“As The Present Now Will Later Be Past…”

Living Donor Liver Transplantation & The Piggy-back Technique

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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)
History

- Pediatric patients
  - Shortage
  - Size mismatch

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

- Split deceased donor liver grafts
  - Ex vivo
    - 1988, R. Pichlmayr, Germany
    - 1990, C. Broelsch, US
  - In situ
    - 1995, X. Rogiers, Germany
    - 1997, J. Goss, UCLA
History

• 1988, São Paulo, Brazil

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

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

Letters to the Editor

LIVER TRANSPLANTATION FROM LIVE DONORS

SIR,—A liver transplant programme in Brazil began in September, 1985, but by November, 1988, only 15 adults and 4 children had been transplanted due to shortage of cadaveric organ donors, a problem faced in many other countries. By the end of the 3rd year of our programme the probability that a potential recipient would die while on the waiting list was 50% for adults and 73% for children.

A technique for liver transplantation from live donors has been developed at our laboratory. Hepatic segments II and III (left lateral) are resected and transplanted to the recipient, whose liver has already been removed with preservation of the entire inferior vena cava. The graft is placed in the hepatic fossa in an obverse position, which favours perfect alignment of the vascular stumps. The risk of haemorrhage in the donor is reduced by a simple device, described elsewhere.1

On Dec 8, 1988, we did our first human liver transplant from a living donor. The recipient was a 43/4-year-old girl in terminal advanced liver failure due to biliary atresia. Her 23-year-old mother, a healthy ABO-identical woman, was the donor. The operation took 18 h. The donor did not need any blood or blood derivatives and was discharged on the 4th postoperative day. The child recovered well at first and the graft started to produce bile soon after the operation. Severe haemolysis resulted from haemolytic antibodies inadvertently transfused in two bags of plasma, with ensuing anuric renal failure. The child died 6 days after the operation during haemodialysis to control metabolic disturbances and fluid overload.

Liver transplantation from a live donor may be life-saving in children with terminal liver disease for whom a cadaveric donor is not available.

Liver Unit, São Paulo University Medical School, 01246 São Paulo, Brazil

SILVANO RAJA
JOSE ROBERTO NERY
SÉRGIO MIES
History

• **1989**, Brisbane, Australia

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

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

• **1993, Niigata, Japan**

• Donor
  – 25-year-old son
  – Left hepatic lobe graft

• Recipient
  – 53-year-old mother
  – Primary biliary cirrhosis

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**THE LANCET**

*Successful living-related partial liver transplantation to an adult patient*

Sir—Living-related liver transplantation (LRLT) has been accepted as an alternative approach to cadaveric liver transplantation in view of the paucity of paediatric cadaveric donors. Although in most cases of LRLT the recipients are children, this procedure could also be considered for adult patients in a critical condition in countries where cadaveric organ procurement is prohibited. Here we describe the clinical course of an adult patient who had LRLT.

Yasuhiko Hashikura, Masatoshi Makuuchi, Seiji Kawasaki, Hidetoshi Matsunami, Toshihiko Iketani, Yuichi Nakazawa, Kendo Kiyosawa, Takafumi Ichida

First Department of Surgery and Second Department of Internal Medicine, Shinshu University School of Medicine, Matsumoto 390, Japan; and Third Department of Internal Medicine, Niigata University School of Medicine, Niigata
History

• **1996**, Hong Kong, China

• Donor
  – 30-year-old brother (74kg)
  – Right hepatic lobe graft (w/ MHV)

• Recipient
  – 28-year-old brother (90kg)
  – Fulminant Wilson’s disease
History

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

Adult-to-Adult Living Donor Liver Transplantation Using Extended Right Lobe Grafts


From the Departments of Surgery*, Anaesthesiology,† Medicine,‡ Diagnostic Radiology,§ Pathology,‖ and Psychiatry,¶ The University of Hong Kong, Queen Mary Hospital, Hong Kong, China

Discussion

DR. RONALD W. BUSUTTIL (Los Angeles, California): I wish to congratulate Dr. Fan for his presentation and thank him for providing me with a manuscript that beautifully details this very complex procedure of living-related liver transplantation using an extended right hepatic lobectomy in adult liver grafting. Clearly one could only justify this procedure in the most desperate of conditions.
History: US

• Adult-to-child
  – 1991, C. Broelsch, University of Chicago
  – 1993, R. Busuttil, UCLA
History: US

- **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
  – \textit{LDLT > DDLT}

• West
  – Brain death laws
  – Promotion and organization of deceased donors
  – \textit{DDLT > LDLT}
# LDLT 2016

