“As The Present Now Will Later Be Past…”

Living Donor Liver Transplantation & The Piggy-back Technique

Joseph DiNorcia, MD
Assistant Professor of Surgery
Division of Liver, Pancreas, and Intestine Transplantation
David Geffen School of Medicine at UCLA

Outline

• Living Donor Liver Transplantation (LDLT)
• Implantation Techniques
• Care of recipients of LDLT
• Care of liver donors

What is living donor liver transplantation?
LDLT

- Donor: health
- Recipient: disease
- Adult-to-child
- Adult-to-adult

History

- 1967
  - Thomas E. Starzl.
  - First.

- 1980s
  - Success & acceptance of liver transplant
  - DEMAND (EXPONENTIAL) ≠ SUPPLY (MINIMAL)
• Pediatric patients
  – Shortage
  – Size mismatch

• Reduced-size deceased donor liver grafts
  – 1984, H. Blumuth, France
  – 1988, C. Broelsch, US

• Split deceased donor liver grafts
  – Ex vivo
    • 1984, R. Pichlmayr, Germany
    • 1990, C. Broelsch, US
  – In situ
    • 1995, X. Rogiers, Germany
    • 1997, J. Gos, UCLA

History

• 1988, São Paulo, Brazil

  • Donor
    – 23-year-old mother
    – Left lateral segment graft

  • Recipient
    – 4-year-old daughter
    – Biliary atresia

History

• 1989, Brisbane, Australia

  • Donor
    – 29-year-old mother
    – Left lateral segment graft

  • Recipient
    – 17-month-old son
    – Biliary atresia
History

1993, Niigata, Japan
- Y. Hashikura, M. Makuuchi, et al.
  Donor
  - 25-year-old son
  - Left hepatic lobe graft
  Recipient
  - 53-year-old mother
  - Primary biliary cirrhosis

1996, Hong Kong, China
- C.M. Lo, S.T. Fan et al.
  Donor
  - 30-year-old brother (74kg)
  - Right hepatic lobe graft (w/ MHV)
  Recipient
  - 28-year-old brother (90kg)
  - Fulminant Wilson’s disease

117th American Surgical Association
- Quebec, Canada, April, 1997

Discussion
History: US

- Adult-to-child
  - 1991, C. Broelsch, University of Chicago
  - 1993, R. Busuttil, UCLA

History: US

- Adult-to-adult
  - 1998, M. Wachs, University of Colorado
    - 2 right hepatic lobe grafts (w/o MHV)
  - 1999, A. Marcos, Medical College of Virginia
    - 25 right hepatic lobe grafts (w/o MHV)
  - 1999, R. Busuttil, UCLA

Today

- 74 countries perform liver transplant
- 27,759 liver transplants in 2015
  - 21% LDLT
- 84,357 kidney transplants in 2015
  - 42% LDKT
“East” and “West”

- **East**
  - HBV, HCV, & HCC
  - Cultural, Religious, Societal Beliefs
  - LDLT > DDLT

- **West**
  - Brain death laws
  - Promotion and organization of deceased donors
  - DDLT > LDLT

**LDLT 2016**

<table>
<thead>
<tr>
<th>West</th>
<th>Middle East</th>
<th>East</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belgium</td>
<td>Egypt 100%</td>
<td>Taiwan &gt;90%</td>
</tr>
<tr>
<td>Canada</td>
<td>Turkey 72%</td>
<td>India &gt;90%</td>
</tr>
<tr>
<td>Brazil</td>
<td>Saudi Arabia 67%</td>
<td>Japan &gt;85%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S. Korea 67%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hong Kong 50%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>China 18%</td>
</tr>
</tbody>
</table>

**US: LDLT**

<table>
<thead>
<tr>
<th>Year</th>
<th>Donor Source</th>
<th>Living Donor</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>4,866</td>
<td>360</td>
</tr>
<tr>
<td>2014</td>
<td>6,402</td>
<td>300</td>
</tr>
<tr>
<td>2013</td>
<td>2,896</td>
<td>141</td>
</tr>
<tr>
<td>2012</td>
<td>2,711</td>
<td>131</td>
</tr>
<tr>
<td>2011</td>
<td>2,143</td>
<td>131</td>
</tr>
<tr>
<td>2010</td>
<td>1,745</td>
<td>131</td>
</tr>
</tbody>
</table>

4.8% in 2017
Perspective

- 2016
  - United States
    - 23 DDLT per million
    - 1 LDLT per million
  - South Korea
    - 9 DDLT per million
    - 19 LDLT per million

Current Statistics in US

- Despite well-organized deceased donation
- 15,000 patients on the waitlist
  - Waitlist mortality is about 20%
- Liver allocation by MELD
  - "Sickest first"
- It works, but misses patients with low MELD scores and significant complications of cirrhosis

US 2017: Adult-to-Child LDLT

- 11
- 9
- 6
- 6
- 17 other centers
US 2017: Adult-to-Adult LDLT

- University of Pittsburgh • 60
- UCSF Transplant • 29
- Mayo Clinic • 26
- University of Colorado Hospital • 16
- NewYork-Presbyterian • 14
- 28 other centers

Which Recipient?

