Developing a Risk Score in Heart Transplantation

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Conflict of Interest Disclosure

• Grant Funding
  – NIH (NHLBI, R01)
  – American Heart Association

• CareDx, Inc: consultant, advisory board, speakers’ bureau
Decline in donor heart utilization nationwide

SRTR data 1995-2010,
All DNDD donors aged 14-70 years

- High: 44% in 1995
- Low: 29% in 2006
- Current: 32%

- Waiting time has increased by 3.5 months for status 1B and 9.3 months for status 2 recipients.
Regional variability in donor heart acceptance for transplant

Advantages of having a risk score

- Tool that can be used “real time” for decision-making during an organ offer
- Applies evidence-based data, using donor and recipient risk factors, to predict transplant outcomes
- Standardize donor heart acceptance across the country
- Improve donor heart utilization
Kidney Donor Risk Index (KDRI)

- Real-time tool that combines donor risk factors to summarize the risk of graft failure after kidney transplant
- A donor with a KDPI of 80% has a higher expected risk of graft failure than 80% of all kidney donors recovered last year
- Launched on-line and as an app
Liver Donor Risk Index (LDRI)
How do we combine donor and recipient risk?

Low risk donor:  
Low risk recipient

High risk donor:  
High risk recipient

High risk donor:  
Low risk recipient

Low risk donor:  
High risk recipient
High risk donor: High risk recipient

**PRO**
- Offer a heart that may have been discarded to a recipient who otherwise may not have been eligible for transplant
- Use “marginal” donor hearts for sickest patients, since they are likely to have a survival benefit, even though post-transplant outcomes may be sub-optimal

**CON**
- Transplanting a high-risk donor heart into a high-risk recipient may be considered an irresponsible accumulation of risk with a high likelihood of patient death after transplant.
High risk donor: Low risk recipient

**PRO**
- Higher likelihood of graft survival

**CON**
- Placing our “best” candidates at a disadvantage?
- Reducing long-term survival
Balancing Risk: Impact of Transplant Center Volume

Does institutional volume impact outcomes after HTx using marginal donor hearts?

- UNOS registry analysis, N=3200, 2000-2010
- Identified marginal donors (>90th percentile in Weiss donor risk index)
- Stratified into tertiles based on transplant center volume (<14, 14-25, >25)
- Examined post-transplant outcomes

Impact of transplant center volume

Marginal vs. Standard Donors

- Recipients of marginal donor hearts were higher risk than recipients of standard donor hearts (IMPACT score 6.2 vs 5.6, p<0.001)

- A higher proportion of HTxs at high volume centers was performed using a marginal donor (high 22.4%, low 16.2%)

- High-volume centers had highest average donor risk index

Impact of transplant center volume

Impact of center volume on 1-year mortality in marginal recipients

1-year survival

Kaplan-Meier Survival (%)
Balancing Risk: Impact of transplant center volume

Conclusions

- Marginal donor heart transplants are more complex (higher donor risk, higher recipient risk, higher complication rates)

- Transplant center experience plays an important role
  - Experienced personnel
  - Experience selecting marginal hearts (e.g. older donors with short ischemic time)
  - Standardized clinical pathways
  - Dedicated ICU and ancillary staff
Balancing Risk

Donor Risk

Recipient Risk

Transplant Center Risk
Looking forward

- High-risk transplants should ideally be performed at high-volume centers.

- Introduction of a risk stratification scheme may prevent penalizing centers that transplant higher risk donors and recipients by accounting for case mix in quality and reimbursement measures.

- Rigorous, high-quality data required to develop a real-time risk score incorporating donor- and recipient-specific variables are lacking
Evidence-Based Evaluation and Acceptance of Donor Hearts for Transplantation

- Funded by National Institutes of Health
- 5-year prospective study
- 5,000 potential heart donors

PI: Kiran Khush, Stanford
Co-I: Darren Malinoski, OHSU
Co-I: Jonathan Zaroff, KPSF
7 participating high-volume OPOs representing 6 UNOS regions
Aim 1: To collect systematic data on cardiac structure and function in a nationally-representative cohort of potential heart donors

- Serial ECG, TnI, BNP during donor management
- Serial TTEs in donors with LV dysfunction (EF<50%) with core interpretation
- Data collection on donor heart acceptance
Aim 1: To collect systematic data on cardiac structure and function in a nationally-representative cohort of potential heart donors

Study Databases

- Stanford REDCap
- DMG Web Portal
Aim 2: To collect real-time detailed data on reasons for donor heart non-acceptance

