Heart Transplantation
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Cardiac transplantation

Evaluation for cardiac transplantation is indicated for carefully selected patients with stage D HF despite GDMT, device, and surgical management.

7.4.6. Cardiac Transplantation: Recommendation

CLASS I

1. Evaluation for cardiac transplantation is indicated for carefully selected patients with stage D HF despite GDMT, device, and surgical management (680). (Level of Evidence: C)

Survival

<table>
<thead>
<tr>
<th></th>
<th>1 Year</th>
<th>3 Year</th>
<th>5 year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>87.8%</td>
<td>78.5%</td>
<td>71.7%</td>
</tr>
</tbody>
</table>
NOTE: This figure includes only the heart transplants that are reported to the ISHLT Transplant Registry. As such, the presented data may not mirror the changes in the number of heart transplants performed worldwide.
UNOS
United Network for Organ Sharing

• Contracted to HHS
• Board reports to Secretary HHS
• Responsible for organ allocation
• Policy/Regulation
• Outcomes: SRTR public reported

• 1.2% of advanced HF population receive donor

119,617 people waiting for a lifesaving transplant
Steve Jobs had a problem. He needed a liver transplant, but people in northern California, where he lived, waited more than 6 years on average before an organ became available. So he got himself listed at a second transplant center, one in Memphis, Tennessee, where average wait times were less than 3 months.\(^1\) 

revise the organ-allocation system so “neither place of residence nor place of listing shall be a major determinant of access to a transplant,”\(^3\) the disparities persist.

The transplant community is considering rule revisions that would reduce these disparities by ensuring that organs are shared the current system, the United States is divided into 58 donation service areas (DSAs) in 11 regions. When a transplantable cadaveric liver, for example, becomes available, it’s offered to patients in the same DSA, with the sickest patients receiving priority. If there’s no suitable recipient in the DSA, the liver is offered within the

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**Median Heart Waiting Time**

<table>
<thead>
<tr>
<th>Location</th>
<th>Waiting Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>8 mo</td>
</tr>
<tr>
<td>Los Angeles</td>
<td>4 mo</td>
</tr>
<tr>
<td>Cleveland</td>
<td>15 mo</td>
</tr>
</tbody>
</table>
Adults Bridged with MCS by Year & Device Type

In USA about HALF of all heart transplant recipients are on durable LVAD prior to transplant
Bridge to Transplant Outcomes 2015-2016

- 34% transplanted at 1 year
- 12% dead at 1 year
- 1% recovery
- 53% waiting

The Journal of Heart and Lung Transplantation 2017 36, 1080-1086 DOI: (10.1016/j.healun.2017.07.005)
Heart Transplant Outcomes

ISHLT Registry

https://www.ishlt.org/registries/slides.asp?slides=heartLungRegistry
Adult and Pediatric Heart Transplants
Median Recipient Age by Location

<table>
<thead>
<tr>
<th>Year</th>
<th>Europe</th>
<th>North America</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>50</td>
<td>55</td>
<td>45</td>
</tr>
</tbody>
</table>

JHLT. 2016 Oct; 35(10): 1149-1205
Adult and Pediatric Heart Transplants
Donor Age by Year of Transplant

Median donor age (years) vs % of transplants

- 0-9
- 10-17
- 18-39
- 40-59
- 60-69
- 70+
- Median Age

JHLT. 2016 Oct; 35(10): 1149-1205
Adult and Pediatric Heart Transplants
Median Donor Age by Location

Europe
North America
Other

Median donor age (years)


2016
JHLT. 2016 Oct; 35(10): 1149-1205
Adult and Pediatric Heart Transplants
Kaplan-Meier Survival by Age Group
(Transplants: January 1982 – June 2015)

Median survival (years):
Adult=10.5; Conditional=13.0;
Pediatric=15.6; Conditional=20.6

p<0.0001
Survival (%)

Adult Heart Transplants
Kaplan-Meier Survival by Donor Age Group
(Transplants: January 1982 – June 2015)

Median survival (years):
0-10=10.6; 11-39=11.5; 40-59=9.7; 60+=7.4

All pair-wise comparisons were significant at p < 0.05 except 0-10 vs. 11-39 and 0-10 vs. 40-59.
Survival (%)