- Pediatric
  - Nearly all
    - Cholestatic, metabolic, & fulminant liver diseases

- Adult
  - Low MELD
    - Complications of cirrhosis
    - Complications of cholestatic liver disease
    - Hepatocellular carcinoma

When DDLT is not immediately available, LDLT can be considered for most patients early in the course of the transplant evaluation.
Which Donor?

<table>
<thead>
<tr>
<th>Step</th>
<th>Psychosocial</th>
<th>Medical</th>
<th>Surgical</th>
<th>Informed consent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>Evaluation and social work with potential donor</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td>Schedule donor by evaluating donor's medical and psychosocial information, and review for psychosocial fitness</td>
</tr>
<tr>
<td>3</td>
<td>Consent and evaluation donor</td>
<td>Schedule for surgery, notification to recipient and family, and obtaining informed consent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td>Schedule operation for potential donor after completion of evaluation and review</td>
</tr>
</tbody>
</table>

Reasons for Non-Acceptance

<table>
<thead>
<tr>
<th>Reason for non-acceptance</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor-related reasons</td>
<td></td>
</tr>
<tr>
<td>Medical</td>
<td>13 (13%)</td>
</tr>
<tr>
<td>Anatomical</td>
<td>15 (15%)</td>
</tr>
<tr>
<td>Liver function</td>
<td>6 (6%)</td>
</tr>
<tr>
<td>Donor declined</td>
<td>56 (56%)</td>
</tr>
<tr>
<td>Psychosocial</td>
<td>55 (55%)</td>
</tr>
<tr>
<td>Recipient-related reasons</td>
<td></td>
</tr>
<tr>
<td>Resuscitated ODEG</td>
<td>21 (21%)</td>
</tr>
<tr>
<td>Death</td>
<td>24 (24%)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>19 (19%)</td>
</tr>
<tr>
<td>Condition improved</td>
<td>6 (6%)</td>
</tr>
<tr>
<td>Condition-related reduced organs</td>
<td>4 (4%)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (3%)</td>
</tr>
</tbody>
</table>

Safety for Both Donor and Recipient

- Center experience >20 cases
- Donor age <40 years
- Donor BMI <30
- Donor macrosteatosis <10%
- Donor remnant liver mass >30%
- (Experienced centers push the limits)
The Operations

- Two experienced surgical teams
- Simultaneous OR
- Orchestrated, step-by-step
  - Recipient hepatectomy
  - Donor hepatectomy
- Communication
  - Coordinate progress
  - Review anatomy
  - Avoid orphan grafts

Adult-to-Child
Adult-to-Adult

1. Adequate graft volume
2. Sufficient inflow
   - PV
   - HA
3. Excellent outflow
   - HV
4. Secure biliary reconstruction

Technically Successful LDLT
Donor-Recipient Graft Matching

• Adult-to-child
  – Graft mass about 1-5% of recipient
  – 10:1 DRWR
  – 60 kg donor for 6 kg baby

• Adult-to-adult
  – Donor needs:
    • 70% hepatectomy maximum!
    • ≥30% remnant
  – Recipient needs:
    • ≥0.8% GRWR
    • 70 kg recipient needs ≥560 g graft

Volumetrics

Results
**Adult-to-Child**

- Adult-to-Adult Living Donor Liver Transplantation (A2ALL)
  - 2002 established by NIH
  - 9 liver transplant centers
  - 14-year retrospective and prospective study
  - 1136 LDLT, 464 DDLT (who had at least 1 donor)
  - 30+ publications
- Donor and recipient LDLT outcomes

**Adult-to-Adult**

- Adult-to-Adult Living Donor Liver Transplantation (A2ALL)
  - 2002 established by NIH
  - 9 liver transplant centers
  - 14-year retrospective and prospective study
  - 1136 LDLT, 464 DDLT (who had at least 1 donor)
  - 30+ publications
  - Donor and recipient LDLT outcomes

**Recipient Morbidity**

- After the 20th case “learning curve”
- Hepatic artery thrombosis
  - 8% LDLT
  - 4% DDLT
- Biliary complications
  - 40% LDLT
  - 25% DDLT
- Overall complications equivalent
  - Time to resolution equivalent
- Re-transplant or death equivalent
Recipient Outcomes

• Compared to undergoing or awaiting DDLT:
  – Decrease in mortality
    • 44% (all cases)
    • 65% (after the ‘learning curve’)
  – Superior survival
    • Highly statistically significant
    • Durable 10 years after transplant
    • Even for lower MELD scores
  – Improves liver graft utility
    • Younger recipients
    • Before disease progression
    – Renal dysfunction
    – Sarcopenia
    – Life support

Donor Safety

• Management of donor risk is paramount

• Counseling potential donors requires comprehensive understanding of the available data on morbidity and mortality

• Informed consent!
Donor Outcomes

- Donor hepatectomy = major operation
- Potential for major morbidity and mortality
- A2ALL 760 donors
  - Overall morbidity = 40%
    • Multiple complications 19%
    • Serious complications 1.1%
    • Complete resolution in 1 year 95%
  - Overall mortality = 0.4%

