tr>
<td>France</td>
<td>SU1</td>
<td>39</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>SU2</td>
<td>8</td>
<td>102</td>
</tr>
<tr>
<td></td>
<td>Regional urgency</td>
<td>9</td>
<td>219</td>
</tr>
<tr>
<td></td>
<td>Non urgent</td>
<td>45</td>
<td>189</td>
</tr>
<tr>
<td>Spain</td>
<td>Urgent 0</td>
<td>14</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Urgent 1</td>
<td>21</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Non Urgent</td>
<td>66</td>
<td>80</td>
</tr>
<tr>
<td>Italy</td>
<td>Urgent</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Non Urgent</td>
<td>86</td>
<td>292</td>
</tr>
</tbody>
</table>

Stehlik J et al J Heart Lung Transplant 2014; 33:977
Distributive justice: set the line to connect competing interests

• Urgency allocation algorithms
  – Need to allocate a scarce resource to individuals at greater need
  – Need to allocate a scarce resource to individuals most likely to get a benefit
  – Need to avoid inequalities in the access to transplant of those who would not meet urgency criteria
Blood group disparities

Italian blood group distribution
- 39% A
- 17% B
- 37% AB
- 7% O

2014-15 HTX blood groups distribution
- 51% A
- 14% B
- 29% AB
- 6% O

Current waitlist blood groups distribution
- 65% A
- 33% B
- 2% AB
And if this little boy were blind?
Survival in HF patients evaluated for transplant (n=500)

- 7 – 9  Low risk
- 10 – 11  Moderate risk
- > 12  High risk

Survival in HF patients evaluated for transplant (n=500)

Follow-up (months)

Survival

- 7 – 9  Low risk
- 10 – 11  Moderate risk
- > 12  High risk

Survival

- 7 – 9  Low risk
- 10 – 11  Moderate risk
- > 12  High risk

Follow-up (months)

Survival
Transplant Benefit at 1 and 5 years

Providing the largest transplant benefit not necessarily provides the best figures on post-transplant survival.
Survival after HT (n=275)

- Low risk
- Moderate risk
- High risk

FUP - death

Prob survival

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

0 10 20 30 40 50 60 70 80 90 100 110 120

92% 89% 88% 86% 69%
Age-stratified comorbidity risk

Masetti M et al. manuscript in preparation
# Frailty and post HT survival

<table>
<thead>
<tr>
<th></th>
<th>Total (n = 34)</th>
<th>Nonfrail or prefrail (n = 25)</th>
<th>Frail (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>49 ± 15</td>
<td>50 ± 14</td>
<td>46 ± 18</td>
</tr>
<tr>
<td>Sex (male:female)</td>
<td>18:16</td>
<td>16:9</td>
<td>2:7</td>
</tr>
<tr>
<td>Intubation, h</td>
<td>28 (103)</td>
<td>27 (98)</td>
<td>110 (116)</td>
</tr>
<tr>
<td>ICU after HTx, d</td>
<td>7 (5)</td>
<td>6 (4)</td>
<td>8 (10)</td>
</tr>
<tr>
<td>LOS after HTx, d</td>
<td>25 (17)</td>
<td>24 (14)</td>
<td>27 (36)</td>
</tr>
<tr>
<td>Survival at 6 mo</td>
<td>93 ± 5%</td>
<td>100%</td>
<td>79 ± 14%</td>
</tr>
<tr>
<td>Survival at 12 mo</td>
<td>86 ± 8%</td>
<td>100%</td>
<td>52 ± 23%</td>
</tr>
</tbody>
</table>

Values are mean ± SD for normally distributed continuous data, median (interquartile range) for non-normally distributed continuous data, and number for categorical data.

HTx indicates heart transplantation; LOS, length of stay.
Donor-recipient match and outcome

Rate of Severe PGD

LR donor to LR recipient (n=211)  HR donor to LR recipient (n=212)  LR donor to HR recipient (n=15)  HR donor to HR recipient (n=33)

Sabatino M et al. manuscript in preparation
Summary

• Thoracic transplantation numbers are stable overall in Europe, with some emerging countries increasing volume and remarkable loss of volume in some other countries.

• Allocation policies are highly variable, but mainly based on a mixed model in which geography prevails on severity (limited number of severity tiers).
Unmet needs

• Shared policies to improve thoracic organ retrieval
• Develop tools to aid clinicians to optimize decision making about appropriate risk matching
  – Balancing the risk of waiting vs. accepting borderline donors (appropriate MCS development)
  – Identify tools to objectively allocate priorities (based on physiology and not on treatment)
  – Auditing systems that set up quality standards with outcome measures accounting for cases complexity, and urgency appropriateness
Question 1

How many urgency tiers are acceptable?
A. 1
B. 2
C. 3
D. more
Question 2

Should the donor risk be considered in the allocation algorithm?

A. Yes
B. No
Question 3

Should the recipient risk enter the allocation algorithm?

A. Yes
B. No