Living donor liver transplantation - current practice & perioperative management

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Thomas E Starzl, MD, PhD, FACS
Transplantation Institute, Pittsburgh, PA.
Vittorio Staudacher 1913-2005
Canine OTLT - University of Milan, 1952
Thomas E. Starzl 1926 – 2017
First LT in humans - University of Colorado, 1963
DDLT Technique

A. Gall bladder removed

B. Donor liver transplanted

- Hepatic artery
- Portal vein
- Common bile duct
- Anastomoses

Diseased liver removed
Developments in immunosuppression prior to first human LT

1. Cytoablation with sublethal doses of total body radiation (450R).
2. 6-MP
3. Azathioprine
4. Prednisone

First liver transplant, 3/1/1963
Child with BA – bled to death in the OR.

Six more attempts made in 1963 (5 in Denver, 1 each in Boston & Paris)
1. All with short term mortality.

In the interim
1. Advances in technique.
2. Further development in immunosuppression – Antilymphocyte globulin (ALG), “triple drug cocktail.”
WHEN I PROMISE TO COME UP WITH AN ORGAN TRANSPLANT PUN

I DE-LIVER
Indications for Liver Transplantation

- Acute Liver Failure
- Chronic Liver Failure
- Neoplastic Liver Disease
- Inborn Errors of Metabolism
Contraindications to LT

- **Absolute**
  - Severe cardiopulmonary disease which is uncorrectable
  - Active extrahepatic malignancy
  - Active substance abuse
  - Active systemic infection

- **Relative**
  - AIDS (less so today)
  - Advanced age
  - Super Obesity
  - Severe psychiatric disease
  - Poor compliance
  - Significant mesenteric vascular thromboses
  - Multiple prior abdominal surgeries
MELD Score and Probability of 3 Month Mortality without Liver Transplant

TRANSPLANT CENTRE

BRING YOUR OWN ORGANS

"I had no idea things were quite so desperate."
Donor types

- Standard criteria – split vs. whole allograft
- PHS increased risk
- DCD
- Expanded criteria donor (ECD)
  - Donor age >70
  - Donor age >60 with significant medical history
  - Donors with HBV/HCV exposure
- Living donor
- Domino donor
Learning to like the "overripe"
Extended criteria donor organs and other utilization challenges
Living Donor Liver Transplant (LDLT)
LDLT Overview

First reported case, Strong et. al. 1989 (pediatric)

First adult LDLT cases in US performed in 1997-98

~5000 performed since in 89 centers

Steady increase in the last five years

Continues to represent a very small component in this country (~5%)

There are individual centers around the world, primarily in Asia, with larger annual cohorts (~75% in South Korea)
LDLT Overview

Similar indications as DDLT

Recipients tend to be “healthier” – less portal hypertension, less metabolic liver derangements, better able to tolerate a smaller graft

Planned operation

Heavy scrutiny

Technically challenging

~80% of donors would donate again

~2 month to return of regular baseline function
LDLT Outcome

Outcomes similar to DDLT

~0.5% mortality, 25-30% morbidity risk for donor

Graft failure occurs in

- 5.9% at 6 months
- 7.1% at one year
- 13.8% at 3 years
- 23.7% at 5 years
- 32.1% at 10 years

Recipient survival

- 5.3% mortality at 6 months
- 7.4% at one year
- 13.1% at 3 years
- 19.7% at 5 years
- 39.5% at 10 years
LDLT Complications

Pulmonary embolism

Myocardial infarction

Peptic ulcer disease

Liver failure

Death
# LDLT Complications

## Table 2
Type of complications of donors in the Adult-to-Adult Living Donor Liver Transplant Cohort Study

<table>
<thead>
<tr>
<th>A2ALL Study, Year of Publication</th>
<th>Number of Donors Who Successfully Donated(^a)</th>
<th>Reported Common Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ghobrial et al, 2008</td>
<td>393</td>
<td>- Bacterial infections (12%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Biliary leaks (9%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Incisional hernias (6%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Pleural effusions requiring intervention (5%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Neuropraxia (4%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Wound infections (3%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Reexplorations (3%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Intraabdominal abscess (2%)</td>
</tr>
</tbody>
</table>

| Abecassis et al, 2012            | 740                                           | - Bacterial infections (12.5%)  |
|                                  |                                               | - Biliary complications (9.7%) |
|                                  |                                               | - Intraoperative complications (6%) |
|                                  |                                               | - Incisional hernias (5.6%)    |
|                                  |                                               | - Pleural effusions (5.3%)     |
|                                  |                                               | - Psychological difficulties (4.1%) |
|                                  |                                               | - Reexplorations (3%)          |

\(^a\) Data from published studies.

