Conflict of Interest Disclosure

- Research support from Astellas (investigator initiated clinical trial)
- No off-label use
Agenda

• Hypertrophy
• Age
• Coronary artery disease
• Dysfunctional donors
• 2007-2014 Snapshot with Donor Sequence Numbers
Left Ventricular Hypertrophy

The Use of Donor Hearts with Left Ventricular Hypertrophy

Daniel Marelli, MD, Hillel Laks, MD, Daniel Fazio, BS, Sara Moore, BA, Jaime Moriguchi, MD, and Jon Kobashigawa, MD


n-=37
Mild vs Mod LVH
P=0.11
Use of Cardiac Allografts With Mild and Moderate Left Ventricular Hypertrophy Can Be Safely Used in Heart Transplantation to Expand the Donor Pool

Sorel Goland, MD, Lawrence S. C. Czer, MD, Robert M. Kass, MD, Robert J. Siegel, MD, James Mirocha, MS, Michele A. De Robertis, RN, Jason Lee, BS, Sharo Raissi, MD, Wen Cheng, MD, Gregory Fontana, MD, Alfredo Trento, MD
Impact of Donor Left Ventricular Hypertrophy on Survival After Heart Transplant

O. Wever Pinzon\textsuperscript{a,b,c}, G. Stoddard\textsuperscript{a}, S. G. Drakos\textsuperscript{a,c}, E. M. Gilbert\textsuperscript{a,b}, J. N. Nativi\textsuperscript{a,b}, D. Budge\textsuperscript{c}, F. Bader\textsuperscript{a,b}, R. Alharethi\textsuperscript{c}, B. Reid\textsuperscript{c}, C. H. Selzman\textsuperscript{a,b}, M. D. Everitt\textsuperscript{d}, A. G. Kfoury\textsuperscript{c} and J. Stehlik\textsuperscript{a,b,*}

- 2626 donors
- 1002 mild LVH, 148 mod-severe LVH
Age and Ischemic Time

Donor age > 55 years

- Absent
- Mild
- Moderate-Severe

Left Ventricular Hypertrophy

Hazard Ratio for Death

Donor age ≤ 55 years

- Absent
- Mild
- Moderate-Severe

Left Ventricular Hypertrophy

Hazard Ratio for Death

Ischemic time ≥ 4h

- Absent
- Mild
- Moderate-Severe

Left Ventricular Hypertrophy

Hazard Ratio for Death

Ischemic time < 4h

- Absent
- Mild
- Moderate-Severe

Left Ventricular Hypertrophy

Hazard Ratio for Death
Impact of Older Donors

CAD of the Donor

Coronary atherosclerosis of the donor heart – impact on early graft failure

Onnen Grauhan, Henryk Siniawski, Michael Dandel, Hans Lehmkuhl, Christoph Knosalla, Miralem Pasic, Yu-Guo Weng, Roland Hetzer


1253 Donor Grafts
(1168 included, 85 excluded)

NDCAS
(n=1086)

grafts with DCAS
(n=82)

DCAS 1
(n=53)

DCAS 2/3
(n=26)

DCAS 123
(n=3)
Single Vessel Disease vs Multivessel

One vessel CAD does not influence survival within limits of selection bias of this study.
Dysfunctional Donors

- Not a new problem

  Donor shortage: use of the dysfunctional donor heart.
  PMID: 8312334
  Related citations

- Likely related to catecholamine surge from brain death
- May be similar to Takosubo / stress cardiomyopathy
**Research Correspondence**

Frequency and Pattern of Left Ventricular Dysfunction in Potential Heart Donors

Implications Regarding Use of Dysfunctional Hearts for Successful Transplantation

*Burhan Mohamedali, MD  Geetha Bhat, PhD, MD
Allan Zelinger, MD

*University of Illinois at Chicago (UIC)

