Living Donor Liver Transplantation

Wits Donald Gordon Medical Centre

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The First

• 1963 C Henry Kempe presented Bennie Solis to Starzl
  
  • University of Colorado
  • Infectious Diseases Specialist
  • Defender of children

• Starzl suggested transplant – Kempe agreed

  • 1981 when moved to Pittsburgh, firmly supported moving program forward

“The Puzzle People”
Bennie

- 3 year old
- BA

“The day he was born, he began his slow walk to Calvary and was almost there...”

Thomas Starzl

- 1st March 1963 attempted first liver transplant
- Died during explant procedure
  - Bleeding
    - Previous surgery
    - PHT
    - Coagulopathy

“The Puzzle People”
The Early Days

- 4 further transplants 1963
- All died complications pulmonary embolic disease
  - EPCA thrombogenic!!!
  - “I saw and talked with the patient......liver making large amounts clear bile.....was in better condition than the surgeons .....”
    Willard Goodwin “The Yellow Paper” May 11 1963

- Self imposed moratorium until first survivor
  - 1967

“Revolution” in management of liver failure
November 2018

- 168 transplants
  - 8 re-transplants

- 101 Deceased Donors 61.6%
  - 50 Whole 30.5%
  - 34 Splits 20.7%
  - 17 Reduced 10.4%

- 65 Living Donors 38.4%

- 20 fulminant hepatic failure
  - 16 well at last follow up
UNIT GROWTH

Number of transplants

Year of transplant

2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017 (1st 6m)
Patient Survival

Percent survival vs. Time

Time

Percent survival
Step 1

1. Successfully implemented LDLT
Context Adult LDLT: Donor outcomes

• Paediatric programme established donor data
• 65 LD hepatectomies
  – Age < 50
  – BMI < 30

• Established protocol
  – Sociomedical questionnaire
  – MDT evaluation
    • Independent transplanting team
  – Anatomical suitability (CT)
    • Volumetric Assessment
Donor Outcomes

- Liver biopsy
  - Only if radiological evidence of steatosis

- Biliary anatomical definition
  - Intra-operative cholangiogram
Donor Outcomes

• 50 female
• 15 male
• 51 parents
  • 43 of these mothers
• Remainder bar 2 were related
• Donor profile impacted by fact that recipients are kids
Theatre Time
## Post Operative Morbidity

<table>
<thead>
<tr>
<th>Total no. of complications</th>
<th>Number</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>20</td>
<td>30.7</td>
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</table>

<table>
<thead>
<tr>
<th>Clavien Grade</th>
<th>Number</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>I</td>
<td>11</td>
<td>55</td>
</tr>
<tr>
<td>II</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>IIIa</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>IIIb</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>IV</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>V</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

### Grade IV Complications

- Bowel perforation with multiple laparotomies, TPN, abdominal wall reconstruction
- Respiratory arrest due to inadvertent opioid overdose
Step 2

1. Successfully implemented LDLT
2. Demonstrated donor safety
Position Statement

• Constraints to Transplant
  – Socioeconomic
  – Religious
  – Cultural beliefs

  Adversely impact deceased organ donation

• Context wait list mortality of 20%
  – LDLT crucial to paediatric population

Fulminant hepatic failure
Adult Need

- 10% Waiting list death
  - As compared to 20%
- Ability improve organ access
- Proven donor outcomes
  - Balance risk of LDLT
    - Wait list death
    - Morbidity and mortality of transplant

Can this experience translate to our adult population?
Step 3

1. Successfully implemented LDLT

2. Demonstrated donor safety

3. Recipient need
Concepts

• Makuuchi et al 1st successful LL A-A LDLT in 1993

• Concerns
  – GRWR < 0.8
  – Survival 82.1% to 54.5% at 3 months!

  Tanaka et al Yonsei Med Journal 2004
  – Similar Kiuchi et al

• Significant trend RL grafts
  – Associated risks
Figure 1: Graft selection algorithm in Kyushu University. *A left lobe graft of GV/SLV <35% was considered to be used when the donor was younger than 40 years old or recipient’s liver function was good or low MELD score without severe portal hypertension. APOLT = auxiliary partial orthotopic liver transplantation
Donor Risk

• 34 RL donor deaths worldwide
• Morbidity
• Difference in opinion between East and West
  – West
    – Significantly increased M and M
  – East
    – No significant difference
• Balance donor safety with recipient outcomes

Increased risk after RL donation must be taken seriously
Retrospective analysis

- 200 LL LDLT’s
- 112 RL LDLT’s

- Donor Morbidity
- Survival
- Complications

Soejima et al. American Journal of Transplantation 2012 (12) 1877 - 1885
Donor Morbidity