Years

1982-1991 (N=570)
1992-2001 (N=995)
2002-2008 (N=739)
2009-6/2015 (N=747)

Median survival (years):

All comparisons were significant at p < 0.05 except 2002-2008 vs. 2009-6/2015.
### Continuous Factors (see figures)

<table>
<thead>
<tr>
<th>Continuous Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipient age</td>
</tr>
<tr>
<td>Recipient creatinine</td>
</tr>
<tr>
<td>Recipient height</td>
</tr>
<tr>
<td>Height difference</td>
</tr>
<tr>
<td>PA systolic pressure</td>
</tr>
<tr>
<td>Transplant center volume</td>
</tr>
<tr>
<td>Total bilirubin</td>
</tr>
</tbody>
</table>
Analysis is limited to patients who were alive at the time of the discharge.
Analysis is limited to patients who were alive at the time of the follow-up.
Adult Heart Transplants

% of Recipients Experiencing *Treated* Rejection Between Transplant Discharge and 1-Year Follow-Up by Maintenance Immunosuppression (Follow-ups: January 2005 – June 2016)

Analysis is limited to patients who were alive at the time of the follow-up.

Treated rejection = Recipient was reported to (1) have at least one acute rejection episode that was treated with an anti-rejection agent; or (2) have been hospitalized for rejection.
Adult Heart Transplants
Relative Incidence of Leading Causes of Death
(Deaths: January 2009 – June 2016)

Since only leading causes of death are shown, the sum of percentages for each time period is less than 100%.
## Adult Heart Transplants
### Post Transplant Malignancy (Transplants: January 1994 – June 2015)

Cumulative Morbidity Rates in Survivors

<table>
<thead>
<tr>
<th>Malignancy/Type</th>
<th>1-Year Survivors</th>
<th>5-Year Survivors</th>
<th>10-Year Survivors</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Malignancy</td>
<td>35,644 (94.8%)</td>
<td>19,728 (84.1%)</td>
<td>7,834 (72.3%)</td>
</tr>
<tr>
<td>Malignancy (all types combined)</td>
<td>1,945 (5.2%)</td>
<td>3,736 (15.9%)</td>
<td>3,001 (27.7%)</td>
</tr>
<tr>
<td><strong>Malignancy Type</strong>*</td>
<td><strong>Skin</strong></td>
<td><strong>Lymphoma</strong></td>
<td><strong>Other</strong></td>
</tr>
<tr>
<td>639 (1.7%)</td>
<td>2,228 (9.5%)</td>
<td>1,999 (18.4%)</td>
<td></td>
</tr>
<tr>
<td>198 (0.5%)</td>
<td>260 (1.1%)</td>
<td>196 (1.8%)</td>
<td></td>
</tr>
<tr>
<td>1,067 (2.8%)</td>
<td>1,458 (6.2%)</td>
<td>1,095 (10.1%)</td>
<td></td>
</tr>
<tr>
<td><strong>Type Not Reported</strong></td>
<td>41 (0.1%)</td>
<td>37 (0.2%)</td>
<td>17 (0.2%)</td>
</tr>
</tbody>
</table>

*Recipients may have experienced more than one type of malignancy so the sum of individual malignancy types may be greater than the total number with malignancy.