**Table 1** Summary of 11 Potential Donors With Cardiac Dysfunction

<table>
<thead>
<tr>
<th>Age (Yrs)</th>
<th>Sex</th>
<th>Cause</th>
<th>Dysfunction Pattern</th>
<th>Peak Troponin I</th>
<th>Peak CK-MB</th>
<th>Pressors</th>
<th>Initial EF</th>
<th>Repeat EF</th>
<th>Repeat EF Time Frame</th>
</tr>
</thead>
<tbody>
<tr>
<td>31</td>
<td>Male</td>
<td>Head trauma</td>
<td>Diffuse global</td>
<td>0.55</td>
<td>7.0</td>
<td>Desmopressin, phenylephrine</td>
<td>34%</td>
<td>45%</td>
<td>10 h</td>
</tr>
<tr>
<td>46</td>
<td>Male</td>
<td>Drug overdose</td>
<td>Diffuse global</td>
<td>9.57</td>
<td>27.6</td>
<td>Dopamine, norepinephrine</td>
<td>40%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>Male</td>
<td>Vehicle accident</td>
<td>Diffuse global</td>
<td>0.36</td>
<td>38.9</td>
<td>Dopamine, phenylephrine</td>
<td>25%</td>
<td>60%</td>
<td>10 h</td>
</tr>
<tr>
<td>20</td>
<td>Male</td>
<td>Gun shot head</td>
<td>Basal</td>
<td>1.55</td>
<td>22.0</td>
<td>Norepinephrine</td>
<td>45%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>Female</td>
<td>Drug overdose</td>
<td>Diffuse global</td>
<td>2.92</td>
<td>6.5</td>
<td>Dopamine, phenylephrine</td>
<td>12%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>Male</td>
<td>Gun shot head</td>
<td>Diffuse global</td>
<td>0.73</td>
<td>33.9</td>
<td>Desmopressin</td>
<td>30%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>55</td>
<td>Female</td>
<td>SAH</td>
<td>Basal</td>
<td>NA</td>
<td>14.7</td>
<td>Desmopressin, phenylephrine</td>
<td>43%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>Male</td>
<td>Gun shot head</td>
<td>Midcavity</td>
<td>4.14</td>
<td>14.1</td>
<td>No pressors</td>
<td>35%</td>
<td>41%</td>
<td>3 h</td>
</tr>
<tr>
<td>63</td>
<td>Male</td>
<td>SAH</td>
<td>Basal</td>
<td>3.22</td>
<td>17.6</td>
<td>Desmopressin</td>
<td>40%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>51</td>
<td>Female</td>
<td>Cardiac arrest</td>
<td>Apical</td>
<td>0.32</td>
<td>14.1</td>
<td>Desmopressin</td>
<td>35%</td>
<td>56%</td>
<td>36 h</td>
</tr>
<tr>
<td>42</td>
<td>Male</td>
<td>Gun shot head</td>
<td>Apical</td>
<td>NA</td>
<td>NA</td>
<td>Phenylephrine</td>
<td>30%</td>
<td>60%</td>
<td>10 h</td>
</tr>
</tbody>
</table>
How Do We Place Available Donors?

- DonorNet launched in 2006 from UNOS
- Assigns PTR (potential transplant recipient) # based on exact priority on the waiting list
- Electronic notification, availability of documents and some images across all US centers
- Simplified notification and communication among the OPO and local coordinators and potentially distant accepting physicians
- Transparent - Can see how many candidates are ahead and behind as well as real time “provisional acceptance” and denial codes
Downsides of Electronic Notifications

• Relies on correct information in chart
  – Echo’s change, details may develop
• Reduces personal element of discussion
• By showing the full list, may create a psychological disincentive to take organs turned down by others
Donor Sequence # and Survival

• Queried UNOS /OPTN for custom dataset with PTR #s
• 13,481 adult heart transplants with PTR data from 5/1/2007 – 3/31/2014
• Disclaimer: Analyses in progress, UNPUBLISHED at this moment
• Accepted at ISHLT 2016 for presentation
### Snapshot 2007-2014: 13,481 Hearts

<table>
<thead>
<tr>
<th>Factor</th>
<th>Range</th>
<th>Mean ± Std Dev</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male Recipient</td>
<td>74%</td>
<td></td>
</tr>
<tr>
<td>Recipient Age</td>
<td>18-79</td>
<td>52.63 ± 12.84</td>
</tr>
<tr>
<td>Days Status 1A Waiting</td>
<td>0-943</td>
<td>24.76 ± 47.27</td>
</tr>
<tr>
<td>Days Status 1B Waiting</td>
<td>0-1904</td>
<td>77.82 ± 141.74</td>
</tr>
<tr>
<td>Days Status 2 Waiting</td>
<td>0-3164</td>
<td>65.88 ± 201.54</td>
</tr>
<tr>
<td>Donor Age</td>
<td>9-66</td>
<td>31.68 ± 11.7</td>
</tr>
<tr>
<td>Male Donor</td>
<td>71%</td>
<td></td>
</tr>
<tr>
<td>Donor Gender Mismatch</td>
<td>74.1%</td>
<td></td>
</tr>
<tr>
<td>Female Donor into Male Recip</td>
<td>14.3%</td>
<td></td>
</tr>
<tr>
<td>Donor HTN</td>
<td>15%</td>
<td></td>
</tr>
<tr>
<td>Donor Smoking hx</td>
<td>14.2%</td>
<td></td>
</tr>
<tr>
<td>Donor Diabetes</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>Donor “CDC High Risk”</td>
<td>10.5%</td>
<td></td>
</tr>
<tr>
<td>Ischemic Time</td>
<td>0.22-12 hours</td>
<td>3.24 ± 1.06</td>
</tr>
<tr>
<td>Donor LVEF</td>
<td>40-81%</td>
<td>61.6 ± 7.1</td>
</tr>
</tbody>
</table>
Donor PTR/ Sequence #