## West
- Belgium 14%
- Canada 13%
- Brazil 8%

## Middle East
- Egypt 100%
- Turkey 72%
- Saudi Arabia 67%

## East
- Taiwan >90%
- India >90%
- Japan >85%
- S. Korea 67%
- Hong Kong 50%
- China 18%
<table>
<thead>
<tr>
<th>Year</th>
<th>Deceased Donor Transplants</th>
<th>Living Donor Transplants</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>6,768</td>
<td>359</td>
</tr>
<tr>
<td>2014</td>
<td>6,450</td>
<td>280</td>
</tr>
<tr>
<td>2013</td>
<td>6,203</td>
<td>252</td>
</tr>
<tr>
<td>2016</td>
<td>7,496</td>
<td>345</td>
</tr>
<tr>
<td>2017</td>
<td>7,715</td>
<td>367</td>
</tr>
<tr>
<td>2017</td>
<td>7,715</td>
<td>367</td>
</tr>
<tr>
<td>Total</td>
<td>50,062</td>
<td>2,337</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
- New York 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>Potential donor</th>
<th>Transplant coordinator</th>
<th>Psychologist</th>
<th>Transplant surgeon</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initiation</strong></td>
<td>Contacts transplant centre Assess ABO compatibility</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Step 1</strong></td>
<td></td>
<td>Informs potential donor Schedules blood work, evaluates donor history and performs routine physical tests</td>
<td>Evaluation and social work interview with potential donor</td>
<td></td>
</tr>
<tr>
<td><strong>Step 2</strong></td>
<td>Contacts past volunteer donor</td>
<td>Schedules lab work*, radiological tests, angiography and biopsy if required†</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Step 3</strong></td>
<td>Opportunity to meet other past volunteer donors</td>
<td></td>
<td>Evaluation and social work interview with potential donor</td>
<td>First surgeon-informed consent from donor obtained</td>
</tr>
<tr>
<td><strong>Step 4</strong></td>
<td></td>
<td>Schedule operation date Potential donor reviewed and reinformed</td>
<td></td>
<td>Second surgeon-informed consent from donor obtained Statement of unsuitability offered to donor</td>
</tr>
</tbody>
</table>

- **Psychosocial**
- **Medical**
- **Surgical**
- **Informed consent**
# Reasons for Non-Acceptance

<table>
<thead>
<tr>
<th>Reason for non-acceptance</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Donor-related reasons</strong></td>
<td></td>
</tr>
<tr>
<td>Medical</td>
<td>173 (17%)</td>
</tr>
<tr>
<td>Anatomical</td>
<td>115 (11%)</td>
</tr>
<tr>
<td>Liver steatosis</td>
<td>65 (6%)</td>
</tr>
<tr>
<td>Donor declined</td>
<td>68 (7%)</td>
</tr>
<tr>
<td>Psychosocial</td>
<td>55 (5%)</td>
</tr>
<tr>
<td><strong>Recipient-related reasons</strong></td>
<td></td>
</tr>
<tr>
<td>Received DDLT</td>
<td>65 (6%)</td>
</tr>
<tr>
<td>Death</td>
<td>24 (2%)</td>
</tr>
<tr>
<td>Too sick</td>
<td>19 (2%)</td>
</tr>
<tr>
<td>Condition improved</td>
<td>8 (1%)</td>
</tr>
<tr>
<td>Condition declined or refused organ</td>
<td>5 (&lt;1%)</td>
</tr>
<tr>
<td>Other</td>
<td>9 (1%)</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 Liver Donor**
- vena cava
- right lobe
- left hepatic vein
- donor left lateral segment is removed
- left bile duct, portal vein and hepatic artery
- common hepatic duct
- portal vein
- common hepatic artery

**Pediatric Liver Recipient**
- piggyback caval anastomosis
- donor left lateral segment
- hepatic artery
- portal vein
- splenic vein
- bile bypasses duodenum and flows directly into jejunum
Adult-to-Adult
Technically Successful LDLT

1. Adequate graft volume

2. Sufficient inflow
   - PV
   - HA

3. Excellent outflow
   - HV

4. Secure biliary reconstruction
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

- 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
  – 6% LDLT
  – 4% DDLT

• Biliary complications
  – 40% LDLT
  – 25% DDLT

• Overall complications equivalent
  – Time to resolution equivalent

• Re-transplant or death equivalent
Recipient Outcomes

- 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
Recipient Outcomes

![Graphs showing survival probabilities for different outcomes: Mortality and Graft Failure, with adjusted and unadjusted HR and p-values.](image-url)
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%
• 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
Minireview

Long-Term Medical and Psychosocial Outcomes in Living Liver Donors

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• 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

FIGURE 1 - Schematic drawing of the implantation of liver graft by conventional technique
Piggy-back Hepatectomy

- Preserve recipient vena cava
- Clamp hepatic veins and anterior vena cava
Piggy-back Implantation
FIGURE 1 - Schematic drawing of the implantation of liver graft by conventional technique

FIGURE 2 - Schematic drawing of the implantation of liver graft by piggyback technique
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
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

Donor liver immediately after donation

Donor liver two months after donation

Left lobe of liver

Common bile duct
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