Living Donor Liver Transplantation for Fulminant Hepatic Failure

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Liver Transplantation for FHF

- FHF is rapidly progressive and irreversible
- Need for liver transplantation is urgent
- It is difficult to obtain grafts in a timely manner from cadaveric donors
- The death rate of patient awaiting for liver transplantation is as high as 40% or 62%.
Rare cadaveric donors in Asia

>80% mortality in the absence of liver transplantation

Almost hopeless wait

Living Donor Liver Transplantation
Living–related Liver Transplantation in FHF
Matsunami et al. Lancet 1992;340:1411

- 15-year-old boy of 48 kg
- Acute liver failure by drug reaction
- Left lobe graft from his father
- 51% of SLV
LDLT for FHF

Advantage

- Availability of graft
  - short waiting time
  - timely transplantation
- Good quality of a graft from a healthy donor
LDLT for FHF

Disadvantage

– Short time to decide the donation
– Short time to evaluate donor candidates
– Donor complications
– Complex surgery
– Recipient complications
– Possible small for size graft
Offer

1st interview and inform
    Family of a recipient
    Family of donor candidates

Medically acceptable recipient &
Definite voluntary willingness of a donor

Recipient transfer & further evaluation

Medical and psychological donor evaluation

Separate donor interview

2nd interview of recipient family & donor

Transplantation
Urgent Living-Donor Evaluation

**Medical**
- Physical ex. & laboratory data
  - Blood type (30min)
  - CBC, coagulation, chemistry (30min)
  - Infection (2hr) HLA (2hr)
  - Occult blood of stool, Urine analysis (5min)

**Radiology**
- Abdominal & chest X-p (5min)
- US screening (20 min)
- CT scan (15min)

**Cardio-pulmonary function check**
- ECG, UCG, spirometry

**Psychological**
- Interview by psychiatrist

**Check steatosis & Anatomy & Volumetry** 1hr

**Decision**
Non-alcoholic Steato-hepatitis

No alcoholic history
No other etiology

Risk factors
diabetes, hyperlipidemia, obesity, hypertension

Symptoms
no specific symptoms and liver failure with cirrhosis

Physical signs
hepatomegaly

Pathology
steatosis and fibrosis

Incidence
unknown in Japan, increasing
Preoperative Assessment of Steatosis with CT Scan

Liver / Spleen ratio of CT value

#1/ #3: 53.9 / 58.9 = 0.91
#2/ #3 : 58.3 / 58.9 = 0.98

Safety value > 1.2
Marginal value 1.0-1.2
Risky value <1.0

Steatosis >> excise, diet >> re-assessment

But, how should we do in an urgent case?
Strategy for Possible Steatosis in an Urgent Case

- High risk donor: alcohol, BMI >28
- Suspected by radiology: US, CT

Evaluation by CT density: liver / spleen ratio (LSR)

<table>
<thead>
<tr>
<th>LSR&lt;1.0</th>
<th>LSR ≥1.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal</td>
<td>Normal LFT</td>
</tr>
</tbody>
</table>

- Liver biopsy
  - No
  - HbA1C, HOMA-IR
    - No
    - OK
    - accept

- No
- OK
- reject

BMI (Rinella. Liver Transplantation 2001;5:409)
Indication for Living Donor Liver Transplantation in Kyoto

Pediatric

Adult

82 cases
Indication and Patient Survival in Children

- Cholestatic
- Metabolic
- Tumor
- Liver cirrhosis
- Fulminant
Indication and Patient Survival in Adults

(%) - 100

(years) - 0 to 5

metabolic
Liver cirrhosis
cholestatic
fulminant
tumor
Etiology of FHF

**<1 y.o.**
- Unknown (15)
- HBV (1)
- HSV (1)

**1~18 y.o.**
- Unknown (15)
- HBV (3)
- Heat stroke (1)
- AIH (2)
- HAV (2)
- Drug induced (3)
- Chrome poison (1)

**≥18 y.o.**
- Unknown (22)
- HBV (16)
Donor

- <1 y.o.
  - Mother (8)
  - Father (8)
  - Ground mother (1)

- 1~18 y.o.
  - Father (9)
  - Spouse (8)
  - Child (9)
  - Sibling (16)
  - Uncle (1)
  - Mother (3)

- ≥18 y.o.
  - Father (8)
  - Spouse (8)
  - Child (9)
  - Sibling (16)
  - Uncle (1)
  - Mother (3)
Blood Type Combination

<1 y.o.
- Identical (10)
- Compatible (3)
- Incompatible (4)

1~18 y.o.
- Identical (13)
- Compatible (6)
- Incompatible (3)

≥18 y.o.
- Identical (35)
- Compatible (9)
- Incompatible (2)
Graft Type

<1 y.o.  1~18 y.o.  ≥18 y.o.
Impact of Recipient Age

• Inferior outcomes of the less-than-1-year-old children

Technical difficulty  →  Vascular thrombosis
Rash deterioration  →  Sepsis
Donor scarcity  →  Haemorrhage
but
Low incidence of ACR
MOF
LDLT for FHF in Children
Lie CL et al. Liver Transplantation 2003;9:1185

- 8 patients (Age: 3 mo–11 years)
- Etiology: drug induced (2), idiopathic (6)
- Outcomes
  - 3 deaths in patients with idiopathic etiology
  - Causes of death
    - Recurrence of acute hepatitis in the 3 months old child
    - Refractory rejection in the 8 months old child
## Result of LDLT for FHF in Children <1y.o.
### -Kyoto Experience-