*Gastroenterol Clin N Am 47 (2018) 297–311*
### LDLT vs. DDLT Complications

#### Table 1
Probability of specific complications in recipients of living or deceased donor liver transplantation

<table>
<thead>
<tr>
<th>Complication</th>
<th>Overall Complication Rate</th>
<th>Log-Rank P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Significantly higher in LDLT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bile leak or biloma</td>
<td>0.26</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Blood infection</td>
<td>0.26</td>
<td>0.0091</td>
</tr>
<tr>
<td>Biliary stricture</td>
<td>0.32</td>
<td>0.0002</td>
</tr>
<tr>
<td>Biliary tree infection</td>
<td>0.14</td>
<td>0.0062</td>
</tr>
<tr>
<td>Hepatic artery thrombosis</td>
<td>0.06</td>
<td>0.0378</td>
</tr>
<tr>
<td><strong>Significantly higher in DDLT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>0.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ascites</td>
<td>0.21</td>
<td>0.0151</td>
</tr>
<tr>
<td>Cardiac complication</td>
<td>0.02</td>
<td>0.0008</td>
</tr>
<tr>
<td>Intraabdominal bleeding</td>
<td>0.05</td>
<td>0.0190</td>
</tr>
</tbody>
</table>

**Table 1** Indications for living donor liver transplantation in the USA

- Low MELD + complications of cirrhosis
- HCC outside tumor criteria with favorable tumor biology
- HCC within tumor criteria in regions with long (>1 year) wait
- Low MELD + cirrhosis + significantly decreased quality of life
- Low MELD + cholestatic liver disease with recurrent cholangitis

MELD, model for end-stage liver disease; HCC, hepatocellular carcinoma.
Challenges to LDLT in the United States

- Prevalence of deceased donor transplantation
- Risk-averse culture
- Steep learning curve
- Diffusion of expertise
- Institutional “burden”
- Acuity of illness in recipient populations
  - Previous surgery, obesity, PVT
- Comorbidities in donor patient population
  - obesity, fatty liver
  - Anatomic variations
  - 60-80% denied after work up completed
First, do no harm*

- Staged evaluation process
- Informed consent at every step
- Independent donor advocate
  - Support for donor / counseling
  - Provide access to prior donors
- Risk stratification including
  - Age
  - Medical / Surgical history
  - ABO compatibility
  - Psychiatric profile
- Diagnostics
  - X-ray, EEG, echocardiogram, CT, MRI/MRCP, blood panels including hypercoagulable workup – factor V Leiden mutation, Protein C, S, ATIII levels
First, do no harm*

- Ethical dilemma
- Opposing interests between donor and recipient needs
  - The more liver you take (the greater the graft to body weight ratio – GRBWR)
  - Improved outcome for recipient
  - Increasing danger for donor

<table>
<thead>
<tr>
<th></th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right Lobe</td>
<td>good volume for recipient</td>
<td>large loss of donor volume (≈70% SLV)</td>
<td>donor to maintain ≥ 30% SLV after donation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>recipient to receive ≈ .8% GRWR</td>
</tr>
<tr>
<td>Left/Caudate Lobe</td>
<td>better volume than left lobe alone helps to</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>overcome SFSS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left Lobe</td>
<td>good volume for small recipients less</td>
<td>small, donated mass/volume risk of SFSS</td>
<td></td>
</tr>
<tr>
<td></td>
<td>donor liver removed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dual Grafts</td>
<td>helps to overcome donor/recipient size mismatch</td>
<td>needs to be performed in highly specialized centers</td>
<td></td>
</tr>
</tbody>
</table>
Balance of Critical Factors for Success in LDLT

The larger the size of the triangle, the greater the functional graft size

Adopted from T. Fishbein
Balance of Critical Factors for Success in LDLT

This is the balance that is necessary for success when using a smaller allograft, e.g., left lobes

Adopted from T. Fishbein
First, do no harm*

Find balance between adequacy for donor and recipient

Asan Medical Center Criteria

\[ \leq 35 \text{ years and no fatty change} \]
- \[ 30\% \text{ remnant liver volume (RLV): Acceptable} \]

\[ \leq 35 \text{ years and } \leq 15\% \text{ fatty change} \]
- \[ 30-35\% \text{ RLV: Acceptable} \]

\[ \leq 35 \text{ years and } \leq 30\% \text{ fatty change} \]
- \[ 35\% \text{ RLV: Acceptable} \]

\[ 35 - 55 \text{ years and } \leq 15\% \text{ fatty change} \]
- \[ >35\% \text{ RLV: Acceptable} \]

Absolute contraindications = BMI > 30 kg/m in age > 30, > 30% steatosis, < 30% RLV
First, do no harm*

ILTS Criteria

- 18-60 years old
- Donor remnant volume no less than 30-35%
- Macrosteatosis > 30% is absolute contraindication
- Separation of donor and recipient teams
- Perioperative plan including pain management
- Anesthesia consultation prior to date of surgery
- “Cooling off period”
First, do no harm* Summary

Attain GRBWR ≥ 0.8%

Donor LRV of ≥ 30%

Donor steatosis ≤ 30 %

Rule out risk of disease transmission

Informed consent on surgical, medical, financial, and psychological risks, including death

0.1 % for left & 0.5% for right liver donors

20 – 35% morbidity rate, including 0.04% transplantation rate

Independent donor advocate

Return to baseline performance & psychological status in ~ 1 year
LDLT Technique

Approximately 60 percent of the donor’s liver is used for transplant.