“Other” includes: prostate (11, 31, 19), adenocarcinoma (7, 2, 1), lung (6, 5, 1), bladder (2, 3, 0), Kaposi’s sarcoma (0, 2, 0), breast (1, 4, 2), cervical (2, 3, 2), colon (2, 4, 3), and renal (2, 6, 1). Numbers in parentheses are those reported within 1 year, 5 years and 10 years, respectively.
Adult Heart Transplants
Cumulative Morbidity Rates in Survivors within 1, 5 and 10 Years Post Transplant  (Transplants: January 1994 – June 2015)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Within 1 Year</th>
<th>Total N with known response</th>
<th>Within 5 Years</th>
<th>Total N with known response</th>
<th>Within 10 Years</th>
<th>Total N with known response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal Dysfunction</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal Creatinine ≤ 2.5 mg/dl</td>
<td>25.7%</td>
<td>(N=34,983)</td>
<td>51.1%</td>
<td>(N=19,655)</td>
<td>68.4%</td>
<td>(N=8,261)</td>
</tr>
<tr>
<td>Creatinine &gt; 2.5 mg/dl</td>
<td>17.2%</td>
<td></td>
<td>32.7%</td>
<td></td>
<td>39.2%</td>
<td></td>
</tr>
<tr>
<td>Chronic Dialysis</td>
<td>6.3%</td>
<td></td>
<td>13.8%</td>
<td></td>
<td>18.7%</td>
<td></td>
</tr>
<tr>
<td>Renal Transplant</td>
<td>1.9%</td>
<td></td>
<td>3.2%</td>
<td></td>
<td>6.7%</td>
<td></td>
</tr>
<tr>
<td>Diabetes*</td>
<td>22.2%</td>
<td>(N=37,659)</td>
<td>35.5%</td>
<td>(N=21,429)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Cardiac Allograft Vasculopathy</td>
<td>7.8%</td>
<td>(N=34,438)</td>
<td>29.3%</td>
<td>(N=16,016)</td>
<td>47.4%</td>
<td>(N=5,468)</td>
</tr>
</tbody>
</table>

* Data are not available 10 years post-transplant.
Cardiac Allograft Vasculopathy

Clinical Presentation

- Since denervated, ischemia is often silent
- New dyspnea
- New heart failure
- New wall motion abnormality
- Graft dysfunction/failure
- New arrhythmia (particularly AF)
- Sudden cardiac death
CAV-Poor Prognostic Indicators

- Early post tx 1-2 yrs-- vasculitis
- Rapid rate of development
- $CAV_3$ (severe)
- Reduced LV ejection fraction
- Restrictive Physiology
- IVUS
  - Change in maximal intimal thickness at a specific site >0.5 mm in the 1st yr post tx
  - Change in percent atheroma volume year 1
Cardiac Allograft Vasculopathy

Treatment

• Palliative
  • Rapamycin/Everolimus
  • PCI
  • CABG (rare)
• Retransplant
Everolimus 1.5 mg with reduced CNI is non inferior to MMF at 12 months and reduces intimal proliferation in de novo heart transplant patients.

### Table 4: Results of the IVUS analysis of the evaluable patients in the IVUS substudy

<table>
<thead>
<tr>
<th>Change from baseline to month 12</th>
<th>Everolimus 1.5 mg (N = 88)</th>
<th>MMF 3g (N = 101)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average MIT (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>0.01 ± 0.02</td>
<td>0.03 ± 0.06</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median (min, max)</td>
<td>0.01 (-0.06, 0.09)</td>
<td>0.02 (-0.12, 0.33)</td>
<td></td>
</tr>
<tr>
<td>Normalized total intimal volume (mm²)</td>
<td>3.40 ± 8.75</td>
<td>11.44 ± 8.07</td>
<td>0.012</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>2.58 (-34.69, 23.14)</td>
<td>6.39 (-23.60, 88.09)</td>
<td></td>
</tr>
<tr>
<td>Median (min, max)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Patients with CAV 12.5% vs 26.7% p=.018

Azathioprine ~50%
Heart Transplant Follow up
Post Heart Transplant Monitoring

- Historical approach is invasive: coronary angiography/IVUS endomyocardial biopsy
- Standard:
  - Cath yearly vs stress imaging
  - IVUS variable
  - 10-12 heart biopsies year 1
The International Society of Heart and Lung Transplantation Guidelines for the care of heart transplant recipients

• **Class IIa:**

  • Treadmill or dobutamine stress echocardiography and myocardial perfusion imaging may all be useful for the detection of CAV in HT recipients unable to undergo invasive evaluation. Non-invasive testing for CAV is technically possible in children.

• **Level of Evidence: B.**
Gene-Expression Profiling for Rejection Surveillance after Cardiac Transplantation

- Management strategy of gene expression blood test and echo versus invasive biopsy
- Low risk heart transplant recipients > 6 months post transplant
- GEP non-inferior to invasive strategy
  - Feasible to reduce morbidity and number of heart biopsies
Summary

• Heart transplantation is the “gold standard” treatment for Stage D advanced heart failure
• Survival and quality of life are excellent
  • Importance of donor and recipient selection
  • Improved immunotherapy
• Donor availability limits the impact as a therapy