CLINICAL—LIVER

Estimates of Early Death, Acute Liver Failure, and Long-term Mortality Among Live Liver Donors

- 4,111 donors
- 7 early deaths
- 0.17% risk of mortality
- Risk did not vary in:
  - Adult-to-child or adult-to-adult
  - Portion of liver donated

Long-Term Medical and Psychosocial Outcomes in Living Liver Donors

- 2016 literature review
- Living liver donors
- Outcomes
  - Medical
  - Psychosocial
Donor: Medical

- Estimated risk of mortality = 0.15%-0.50%
  - Highest risk in the first 90 days
- Average risk of complications = 15%-25%
  - 40% risk in adult-to-adult
- Risk of near-miss events = 1%
- One year post-donation:
  - Lab abnormalities normalize (except platelets)
  - Liver remnant regeneration complete

Donor: Psychosocial

- Majority (>90%) do not regret donation
- HR-QOL meet or exceed general population
- Improved relationship with recipient
- Donation-specific challenges:
  - Lingering physical symptoms (~1/3)
  - Financial burdens (~1/3)
  - Depression or anxiety exacerbation (~1/4)

Innovation

- 2001, S. Lee, Korea
  - Dual grafts
- 2002, D. Cherqui, France
  - Laparoscopic donor LLS
- 2004, N. Jabbour, US
  - Jehovah’s Witness
- 2008, S. Lee, Korea
  - Donor exchange
- 2013, B. Samstein (US), O. Soubrane (France)
  - Laparoscopic donor hepatic lobectomy
LDLT Conclusions

• Important, underutilized gift of life
• Proven transplantation option
• Strategy to address the organ shortage
• Lower waitlist suffering and mortality
• Equivalent or better survival than DDLT

Implantation Techniques

• Standard (bi-caval)
• Piggy-back (cavo-cavostomy)
Standard Hepatectomy

- Clamp both suprahepatic and infrahepatic IVC
- Retrohepatic caval resection

Veno-venous Bypass
Standard Implantation

Piggy-back Hepatectomy

- Preserve recipient vena cava
- Clamp hepatic veins and anterior vena cava
Piggy-back Implantation

A  B
Advantages

- Greater hemodynamic stability
  - Preserve venous return to the heart
  - Preserve venous drainage of the kidneys
  - Avoid veno-venous bypass
    - The trauma!
    - The aftermath!
- Shorter warm ischemic time
  - One caval anastomosis in more favorable orientation
- Shorter anhepatic phase
- Less blood loss
- Fewer transfusions

Advantages

- Less RP dissection
  - Less bleeding
  - No RP closure
  - Large livers
  - No Gore-Tex!

Advantages

- Less postoperative renal dysfunction
- Shorter ICU length of stay
- Decreased costs
Advantages

- Living donor liver transplantation
- Split liver transplantation
- Re-transplantation
- Donor-recipient cava size mismatch
- Complex hepatobiliary surgery

Challenges

- Longer hepatectomy?
- Hepatic vein outflow obstruction?
- Enlarged caudate lobe?
- Fulminant liver failure?
- Budd-Chiari syndrome
- Juxtacaval malignancy

Data?

- Cochrane review 2011
  - 2 randomized trials (106 patients, 53 piggy-back)
  - Standard with VVB compared to piggy-back
  - Bias
  - Data do not recommend or refute piggy-back

Implantation Conclusions

• Case by case evaluation

• Proficiency in all techniques

• Requirement for living donor and split liver transplantation

Care of LDLT Recipient

• Healthier recipients (low MELD)

• Treat as a healthy liver transplant recipient, but with high index of suspicion!

• Understand the graft anatomy
Care of LDLT Recipient

- Smaller liver volume
  - Avoid volume overload
  - Early nutrition
  - Phosphorus repletion

- Smaller vasculature
  - Liver ultrasound POD#1 and PRN
  - Anti-coagulation PRN
  - Anti-platelet PRN

- Smaller bile duct(s)
  - Ursodiol
  - Two drains: 1. Biliary reconstruction & 2. Cut surface
  - HIDA

Care of LDLT Recipient

- Slower graft function
  - INR
  - Total bilirubin
  - Lower initial tacrolimus doses
  - Patience!

- Small-for-Size Syndrome
  - Octreotide
  - Splenic artery embolization

Care of Liver Donors

- Healthy patients!

- Treat as healthy, but with high index of suspicion!

- Understand liver remnant anatomy
Care of Liver Donors

- Analgesia
  - Epidural or PCA
  - Toradol ok
- One JP drain by cut surface
- Minimal labs
  - Phosphorus repletion
- Prophylaxis
  - Early ambulation, SCD, heparin/Lovenox, IS
- Facilitate visiting the recipient

Conclusion

- Global human crisis → global collaboration
- Build on past experience
- Challenge standard concepts
- Courage, creativity, & resilience
- Family, friends, loved ones, and strangers
- Rich history-in-the-making
- Leadership, innovation, and research
- Transplantation!
“For the times they are a-changin’.”

~Bob Dylan, 1963

Thank you