Hepatic artery connection
Portal vein connection
Vena cava
Aorta

Living donor liver transplant (recipient)
DDLT vs. LDLT Technique

- Portion of donor’s vena cava is connected to recipient’s hepatic vein trunk
- Approximately 60 percent of the donor’s liver is used for transplant
- Living donor liver transplant (recipient)

Keck School of Medicine of USC
LDLT Anatomy

A) Left lateral section (S2 and 3)
B) Left lobe (S2, 3 and 4)
   With/without MHV
   With/without caudate
C) Right lobe (S5, 6, 7 and 8)
   With/without MHV
D) Right posterior (S6 and 7)
E) Right trisegment (S4-8)
LDLT Anatomy

Right segment

Left segment
LDLT Donor Hepatectomy – hepatic hilum
Donor cholangiogram
LDLT Donor “back table” preparation
LDLT Recipient – venous outflow
LDLT Recipient – portal inflow
LDLT Recipient – arterial inflow
LDLT Recipient – reperfusion
Post operative care of the donor

ICU monitoring

Pain management

Prophylaxis for DVT and stress peptic ulcers

Monitoring for adequate liver function – LFTs, coagulation panel etc

Donor imaging to look for biliary leak – HIDA scan + US

Most donor labs normalize in 3-6 months

Close outpatient monitoring for at least two years
Donor complications & outcomes – A2ALL

Bacterial infections 12.5%

Biliary leak 9.7%

Incisional hernias 6%

Residual disability, liver failure, death (0.2-0.4%) 1%

Psychological difficulties 4.1%

Financial concerns in 75%, including donation related medical in 37%

90% felt optimistic about donation in long term follow ups
**Brief Communication**

**To Do or Not to Do Living Donor Hepatectomy in Jehovah’s Witnesses: Single Institution Experience of the First 13 Resections**

Table 1: Demographic data of the of living donors

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Relationship to recipient</th>
<th>Portion of the liver procured</th>
<th>% liver removed</th>
<th>Real weight of liver (g)</th>
<th>Time of recipient follow-up (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24</td>
<td>F</td>
<td>Mother</td>
<td>LLS</td>
<td>18</td>
<td>278</td>
<td>1877</td>
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<tr>
<td>2</td>
<td>45</td>
<td>F</td>
<td>Grand Mother</td>
<td>LLS</td>
<td>14</td>
<td>175</td>
<td>1382</td>
</tr>
<tr>
<td>3</td>
<td>33</td>
<td>M</td>
<td>Father</td>
<td>LLS</td>
<td>22</td>
<td>305</td>
<td>1281</td>
</tr>
<tr>
<td>4</td>
<td>29</td>
<td>F</td>
<td>Mother</td>
<td>LLS</td>
<td>17</td>
<td>265</td>
<td>247</td>
</tr>
<tr>
<td>5</td>
<td>57</td>
<td>F</td>
<td>Mother</td>
<td>RL</td>
<td>67</td>
<td>775</td>
<td>1911</td>
</tr>
<tr>
<td>6</td>
<td>26</td>
<td>M</td>
<td>Half Brother</td>
<td>RL</td>
<td>63</td>
<td>1120</td>
<td>1496</td>
</tr>
<tr>
<td>7</td>
<td>18</td>
<td>M</td>
<td>Son</td>
<td>RL</td>
<td>65</td>
<td>950</td>
<td>1414</td>
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<tr>
<td>8</td>
<td>53</td>
<td>M</td>
<td>Friend</td>
<td>RL</td>
<td>60</td>
<td>820</td>
<td>1297</td>
</tr>
<tr>
<td>9</td>
<td>44</td>
<td>F</td>
<td>Wife</td>
<td>RL</td>
<td>62</td>
<td>900</td>
<td>1290</td>
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<tr>
<td>10</td>
<td>42</td>
<td>M</td>
<td>Son</td>
<td>RL</td>
<td>65</td>
<td>965</td>
<td>1194</td>
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<td>11</td>
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<td>RL</td>
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<td>13</td>
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<td>F</td>
<td>Friend</td>
<td>RL</td>
<td>59</td>
<td>935</td>
<td>261</td>
</tr>
<tr>
<td>Mean</td>
<td>37</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1160.38</td>
</tr>
</tbody>
</table>

M = male; F = female; LLS = left lateral segment; RL = right lobe.
TEAM EFFORT

Thank You
Session Survey

Kambiz Etessami, MD | April 20th 8:00 AM-8:45 AM