• Left
  – 36.0%

• Right
  – 34.8%

• Discussion point as strong argument in US that morbidity significantly higher with RL

Soejima et al. American Journal of Transplantation 2012 (12) 1877 - 1885
# Recipient Survival

<table>
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<tr>
<th></th>
<th>LL</th>
<th>RL</th>
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<tbody>
<tr>
<td>1 Year</td>
<td>85.6%</td>
<td>89.8%</td>
</tr>
<tr>
<td>5 Year</td>
<td>77.9%</td>
<td>71.3%</td>
</tr>
<tr>
<td>10 Year</td>
<td>69.5%</td>
<td>70.7%</td>
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- Wide Caval anastomosis
- SAL (8%) – abandoned
- Splenectomy (36%)
- 2 HPCS

Soejima et al. American Journal of Transplantation 2012 (12) 1877 - 1885
MELD > 30 = Consider RL over LL

Soejima et al. American Journal of Transplantation 2012 (12) 1877 - 1885
- 528 recipients

- Patient survival
  - 1, 3, 5, and 10 years

- 87.8%
- 81.8%
- 79.4%
- 72%

Soejima et al. Transplantation 2018 102 (9) e382 – e391
LARGE FOR SIZE SYNDROME

- 8 cases
  - 4 Whole grafts
  - 1 Living Donor
    - Radiology
- 2 split
- 1 CLKT
• Alluded to ductal diameter of 150 microns as potentially prognostic for drainage

  • 10 of 14 with ducts > 200μ drained
  • Only 1 of 13 < 150μ

“Size may be of great significance”

• All cured cases surgery before 4 months of age

“Not a few cases .... Might be curable if portoenterostomy carried out before 4 months of age, preferably within 3 months after birth”

Kasai et al. *Journal of Paediatric Surgery* 1968 3 (6) 665 -675
Small For Size Syndrome

Segment 2: 50% 325.1 cc
Segment 3: 50% 211.0 cc
Total: 536.0 cc
Kyoto: Poor Outcomes......

- Initial graft loss: 54% at 3 months
- Patient Mortality at 90 days: 45.5%

Tanaka et Al. Yonsei Medical Journal 2004 1089 - 1094
SFSS

• Not purely a function of size
  • Primary Graft Dysfunction
    – Technical
    – Anatomical
    – Immunological
    – Hepatitis related issues

• Inpatient status
• Donor age > 45
• MELD > 20
• PVP > 20mmHg
• Blood loss > 10 litres

Ikegami et al. Am J Transplant 2012 12 1886 – 1897

RISK FACTORS

Ikegami et al. Journal of the American College of Surgeons 2013 216(3) 353 - 362
Consolidation

• Approach to optimizing outcomes and preventing recipient morbidity
  – Graft Inflow Modulation/Portal Flow Modulation
    • Applied to individual patient
  – Variety of techniques
    • **Indirect**
      – Hepatic Venous Outflow optimization
      – Splenic Artery Ligation
      – Splenectomy
      – Shunt ligation
    • **Direct**
      – Hemi Porto Caval Shunt
Cumulative Graft Survival

Ikegami et al. Journal of the American College of Surgeons 2013 216(3) 353 - 362
Conclusion

Tanaka et al 2004

Ikegami et al 2013
PVP Modulation

ACCESS TO TRANSPLANTATION

Number of transplants
public sector
private sector

Number of transplants
0 5 10 15 20 25 30

2004 - Establishment of first public sector transplant
2005 - Use of local cadaveric donors
2006 - Increase in public sector transplants
2007 - Further expansion of public sector transplants
2008 - Establishment of living donor transplantation
2009 - Expansion of living donor transplantation
2010 - Continued increase in public sector transplants
2011 - Introduction of additional public sector programs
2012 - Further growth in public sector transplants
2013 - Expansion of private sector transplants
2014 - Peak in private sector transplants
2015 - Reduction in private sector transplants
2016 - Continued stabilization of private sector transplants
2017 - Further increases in public sector transplants
WDGMC Transplant Unit

• Proven donor safety large cohort living donors

• Significant impact organ availability
  • Organ of choice 40% paediatric patients

• Despite lower wait list mortality
  • Similar pressure DD organs adult population

• Appropriate embark adult LDLT programme
Figure 1: Graft selection algorithm in Kyushu University. *A left lobe graft of GV/SLV <35% was considered to be used when the donor was younger than 40 years old or recipient’s liver function was good or low MELD score without severe portal hypertension. APOLT = auxiliary partial orthotopic liver transplantation