<table>
<thead>
<tr>
<th>RECIPIENT ISSUES</th>
<th>DONOR ISSUES</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Recipient DNR</td>
<td>□ Donor age</td>
</tr>
<tr>
<td>□ Unavailable</td>
<td>□ Gender male</td>
</tr>
<tr>
<td>□ Declined</td>
<td>□ Female</td>
</tr>
<tr>
<td>□ Recipient's condition improved, transplant not needed</td>
<td>□ Height disparity</td>
</tr>
<tr>
<td>□ Multiple organ transplant</td>
<td>□ Weight disparity</td>
</tr>
<tr>
<td>□ Recipient declined due to high risk donor</td>
<td>□ Public Health Service (PHS) high risk:</td>
</tr>
<tr>
<td>□ Medical urgency of another potential recipient</td>
<td>- HIV</td>
</tr>
<tr>
<td>□ Other (specify)</td>
<td>□ Hep B</td>
</tr>
<tr>
<td></td>
<td>□ Hep C</td>
</tr>
<tr>
<td></td>
<td>□ HIV Drug</td>
</tr>
<tr>
<td></td>
<td>□ Renal failure</td>
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<tr>
<td></td>
<td>□ Other</td>
</tr>
<tr>
<td></td>
<td>□ Social history:</td>
</tr>
<tr>
<td></td>
<td>□ Alcohol use</td>
</tr>
<tr>
<td></td>
<td>□ Drug use:</td>
</tr>
<tr>
<td></td>
<td>□ Other</td>
</tr>
<tr>
<td></td>
<td>□ Infectious disease:</td>
</tr>
<tr>
<td></td>
<td>□ Other</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TRANSPLANT CENTER ISSUES</th>
<th>HISTOCOMPATIBILITY REASONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Surgeon unavailable</td>
<td>□ ABO incompatible</td>
</tr>
<tr>
<td>□ Heavy workload in OR</td>
<td>□ Positive crossmatch</td>
</tr>
<tr>
<td>□ Distance too far</td>
<td>□ Number of HLA mismatches unacceptable</td>
</tr>
<tr>
<td>□ Exceeded 1 hour response time</td>
<td>□ No serum for crossmatching</td>
</tr>
<tr>
<td>□ Logistics (specify)</td>
<td>□ High OPA</td>
</tr>
<tr>
<td>□ Minimum acceptance criteria not met</td>
<td>□ Other (specify)</td>
</tr>
<tr>
<td>□ Other (specify)</td>
<td>□ Other (specify)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>OTHER</th>
<th>OTHER</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Specify:</td>
<td>□ Specify:</td>
</tr>
</tbody>
</table>

| Survey Completed by: □ Surgeon □ Surgical Fellow □ Cardiologist □ Cardiology Fellow □ NP □ Nurse Coord. |
|--------------------------------------------------|--------------------------------------------------|
| Offer made to □ Surgeon □ Surgical Fellow □ Cardiologist □ Cardiology Fellow □ NP □ Nurse Coord. |
| Potential transplant recipient number: ___ Sequence/Rank No. ___ |
| Donor UNOS ID: ___ |
| Data: Time: Transplant Center: ___ |

CUTTING EDGE OF TRANSPLANTATION 2016
RESOLVING THE ORGAN SHORTAGE
PRACTICE | POLICY | POLITICS
Aim 3: To develop clinical tools to assist transplant centers with real-time decisions about donor heart acceptance

- Risk models for recipient outcomes, given donor and recipient characteristics at the time of an organ offer
## Sample Donor Heart Report

### Donor Characteristics:

<table>
<thead>
<tr>
<th>Age</th>
<th>Gender</th>
<th>Cause of Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>45</td>
<td>Male</td>
<td>Stroke</td>
</tr>
</tbody>
</table>

### Donor Health:

<table>
<thead>
<tr>
<th>Hypertension</th>
<th>Diabetes</th>
<th>Coronary Artery Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

### Echo Results:

<table>
<thead>
<tr>
<th>Ejection Fraction</th>
<th>Regional Wall Motion Abnormalities</th>
<th>Left Ventricular Hypertrophy</th>
</tr>
</thead>
<tbody>
<tr>
<td>58%</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

A heart with these characteristics has been transplanted 83% of the time. 97% of patients with a similar heart survive at least 30 days and 92% survive 1 year. It is expected that you would have to wait on average 6 months to be offered a more desirable heart.
Study Goals

• Standardized data collection on donor characteristics nationwide
• To study prevalence and reversibility of cardiac dysfunction after brain death
• To identify biomarkers that define organ quality
• Detailed examination of current donor heart acceptance practices
• To identify donor predictors of recipient outcomes
• To develop tools that can be used real-time in decision making for donor heart acceptance
Thank you