Quantiles

<table>
<thead>
<tr>
<th>Percentile</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>100.0%</td>
<td>maximum 1263</td>
</tr>
<tr>
<td>99.5%</td>
<td>291.28</td>
</tr>
<tr>
<td>97.5%</td>
<td>84</td>
</tr>
<tr>
<td>90.0%</td>
<td>27</td>
</tr>
<tr>
<td>75.0%</td>
<td>quartile 10</td>
</tr>
<tr>
<td>50.0%</td>
<td>median 3</td>
</tr>
<tr>
<td>25.0%</td>
<td>quartile 1</td>
</tr>
<tr>
<td>10.0%</td>
<td>1</td>
</tr>
<tr>
<td>2.5%</td>
<td>1</td>
</tr>
<tr>
<td>0.5%</td>
<td>1</td>
</tr>
<tr>
<td>0.0%</td>
<td>minimum 1</td>
</tr>
</tbody>
</table>

Summary Statistics

Mean 13.364236
Std Dev 45.689345
Std Err Mean 0.395538
Upper 95% Mean 14.139546
Lower 95% Mean 12.588925
N 13343
Survival, n=13,438, 2007-2014

74.5% Survival
Sequence #: Survival Similar

- For Sequence > 10 and Sequence 1-10, the survival rates are similar with a p-value of 0.21.
- For Sequence > 30 and Sequence 1-30, there is a slight difference with a p-value of 0.10.

Graph showing survival rates over years post transplant.
<table>
<thead>
<tr>
<th>Factor</th>
<th>Mean (Seq 1-30)</th>
<th>Mean (Seq ≥ 31)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipient ABO O</td>
<td>38.13%</td>
<td>46.13%</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Recipient ABO AB</td>
<td>6.00%</td>
<td>1.98%</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Recipient Age</td>
<td>52.41 ± 12.90</td>
<td>55.05 ± 11.98</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Donor Age</td>
<td>31.18 ± 11.47</td>
<td>36.70 ± 12.83</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>CDC High Risk</td>
<td>10.20%</td>
<td>16.61%</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>UNOS Status 1A Days</td>
<td>25.79 ± 47.65</td>
<td>13.28 ± 39.37</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>UNOS Status 1B Days</td>
<td>79.44 ± 143.40</td>
<td>60.27 ± 121.37</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Miles to Donor Hospital</td>
<td>164.77 ± 200.20</td>
<td>376.81 ± 273.75</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Donor Gender: Male</td>
<td>73.00%</td>
<td>50.69%</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Donor Hx Hypertension</td>
<td>13.32%</td>
<td>26.16%</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Ischemic Time</td>
<td>3.19 hr ± 1.05</td>
<td>3.76 hr ± 0.98</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>LVEF</td>
<td>61.70 %± 7.08</td>
<td>61.07 %± 7.21</td>
<td>p=0.005</td>
</tr>
</tbody>
</table>
Outcomes With Traditional Risk Groups

Donor CDC High Risk

P=NS
Outcomes With Traditional Risk Groups

Female Donor / Male Recipient

Survival

Days Post Transplant

P=NS
Diabetic Donor

p=0.07
Hypertension Hx in Donor

![Graph showing survival rates over days post transplant with p=0.009]
Why Don’t We Use High Sequence Donors?
Unintended Consequences

• DonorNet transparency and sequences should have made increased efficiency
• Utilization should have gone up
• As we embark on a drastic reworking of allocation and geographic distribution for hearts in the US we must be mindful of unintended consequences
Conclusions

• We will never have sufficient donors to meet the demand for this life saving therapy
• We must use evidence to see that we are leaving donors that could be utilized safely.
• Sequence # could be a way of identifying “extended criteria donors” and potentially moving them out of the UNOS PSR assessment to encourage use in a trial setting.