<table>
<thead>
<tr>
<th>Etiology</th>
<th>outcome</th>
<th>Causes of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV(1)</td>
<td>alive</td>
<td></td>
</tr>
<tr>
<td>HSV(1)</td>
<td>alive</td>
<td></td>
</tr>
<tr>
<td>unknown(15)</td>
<td>alive (4) (normal LFT [1] and waiting for re-Tx [2])</td>
<td>dead (11) recurrent hepatitis (5) refractory ACR (1) chronic rejection (1) EBV hepatitis (1) MOF after Rota-virus infection (2) HAT (1)</td>
</tr>
<tr>
<td>Etiology</td>
<td>Biopsy findings</td>
<td></td>
</tr>
<tr>
<td>---------------</td>
<td>------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>HBV (1)</td>
<td>no biopsy</td>
<td></td>
</tr>
<tr>
<td>HSV (1)</td>
<td>no biopsy</td>
<td></td>
</tr>
<tr>
<td>unknown (15)</td>
<td>moderate ACR (4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>severe ACR (7)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>chronic rejection (1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>hepatitis (7)</td>
<td></td>
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<tr>
<td></td>
<td>massive necrosis (4)</td>
<td></td>
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</tbody>
</table>
A Case of FHF

5 months old girl, 7.8 kg, unknown etiology
Donor: mother, identical blood type

Day 12

- moderate ACR with lobula inflammation

Day 24

- severe ACR with hepatocyte dropout, simulating “recurrent fulminant hepatitis
LDLT for FHF with unknown etiology in Children <1y.o.

- Poor outcomes
- Strong immunosuppression is required
- No strategy for recurrent hepatitis
LDLT for FHF in Kyoto

Coma grade

- II (12)
- III (19)
- IV (13)

Hyperacute (9)
Acute (21)
Subacute (12)

Adult cases

Type

Subacute (12)
Acute (21)
Hyperacute (9)

jaundice
hyper 7d acute 28d subacute

encephalopathy
Hoofnalge 1991
Neurological Death after LDLT

• Reported incidence: 4 ~ 11%
• Kyoto Experience
  – Incidence: 5%
  – All adult patients
  – GBWR: 0.73 ~ 1.24%
  – Preoperative coma grade: III (1), IV (3)
How much volume do we need for adult patients with FHF?

• **Left lobe:**
  – 23%-54% SLV
    • Nishizaki et al. Surgery 2002;131:182
  – >35%
    • Miwa et al. Hepatology 1999;30:1521

• **Right Lobe**
  – 40% and more is favorable
    • Liu et al. British J Surgery 2002;89:317

• **Right or left or APOLT ?**
Graft Type and Patient Survival

- Right Lobe
- Left Lobe
- APOLT

Years
GBWR = graft weight/recipient weight x 100 (%)
GBWR and Patient Survival

GBWR < 0.8%
GBWR 0.8-1.0%
GBWR >1.0%

P<0.05

Years
How much volume do we need for adult patients with FHF?

Answer

• There is no difference between left lobe and right lobe when the graft volume is enough.
• The safe limit is GBWR of 0.8.
• Grafts with GBWR of 0.8 should be used even in APOLT.
Risk Factors in Adults
-Kyoto Experience-

• Preoperative factors
  – Other organ dysfunction
    • Renal dysfunction: Cre>2.0, with dialysis
    • Respiratory dysfunction: on ventilator
    • Pancreatitis
  – Preoperative steroid administration > 20 days
  – MELD $\geq 25 \ (p=0.054)$

• Operative factors
  – Small for size: GBWR < 0.8
Small-for-size Syndrome

- Prolonged cholestasis
- Coagulopathy
- Massive ascites
- Gastrointestinal bleeding
- Renal dysfunction
Strategy for Small for Size Graft

• Monitoring
  PV pressure < 20cmH₂O

• Surgery
  – Outflow
    wide anastomosis
    reconstruction of HVs draining to MHV
    right lobe graft with MHV
  – Inflow
    splenic artery ligation
    porto-caval shunt
Small-for-size partial liver graft in an adult recipient; a new transplant technique

O. Boillot, et al., The LANCET; vol. 359 (2002)
A Case of Heat Stroke

- **Recipient**
  - 16y.o. boy
  - Heat stroke with liver & kidney failure
  - Come grade IV
  - 79kg in body weight

- **Donor**
  - Patient's mother
  - 51kg in body weight

- **GBWR: 0.62 (496g)**
Effect of Inflow Moduration for Small for Size

Partial porto-caval shunt

Recipient left PV

![Graph showing ALT, T-Bil, and PT over POD](chart.png)
Musts in LDLT for FHF

• Aim 1: Timely LDLT
  – Offer to LDLT center ASAP
  – Inform family about an option of LDLT ASAP
  – Evaluate donor candidate quickly

• Aim 2: Donor safety & ethics
  – Inform donor risks as well as recipient benefits
  – Do not rush donor candidates to decide organ donation
  – Evaluate donor candidate without omission
  – Secure residual liver volume ≥30%

• Aim 3: Enough graft & residual liver volume
  – Choose graft type with GBWR > 0.8
  – Choose appropriate procedures in case of small for size graft
Donor Evaluation in LDLT for FHF

Save recipient

Donor safety